

## Nationale VersorgungsLeitlinie

COPD

Leitlinienreport




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Die Nationale VersorgungsLeitlinie COPD wird mit folgenden Komponenten publiziert:

- Langfassung: Graduierte Empfehlungen und Darstellung der Evidenzgrundlage (Evidenz und weitere Erwägungen);
- Kurzfassung: Übersicht der graduierten Empfehlungen;
- Leitlinienreport (das vorliegende Dokument);
- Patientenleitlinie;
- weitere Patientenmaterialien wie Patientenblätter und Kurzinformationen.

Alle Fassungen sind zugänglich über das Internetangebot des NVL-Programms [www.leitlinien.de/copd](http://www.leitlinien.de/copd).

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### Besonderer Hinweis

Die Medizin unterliegt einem fortwährenden Entwicklungsprozess, sodass alle Angaben, insbesondere zu diagnostischen und therapeutischen Verfahren, immer nur dem Wissensstand zur Zeit der Drucklegung der VersorgungsLeitlinie entsprechen können. Hinsichtlich der angegebenen Empfehlungen zur Therapie und der Auswahl sowie Dosierung von Medikamenten wurde die größtmögliche Sorgfalt beachtet. Gleichwohl werden die Nutzenden aufgefordert, die Beipackzettel und Fachinformationen der pharmazeutischen Unternehmen zur Kontrolle heranzuziehen und im Zweifelsfall entsprechende Fachleute zu konsultieren. Fragliche Unstimmigkeiten sollen bitte im allgemeinen Interesse der NVL-Redaktion mitgeteilt werden.

Die Nutzenden selbst bleiben verantwortlich für jede diagnostische und therapeutische Applikation, Medikation und Dosierung.

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## Inhaltsverzeichnis

Impressum .....	1
1 Programm für Nationale VersorgungsLeitlinien .....	4
2 Zielsetzung .....	5
3 Adressat*innen.....	5
4 Zusammensetzung der Leitliniengruppe .....	6
5 Patient*innenbeteiligung.....	11
6 Auswahl und Bewertung der Evidenz.....	11
7 Formulierung von Empfehlungen.....	14
8 Entwicklung und Konsentierung .....	15
9 Externe Begutachtung .....	17
10 Redaktionelle Unabhängigkeit .....	17
11 Gültigkeit und Aktualisierung.....	18
12 Anwendung und Verbreitung .....	18
12.1 Materialien und Formate .....	18
12.2 Implementierung und Öffentlichkeitsarbeit .....	20
13 Evaluation.....	21
Tabellenverzeichnis.....	22
Anhang.....	23
Anhang 1 Darstellung von Interessenkonflikten .....	23
Anhang 2 Endpunktgraduierung.....	64
Anhang 3 Recherchestrategien .....	64
Anhang 4 Evidenztabelle Definition und Epidemiologie .....	123
Anhang 5 Evidenztabelle Diagnostik und Monitoring .....	123
Anhang 6 Evidenztabelle Tabakentwöhnung .....	151
Anhang 7 Evidenztabelle Nicht-medikamentöse Therapie und Rehabilitation .....	174
Anhang 8 Evidenztabelle Medikamentöse Therapie .....	225
Anhang 9 Evidenztabelle Medizinische Rehabilitation .....	286
Anhang 10 Evidenztabelle Versorgungskoordination .....	300
Anhang 11 Kommentare aus der öffentlichen Konsultation .....	310
Literatur .....	345

# 1 Programm für Nationale VersorgungsLeitlinien

Im Rahmen des Programms für Nationale VersorgungsLeitlinien (NVL) von Bundesärztekammer (BÄK), Kassenärztlicher Bundesvereinigung (KBV) und Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) haben die zuständigen Fachgesellschaften und Organisationen inhaltliche Eckpunkte für die 2. Auflage der NVL COPD konsentiert. Die Beteiligung von Patient\*innen wird durch die Kooperation mit der Bundesarbeitsgemeinschaft Selbsthilfe (BAG SELBSTHILFE) gewährleistet.

Die Überarbeitung der NVL COPD erfolgt modular. Die 2. Auflage beinhaltet die Kapitel:

- „Definition und Epidemiologie“;
- „Diagnostik und Monitoring“;
- „Tabakentwöhnung“;
- „Nicht-medikamentöse Therapie“;
- „Medikamentöse Therapie“;
- „Medizinische Rehabilitation“ und
- „Versorgungskoordination“.

Sie ist Teil eines späteren Gesamtdokumentes. Weitere Themen werden im Rahmen der nächsten Auflagen bearbeitet und veröffentlicht (siehe auch Übersicht ausstehender Themen in der NVL).

Das NVL-Programm zielt auf die Entwicklung und Implementierung versorgungsbereichsübergreifender Leitlinien zu ausgesuchten Erkrankungen hoher Prävalenz unter Berücksichtigung der Methoden der Evidenzbasierten Medizin (EbM). Insbesondere sind NVL inhaltliche Grundlage für die Ausgestaltung von Konzepten der strukturierten und integrierten Versorgung [1].

Ziele des NVL-Programms sind insbesondere:

- Empfehlungen zu versorgungsbereichsübergreifenden Vorgehensweisen für prävalente Erkrankungen entsprechend dem besten Stand der medizinischen Erkenntnisse unter Berücksichtigung der Kriterien der Evidenzbasierten Medizin zu erarbeiten und formal zu konsentieren;
- Empfehlungen hinsichtlich der Abstimmung und Koordination der an der Versorgung beteiligten Fachdisziplinen und weiterer Fachberufe im Gesundheitswesen in den verschiedenen Versorgungsbereichen zu geben;
- durch Einbeziehung aller an der Versorgung beteiligten Disziplinen, Organisationen und Patient\*innen eine effektive Verbreitung und Umsetzung der Empfehlungen zu ermöglichen;
- Berücksichtigung von NVL-Empfehlungen in der ärztlichen Aus-, Fort- und Weiterbildung und in Qualitätsmanagementsystemen sowie bei Verträgen zur Integrierten Versorgung oder strukturierten Behandlungsprogrammen;
- Unterstützung der gemeinsamen Entscheidungsfindung zwischen Ärzt\*innen und Patient\*innen durch qualitativ hochwertige Patienteninformationen und Entscheidungshilfen.

Auf diesem Weg soll die Qualität der Versorgung verbessert und die Stellung der Patient\*innen gestärkt werden. Zudem wird von der Berücksichtigung der Empfehlungen eine Effizienzsteigerung im Gesundheitswesen erwartet.

Die Erarbeitung der NVL erfolgt unter wesentlicher Berücksichtigung der Konzepte des Internationalen Leitlinien-Netzwerks GIN [2], der Leitlinien-Empfehlungen des Europarats [3], der Beurteilungskriterien für Leitlinien von BÄK und KBV [4], des Deutschen Leitlinienbewertungsinstruments DELBI von ÄZQ und AWMF [5,6] sowie des AWMF-Regelwerks Leitlinien [7].

Die grundlegende methodische Vorgehensweise ist im NVL-Methodenreport [8] beschrieben. Die spezifische methodische Vorgehensweise beschreibt das hier vorliegende Dokument, das einen essentiellen Bestandteil der Leitlinie darstellt.

### Leitlinien als Entscheidungshilfen

Bei einer NVL handelt es sich um eine systematisch entwickelte Entscheidungshilfe über die angemessene ärztliche Vorgehensweise bei speziellen gesundheitlichen Problemen im Rahmen der strukturierten medizinischen Versorgung und damit um eine Orientierungshilfe im Sinne von „Handlungs- und Entscheidungsvorschlägen“, von denen in begründeten Fällen abgewichen werden kann oder sogar muss [4].

Die Entscheidung darüber, ob einer bestimmten Empfehlung gefolgt werden soll, muss individuell unter Berücksichtigung der bei der jeweiligen Patientin beziehungsweise dem jeweiligen Patienten vorliegenden Gegebenheiten und Präferenzen sowie der verfügbaren Ressourcen getroffen werden [3].

Eine NVL wird erst dann wirksam, wenn ihre Empfehlungen bei der Versorgung von Patient\*innen Berücksichtigung finden. Die Anwendbarkeit einer Leitlinie oder einzelner Leitlinienempfehlungen muss in der individuellen Situation geprüft werden nach den Prinzipien der Indikationsstellung, Beratung, Präferenzermittlung und partizipativen Entscheidungsfindung [7,9].

Ebenso wie bei jeder anderen medizinischen Leitlinie handelt es sich bei einer NVL explizit nicht um eine Richtlinie im Sinne einer Regelung des Handelns oder Unterlassens, die von einer rechtlich legitimierten Institution konsentiert, schriftlich fixiert und veröffentlicht wurde, für den Rechtsraum dieser Institution verbindlich ist und deren Nichtbeachtung definierte Sanktionen nach sich zieht [4].

## 2 Zielsetzung

Nationale Versorgungsleitlinien sollen die Versorgung von Patient\*innen in Deutschland verbessern durch aktuelle wissenschaftlich begründete Empfehlungen zu Diagnostik, Behandlung und Rehabilitation sowie für ein strukturiertes und optimiertes Management der Erkrankung. Dazu gehört insbesondere auch eine verbesserte Kommunikation zwischen den Behandelnden über alle Sektoren- und Fächergrenzen hinaus sowie der Einbezug der Patient\*innen in alle Behandlungsentscheidungen.

Darüber hinaus erhoffen sich die Autor\*innen und die herausgebenden Organisationen der Nationalen Versorgungsleitlinie COPD konkret:

- Eine Verbesserung der Diagnostik. Dies beinhaltet die möglichst frühe Diagnose der Erkrankung, eine angemessene Verlaufskontrolle aber auch die Vermeidung von Über- und Unterdiagnostik durch Verwendung angemessener Referenzwerte für die Spirometrie.
- Eine Optimierung des Therapiemanagements: insbesondere eine an die individuellen Voraussetzungen jedes Patienten beziehungsweise jeder Patientin angepasste Therapie die auch das Potenzial nichtmedikamentöser Verfahren ausschöpft sowie wichtige Aspekte wie Multimorbidität angemessen berücksichtigt.
- Eine Optimierung des Managements der Komorbiditäten, insbesondere der Umgang mit Angst und Depression, Osteoporose, Schmerz.
- Die Stärkung der Arzt-Patienten-Kommunikation mit dem Ziel, die Adhärenz zu gemeinsam vereinbarten Therapiezielen zu fördern und die vorausschauende Planung der Behandlung zu fördern.
- Die Förderung des Verständnisses von COPD als eine chronische Erkrankung, die dauerhafter Betreuung insbesondere auch palliativmedizinischer Versorgung bedarf.
- Die Förderung von Aufklärung über und Motivation zu lebensstilbezogener Anpassung: Dies betrifft körperliche Aktivität und Training sowie insbesondere die Beachtung des großen Stellenwerts der Tabakentwöhnung.

## 3 Adressat\*innen

Die Empfehlungen der NVL COPD richten sich an

- alle Ärzt\*innen, die in den von der NVL angesprochenen Versorgungsbereichen tätig sind (z. B. Allgemeinmedizin, Arbeitsmedizin, Innere Medizin, Pneumologie, Physikalische Medizin und Rehabilitation, Psychosomatik);
- die nicht-ärztlichen Fachberufe, die in den von einer NVL angesprochenen Versorgungsbereichen als Kooperierende der Ärzteschaft tätig sind (z. B. Apotheker\*innen, Physiotherapeut\*innen, Psychotherapeut\*innen);
- betroffene Patient\*innen sowie ihr persönliches Umfeld (z. B. Partner\*innen, Kinder) unter Nutzung von speziellen Patientenleitlinien und Patienteninformationen.

Die NVL COPD richtet sich weiterhin an

- die Vertragsverantwortlichen von „Strukturierten Behandlungsprogrammen“ und „Integrierten Versorgungsverbänden“;
- die medizinischen wissenschaftlichen Fachgesellschaften und andere Herausgeber von Leitlinien, deren Leitlinien ihrerseits die Grundlage für die NVL bilden können;
- die Kostenträger im Gesundheitssystem;
- die Öffentlichkeit zur Information über gute medizinische Vorgehensweise.

## 4 Zusammensetzung der Leitliniengruppe

Primäre Ansprechpartner\*innen bei der Benennung von Leitlinienautor\*innen sind die Mitgliedsgesellschaften der AWMF sowie die Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ). Die an der Versorgung von Patient\*innen mit COPD maßgeblich beteiligten Fachgesellschaften wurden durch das ÄZQ angesprochen und um Entsendung von Mandatsträger\*innen in die Leitliniengruppe gebeten. Die Nominierung liegt im Verantwortungsbereich der angesprochenen medizinischen wissenschaftlichen Fachgesellschaften. Die Leitliniengruppe wurde multidisziplinär zusammengesetzt.

Bei der Erstellung der 2. Auflage der NVL COPD vertretene Fachgesellschaften/Organisationen:

- Akademie für Ethik in der Medizin e. V. (AEM);
- Arzneimittelkommission der Deutschen Apotheker (AMK);
- Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ);
- Bundesarbeitsgemeinschaft SELBSTHILFE e. V. (BAG Selbsthilfe);
- Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin e. V. (DEGAM);
- Deutsche Gesellschaft für Geriatrie e. V. (DGG);
- Deutsche Gesellschaft für Gerontologie und Geriatrie e. V. (DGGG);
- Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie e. V. (DGHNOKHC);
- Deutsche Gesellschaft für Innere Medizin e. V. (DGIM);
- Deutsche Gesellschaft für Palliativmedizin e. V. (DGP);
- Deutsche Gesellschaft für Pflegewissenschaft e. V. (DGP);
- Deutsche Gesellschaft für Physikalische und Rehabilitative Medizin e. V. (DGPRM);
- Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin e. V. (DGP);
- Deutsche Gesellschaft für Psychosomatische Medizin und Ärztliche Psychotherapie e. V. (DGPM);
- Deutsche Gesellschaft für Rehabilitationswissenschaften e. V. (DGRW);
- Deutsche Gesellschaft für Schlafforschung und Schlafmedizin e. V. (DGSM);
- Deutsche Röntgengesellschaft e. V. (DRG);
- Deutscher Verband für Physiotherapie e. V. (ZVK);
- Deutsches Kollegium für Psychosomatische Medizin und Psychotherapie (DKPM);
- Gesellschaft für Phytotherapie e. V. (GPT).

In der ersten Sitzung zur Aktualisierung der NVL COPD, 2. Auflage am 22.01.2018 wurde die Repräsentativität der Gruppe zur Überarbeitung der NVL durch die Leitliniengruppe geprüft. Folgende Fachgesellschaften/Organisationen wurden neu aufgenommen:

- Deutsche Atemwegsliga e. V.;
- Deutsche Forschungsgruppe Pneumologie in der Primärversorgung e. V. (DFPP);
- Deutsche Gesellschaft für Arbeitsmedizin und Umweltmedizin e. V. (DGAUM);
- Deutsche Gesellschaft für Internistische Intensivmedizin und Notfallmedizin e. V. (DGIIN);
- Deutsche Gesellschaft für Kardiologie – Herz und Kreislaufforschung e. V. (DGK);
- Deutsche Gesellschaft für Nikotin- und Tabakforschung e. V. (DGNTF);

- Deutsche Gesellschaft für Thoraxchirurgie e. V. (DGT);
- Deutsche Interdisziplinäre Gesellschaft für Außerklinische Beatmung e. V. (DIGAB).

Im Laufe der Aktualisierung wurden folgende Fachgesellschaften nachbenannt:

- Deutsche Gesellschaft für Psychologie e. V. (DGPs);
- Deutsche Gesellschaft für Suchtforschung und Suchttherapie e. V. (DG-Sucht).

BÄK und KBV haben zur Begleitung des Aktualisierungsprozesses der NVL COPD diskontinuierlich Referent\*innen aus den zuständigen Dezernaten in die Sitzungen der Leitliniengruppe als Beobachter\*innen entsandt.

In Tabelle 1 werden alle Vertreter\*innen der Fachgesellschaften aufgeführt, die an der Erstellung der 2. Auflage der NVL COPD und dem formalen Konsensusverfahren beteiligt waren. Autor\*innen, die an der vorherigen Auflage beteiligt waren, sind im jeweiligen Leitlinienreport dokumentiert [10].

**Tabelle 1: Vertreter\*innen der Fachgesellschaften/Organisationen**

Fachgesellschaft/ Organisation	Funktion in der Leitliniengruppe	Experte/Expertin	Arbeitsgruppen zur Aktualisierung (2. Auflage)
Akademie für Ethik in der Medizin (AEM)	Erstbenannte Vertreterin der Fach- gesellschaft	Dr. Elisabeth Heis- ter	Nicht-medikamentöse Therapie, Rehabilitation Respiratorische Insuffizienz
Akademie für Ethik in der Medizin (AEM)	Stellvertreter der Erstbenannten	Prof. Dr. Alfred Si- mon	Nicht-medikamentöse Therapie, Rehabilitation
Arzneimittelkommission der Deutschen Apotheker (AMK)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Martin Schulz	Medikamentöse Therapie Versorgungskoordination
Arzneimittelkommission der Deutschen Apotheker (AMK)	Stellvertreter des Erstbenannten	Dr. Eric Martin	Medikamentöse Therapie Versorgungskoordination
Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Harald Schäfer	Diagnostik Medikamentöse Therapie
Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ)	Stellvertreter des Erstbenannten	Prof. Dr. Klaus Dal- hoff	-
Deutsche Atemwegsliga	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Carl-Peter Criée	Diagnostik Nicht-medikamentöse Therapie, Rehabilitation Respiratorische Insuffizienz Medikamentöse Therapie Aktualisierung Definition
Deutsche Atemwegsliga	Stellvertreterin des Erstbenannten	Prof. Dr. Andrea Koch (bis März 2019) <sup>1</sup>	-
Deutsche Forschungs- gruppe Pneumologie in der Primärversorgung (DFPP)	Erstbenannter Vertreter der Fachgesellschaft	Dr. Michael Weber	Diagnostik Nicht-medikamentöse Therapie, Rehabilitation Medikamentöse Therapie
Deutsche Forschungs- gruppe Pneumologie in der Primärversorgung (DFPP)	Stellvertreter des Erstbenannten	Dr. Andreas Hellmann	Diagnostik Tabakentwöhnung Respiratorische Insuffizienz Versorgungskoordination



Fachgesellschaft/ Organisation	Funktion in der Leitliniengruppe	Experte/Expertin	Arbeitsgruppen zur Aktualisierung (2. Auflage)
Deutsche Forschungs- gruppe Pneumologie in der Primärversorgung (DFPP)	2. Stellvertreter des Erstbenannten	Dr. Thomas Hering (ab Oktober 2019)	Tabakentwöhnung
Deutsche Gesellschaft für Allgemeinmedizin und Fa- milienmedizin (DEGAM)	Erstbenannter Vertreter der Fachgesellschaft	Univ.-Prof. Dr. Antonius Schneider	-
Deutsche Gesellschaft für Allgemeinmedizin und Fa- milienmedizin (DEGAM)	Stellvertreter des Erstbenannten	Prof. Dr. Michael Freitag, MPH	Diagnostik Medikamentöse Therapie Versorgungskoordination
Deutsche Gesellschaft für Allgemeinmedizin und Fa- milienmedizin (DEGAM)	2. Stellvertreter des Erstbenannten	Univ.-Prof. Dr. Daniel Kotz, PhD, MPH (ab August 2019)	Tabakentwöhnung
Deutsche Gesellschaft für Arbeitsmedizin und Um- weltmedizin (DGAUM)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Dennis Nowak	Tabakentwöhnung
Deutsche Gesellschaft für Arbeitsmedizin und Um- weltmedizin (DGAUM)	Stellvertreter des Erstbenannten	Univ.-Prof. Dr. Thomas Kraus	-
Deutsche Gesellschaft für Geriatric (DGG)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Hans Jürgen Heppner	-
Deutsche Gesellschaft für Geriatric (DGG)	Stellvertreter des Erstbenannten	PD Dr. Helmut Frohnhofen	Diagnostik
Deutsche Gesellschaft für Gerontologie und Geriatric (DGGG)	Erstbenannte Vertreterin der Fachgesellschaft	Dr. Katrin Knoll	-
Deutsche Gesellschaft für Gerontologie und Geriatric (DGGG)	Stellvertreter der Erstbenannten	Dr. Manfred Gogol	-
Deutsche Gesellschaft für Hals-Nasen-Ohren-Heil- kunde, Kopf- und Hals-Chi- rurgie (DGHNOKHC)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Andreas Neumann	-
Deutsche Gesellschaft für Innere Medizin (DGIM)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Stefan Andreas	Tabakentwöhnung Medikamentöse Therapie
Deutsche Gesellschaft für Internistische Intensivmedi- zin und Notfallmedizin (DGIIN)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Tobias Welte	-
Deutsche Gesellschaft für Internistische Intensivmedi- zin und Notfallmedizin (DGIIN)	Stellvertreter des Erstbenannten	Prof. Dr. Claus F. Vogelmeier	Aktualisierung Definition
Deutsche Gesellschaft für Kardiologie – Herz und Kreislaufforschung (DGK)	Erstbenannter Vertreter der Fachgesellschaft	PD Dr. Tobias J. Lange	Diagnostik

Fachgesellschaft/ Organisation	Funktion in der Leitliniengruppe	Experte/Expertin	Arbeitsgruppen zur Aktualisierung (2. Auflage)
Deutsche Gesellschaft für Nikotin- und Tabakfor- schung (DGNTF)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. David Groneberg	Tabakentwöhnung
Deutsche Gesellschaft für Nikotin- und Tabakfor- schung (DGNTF)	Stellvertreter des Erstbenannten	Dr. Ulf Ratje (bis Juni 2018) <sup>1</sup>	-
Deutsche Gesellschaft für Palliativmedizin (DGP)	Erstbenannte Vertreterin der Fach- gesellschaft	Prof. Dr. Claudia Bausewein, PhD	Nicht-medikamentöse Therapie, Rehabilitation Respiratorische Insuffizienz
Deutsche Gesellschaft für Palliativmedizin (DGP)	Stellvertreterin der Erstbenannten	Dr. Wiebke Nehls	Nicht-medikamentöse Therapie, Rehabilitation
Deutsche Gesellschaft für Pflegerwissenschaften (DGP)	Erstbenannte Vertreterin der Fachgesellschaft	Christiane Freitag, B.A.	Tabakentwöhnung Nicht-medikamentöse Therapie, Rehabilitation
Deutsche Gesellschaft für Physikalische und Rehabi- litative Medizin (DGPRM)	Erstbenannter Vertreter der Fachgesellschaft	Dr. Konrad Schultz	Tabakentwöhnung Nicht-medikamentöse Therapie, Rehabilitation
Deutsche Gesellschaft für Pneumologie und Beat- mungsmedizin (DGP)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Heinrich Worth	Diagnostik Tabakentwöhnung Nicht-medikamentöse Therapie, Rehabilitation Respiratorische Insuffizienz Aktualisierung Definition
Deutsche Gesellschaft für Pneumologie und Beat- mungsmedizin (DGP)	Stellvertreter des Erstbenannten	PD Dr. Henrik Watz	Diagnostik Medikamentöse Therapie
Deutsche Gesellschaft für Pneumologie und Beat- mungsmedizin (DGP)	2. Stellvertreter des Erstbenannten	Dr. Andrés de Roux (ab März 2018)	Diagnostik Medikamentöse Therapie Versorgungskoordination
Deutsche Gesellschaft für Psychologie (DGPs)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Stephan Mühlig (ab August 2019)	Tabakentwöhnung
Deutsche Gesellschaft für Psychosomatische Medizin und Ärztliche Psychothera- pie (DGPM)	Erstbenannte Vertreterin der Fachgesellschaft	PD Dr. Cora Weber (ab April 2018)	Diagnostik Nicht-medikamentöse Therapie, Rehabilitation Versorgungskoordination
Deutsche Gesellschaft für Psychosomatische Medizin und Ärztliche Psychothera- pie (DGPM)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Hans Christian Deter (bis März 2018) <sup>1</sup>	-
Deutsche Gesellschaft für Rehabilitationswissenschaf- ten (DGRW)	Erstbenannter Vertreter der Fachgesellschaft	Dr. Konrad Schultz	Tabakentwöhnung Nicht-medikamentöse Therapie, Rehabilitation
Deutsche Gesellschaft für Schlafforschung und Schlafmedizin (DGSM)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Georg Nilius	Diagnostik Nicht-medikamentöse Therapie, Rehabilitation Respiratorische Insuffizienz

Fachgesellschaft/ Organisation	Funktion in der Leitliniengruppe	Experte/Expertin	Arbeitsgruppen zur Aktualisierung (2. Auflage)
Deutsche Gesellschaft für Suchtforschung und Sucht- therapie (DG-Sucht)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Anil Batra (ab August 2019)	Tabakentwöhnung
Deutsche Gesellschaft für Thoraxchirurgie (DGT)	Erstbenannter Vertreter der Fachgesellschaft	Dr. Stephan Eggeling	-
Deutsche Gesellschaft für Thoraxchirurgie (DGT)	Stellvertreter des Erstbenannten	PD Dr. Stefan Welter	-
Deutsche Interdisziplinäre Gesellschaft für Außerklini- sche Beatmung (DIGAB)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Jan H. Storre	Nicht-medikamentöse Therapie, Rehabilitation Respiratorische Insuffizienz
Deutsche Interdisziplinäre Gesellschaft für Außerklini- sche Beatmung (DIGAB)	Stellvertreter des Erstbenannten	Prof. Dr. Michael Dreher	Nicht-medikamentöse Therapie, Rehabilitation Respiratorische Insuffizienz Aktualisierung Definition
Deutsche Röntgengesell- schaft (DRG)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Claus Peter Heußel	Tabakentwöhnung Nicht-medikamentöse Therapie, Rehabilitation
Deutsche Röntgengesell- schaft (DRG)	Stellvertreter des Erstbenannten	Prof. Dr. Hans-Ul- rich Kauczor	Diagnostik
Deutscher Verband für Physiotherapie (ZVK)	Erstbenannter Vertreter der Fachgesellschaft	Jan Kaufmann	Nicht-medikamentöse Therapie, Rehabilitation Versorgungskoordination
Deutsches Kollegium für Psychosomatische Medizin und Psychotherapie (DKPM)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Thomas Ritz (ab April 2018)	Diagnostik Nicht-medikamentöse Therapie, Rehabilitation
Deutsches Kollegium für Psychosomatische Medizin und Psychotherapie (DKPM)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Hans Christian Deter (bis März 2018) <sup>1</sup>	-
Gesellschaft für Phytothe- rapie (GPT)	Erstbenannter Vertreter der Fachgesellschaft	Prof. Dr. Jost Langhorst	-
Gesellschaft für Phytotherapie (GPT)	Stellvertreterin des Erstbenannten	Dr. Petra Klose	Nicht-medikamentöse Therapie, Rehabilitation Medikamentöse Therapie
Deutsche PatientenLiga Atemwegserkrankungen (DPLA)	Erstbenannter Vertreter	Dr. Michael Köhler	Tabakentwöhnung Nicht-medikamentöse Therapie, Rehabilitation Medikamentöse Therapie

<sup>1</sup> Die aufgeführten Expert\*innen wurden für die NVL COPD benannt, waren jedoch nicht an der Erstellung beteiligt.

Frau Claudia Meiling vom Deutschen Verband der Ergotherapeuten unterstützte die Arbeitsgruppe Nicht-medikamentöse Therapie als externe Expertin bei der Erarbeitung des Kapitels Ergotherapie.

**Tabelle 2: Methodik, Redaktion und Moderation**

Redaktion und Moderation		
Sabine Schüler	Ärztliches Zentrum für Qualität in der Medizin (ÄZQ)	Literaturrecherche, Evidenzaufbereitung, Methodische Begleitung, Redaktion, Moderation
Corinna Schaefer	Ärztliches Zentrum für Qualität in der Medizin (ÄZQ)	Methodische Begleitung, Redaktion, Moderation, Redaktion Patientenmaterialien
Isabell Vader, MPH (bis 01/2021)	Ärztliches Zentrum für Qualität in der Medizin (ÄZQ)	Literaturrecherche, Evidenzaufbereitung, Moderation
Dr. Susanne Blödt, MScPH	Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)	Methodische Begleitung
Dr. Monika Nothacker, MPH	Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)	Moderation

## 5 Patient\*innenbeteiligung

Neben der wissenschaftlichen Evidenz und den ärztlichen Erfahrungen stellen die Erfahrungen und Lösungsvorschläge von Patient\*innen(-organisationen) im Hinblick auf die Versorgungssituation bei der betreffenden Erkrankung eine wertvolle Informationsquelle für Leitlinien dar [11]. Vor diesem Hintergrund haben BÄK, KBV und AWMF die konsequente Beteiligung von Patient\*innen am NVL-Programm beschlossen. Patient\*innen sind regelhaft beteiligt an der NVL-Erstellung, am externen Begutachtungsverfahren und an der Erstellung von Patientenleitlinien (siehe Kapitel 12.1 Materialien und Formate) zur entsprechenden NVL. Die Benennung von Patientenvertreter\*innen erfolgt nach einem transparenten, standardisierten Verfahren (siehe Handbuch Patientenbeteiligung [12]) über die Dachverbände der Selbsthilfeorganisationen:

- Bundesarbeitsgemeinschaft Selbsthilfe (BAG SELBSTHILFE);
- Deutsche Arbeitsgemeinschaft Selbsthilfegruppen (DAG SHG);
- Forum chronisch kranker und behinderter Menschen im Paritätischen Gesamtverband).

Die Interessenvertretung der an COPD erkrankten Patient\*innen übernahm Herr Dr. Michael Köhler von der Deutschen PatientenLiga Atemwegserkrankungen (DPLA).

## 6 Auswahl und Bewertung der Evidenz

### Quell- und Referenzleitlinien

Die strukturierte Suche nach Leitlinien zum Thema COPD bei fachübergreifenden und fachspezifischen Leitlinien-datenbanken und -anbietern erbrachte 18 Treffer, welche als potentielle Grundlage für eine Leitliniensynopse geeignet waren. Bei näherer Betrachtung ergab sich jedoch, dass die Qualität der Leitlinien – insbesondere in den Bereichen „methodische Exaktheit“ und „redaktionelle Unabhängigkeit“ zumeist unzureichend war.

Aufgrund dieser Überlegungen wurde auf eine Leitlinienadaptation verzichtet und stattdessen für die gesamte NVL eine strukturierte Recherche nach aggregierter Evidenz durchgeführt. Für einzelne Fragestellungen wurde auf Referenzleitlinien Bezug genommen. Die Bewertung und Auswahl der internationalen Quell- und Referenzleitlinien wird strukturiert im Anhang 3.1 dargestellt. Aus dem deutschen Versorgungskontext stammende Leitlinien (AWMF-Leitlinienregister, [www.awmf.org/leitlinien.html](http://www.awmf.org/leitlinien.html)) wurden, da sie bereits seitens der AWMF umfassend begutachtet wurden, nicht zusätzlich bewertet.

### Strukturierte Recherche

Für die gesamte NVL COPD wurde aggregierte Evidenz zum Thema COPD in der Cochrane-Datenbank recherchiert. Die gefundenen Publikationen wurden zweistufig, als Titel/Abstract und im Volltext gesichtet. Die eingeschlossenen systematischen Reviews wurden bewertet und die Ergebnisse extrahiert. In den Evidenztabelle wurde die empfehlungsrelevante Evidenz ausführlich dargestellt. Eine Übersicht der Literatursichtung sowie Evidenztabelle befinden sich im Anhang.

Für weitere Fragestellungen erfolgte in einem zweistufigen Vorgehen zunächst eine strukturierte Suche nach HTA-Berichten oder systematischen Übersichtsarbeiten, die durch das IQWiG (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen), das National Institute for Health and Care Excellence (NICE), die Agency for Healthcare Research and Quality (AHRQ) oder die Cochrane Collaboration erstellt wurden. Diese Institutionen wurden auf Grund ihrer evidenzbasierten Vorgehensweise, ihrer hohen Berichtsqualität, ihrer wissenschaftlichen Unabhängigkeit und – im Falle des IQWiG und NICE – ihres Bezugs zum deutschen bzw. europäischen Versorgungskontext als primäre Quellen systematischer Übersichtsarbeiten ausgewählt.

Zu folgender Fragestellung wurde eine strukturierte Recherche auf Basis aggregierter Evidenz durchgeführt:

- Häusliche Trainingstherapie bei Patient\*innen mit COPD, Anhang 3.12

### Systematische Evidenzrecherche

Eine zusätzliche systematische Recherche erfolgte bei Fehlen thematisch passender Übersichtsarbeiten von Cochrane. Systematische Recherchen wurden in Medline via Pubmed und der Cochrane-Datenbank durchgeführt. Die gefundenen Publikationen wurden zweistufig, als Titel/Abstract und im Volltext gesichtet. Die eingeschlossenen systematischen Übersichtsarbeiten und Primärstudien wurden bewertet und die Ergebnisse extrahiert. In den Evidenztabelle wurde die empfehlungsrelevante Evidenz ausführlich dargestellt.

Zu folgenden Themen wurden systematische Recherchen durchgeführt:

- Diagnostische Verfahren, Anhang 3.4;
- Über-/Unterdiagnose, Anhang 3.5;
- Phänotypisierung mittels Computertomographie, Anhang 3.6;
- Cut-Off Symptomerfassung, Anhang 3.7;
- Angst/Depression, Anhang 3.8;
- Ganzkörpervibration, Anhang 3.11;
- Atemtechniken, Anhang 3.13;
- Patientenschulung, Anhang 3.14;
- Ernährung, Anhang 3.15;
- Gerätebasiertes Training, Anhang 3.16;
- Telemedizin, Anhang 3.17;
- Triple-Therapie, Anhang 3.18;
- kardiale Nebenwirkungen bei inhalativer Dauertherapie mit einem LAMA oder LABA, Anhang 3.19;
- Eosinophile, Anhang 3.20;
- Roflumilast, Anhang 3.21;
- Mukolytika, Anhang 3.23;
- Wechsel des Inhalationssystems ohne erneute Instruktion, Anhang 3.24.

Für folgende Fragestellungen wurden aufgrund ihrer Übertragbarkeit auf Patient\*innen mit COPD systematische Recherchen der NVL Asthma [13] herangezogen:

- Asthma COPD Overlap, Anhang 5.1;
- Wirksamkeit von Instruktionen in Inhalationssysteme, Anhang 3.22;
- Auswirkungen des Wechsels von Inhalationssystemen ohne erneute Instruktion, Anhang 3.24.

Die Recherchedokumentationen zu den jeweiligen systematischen Recherchen sind im Leitlinienreport der NVL Asthma [14] ([www.leitlinien.de/asthma](http://www.leitlinien.de/asthma)) einzusehen.

In Zusammenarbeit mit der Cochrane Airways Group wurde eine systematische Update-Recherche eines Cochrane Reviews zur Wirksamkeit verhaltensbezogener und/oder pharmakologischer Maßnahmen zur Raucherentwöhnung bei rauchenden Patient\*innen mit COPD [15] durchgeführt. Für ein Suchupdate wurde die damals verwendete Suchstrategie seitens der Cochrane Airways Group erneut umgesetzt. Die Ergebnisse dieser Update-Suche wurden dem ÄZQ zur Verfügung gestellt. Die Sichtung im Titel/Abstract und im Volltext, sowie die Bewertung und Extraktion erfolgte durch das ÄZQ (Anhang 3.9).

Im Rahmen der Aktualisierung der S3-Leitlinie „Rauchen und Tabakabhängigkeit: Screening, Diagnostik und Behandlung“ [16] wurde eine systematische Update-Recherche bezüglich der Nutzung von E-Zigaretten durchgeführt. Die identifizierten Volltexte wurden dem ÄZQ zur Verfügung gestellt (Anhang 3.10).

Der Leitlinienkoordinator der S3-Leitlinie „Tabakentwöhnung bei COPD“ [17], welcher auch Mitglied der Leitliniengruppe der NVL COPD ist, stellte die Evidenz zu möglichen motivierenden Effekten der Besprechung von Lungenfunktion oder CO-Werten mit den Patient\*innen zur Verfügung (Anhang 6.3). Weitere Informationen zu dieser systematischen Recherche finden sich unter [www.awmf.org/leitlinien/detail/II/020-005.html](http://www.awmf.org/leitlinien/detail/II/020-005.html).

Selektiv recherchierte Arbeiten wurden in Ausnahmen ergänzend für den Hintergrundtext herangezogen, wenn sie aus Sicht der Leitliniengruppe im medizinischen Diskurs von besonderer Bedeutung waren (z. B. RCT zum Effekt von Metoprolol hinsichtlich des Exazerbationsrisikos bei Patient\*innen mit moderater bis schwerer COPD) oder auf einzelne praxisrelevante Aspekte eingingen.

### Weitere Quellen

Zur Aktualisierung des Kapitels Epidemiologie wurde gezielt nach epidemiologischen Daten aus dem deutschen Versorgungskontext gesucht. Als aktuellste verfügbare Daten wurden die Ergebnisse der Querschnittstudie GEDA 2014/2015-EHIS [18] sowie Auswertungen des Zi (Zentralinstitut für die kassenärztliche Versorgung in Deutschland) von bundesweiten vertragsärztlichen Abrechnungsdaten [19] herangezogen.

Für ausgewählte Fragestellungen wurden Veröffentlichungen der European Medicines Agency (EMA) und des Gemeinsamen Bundesausschusses (G-BA) gezielt durchsucht.

### Evidenzbewertung

Die methodische Bewertung der recherchierten Übersichtsarbeiten erfolgte zunächst mit dem AMSTAR-Tool [20]. Bewertet wurden elf Fragen zur methodischen Qualität der systematischen Übersichtsarbeit mit den Kategorien ja, nein, nicht anwendbar und nicht beantwortbar. Gezählt wurden die Ja-Antworten. Von den Entwicklern wurde kein Cut-off-Wert für methodisch gute Arbeiten festgelegt. Innerhalb der Leitliniengruppe wurde ein Cut-off-Wert von 6 für den Einschluss einer Arbeit festgelegt. Zudem musste das Kriterium 7 „Qualitätsbewertung der eingeschlossenen Primärstudien“ erfüllt sein, um in die Evidenzsynthese eingeschlossen zu werden.

Im Verlauf der Arbeiten an der NVL COPD wurde die Bewertung systematischer Übersichten dann mit der aktualisierten Version – AMSTAR-2-Tool [21] – entsprechend durchgeführt. Bewertet wurden nun sechzehn Fragen zur methodischen Qualität der systematischen Übersichtsarbeit mit den Kategorien „ja“, „partiell ja“, „nein“ oder „nicht anwendbar“. Bewertet wurden die als kritische Domänen bezeichneten Fragen sowie die nicht-kritischen Domänen nach den vorgeschlagenen Bewertungskategorien „High“, „Moderate“, „Low“ und „Critically low“. Dabei durften für die Kategorie „High“ keine kritische Domäne oder eine nicht-kritische Domäne verletzt sein, für die Kategorie „Moderate“ mehr als eine nicht-kritische Domäne, für die Kategorie „Low“ eine kritische Domäne und für die Kategorie „Critically low“ mehr als eine kritische Domäne. Wird eine systematische Übersichtsarbeit mit „Critically low“ bewertet, führt dies nicht automatisch zum Ausschluss. Gegebenenfalls werden im Einzelfall die nicht erfüllten Kriterien individuell kritisch geprüft.

Die methodische Bewertung der randomisierten kontrollierten Studien erfolgte in Anlehnung an das Cochrane Risk of Bias Tool, wobei die Domänen „Selection bias“, „Performance bias“, „Detection bias“, „Attrition bias“, „Reporting bias“ sowie „andere Bias-Ursachen“ jeweils mit „hoch“, „niedrig“ oder „unklar“ bewertet wurden [22]. Die Bewertung von nicht randomisierten Studien erfolgte entsprechend den Empfehlungen zur „Bewertung des Biasrisikos (Risiko systematischer Fehler) in klinischen Studien: ein Manual für die Leitlinienerstellung“ [23]; diagnostische Studien wurden mit dem QUADAS-2-Tool bewertet [24].

### Evidenzqualität

Für den Fall, dass eine Bewertung nach GRADE bereits durch die Autor\*innen der systematischen Übersichtsarbeit erfolgt war, wurde diese übernommen. Wenn eine Bewertung nach GRADE nicht zur Verfügung stand, oder Primärstudien aus systematisch durchgeführten Recherchen für die Formulierung von Empfehlungen herangezogen wurden, wurde die Präzision, Direktheit und Konsistenz der Evidenz, sowie endpunktbezogene Studienqualität betrachtet und narrativ beschrieben. Daraus ergab sich eine Bewertung der Evidenzqualität in Anlehnung an GRADE von hoch bis sehr gering. Eigene GRADE-Bewertungen wurden nicht vorgenommen, da auch keine eigenen Metaanalysen durchgeführt wurden.

### Endpunktgraduierung

In der Auftaktsitzung zur NVL COPD, 2. Auflage wurden klinisch relevante Endpunkte gesammelt (Anhang 2) und in einer elektronischen Abstimmung in Anlehnung an die Empfehlungen von GRADE priorisiert [25]. Die Endpunkte „krankheitsspezifische Mortalität“, „Symptomatik: Atemnot, Husten und Auswurf“, „Mobilität/Funktionalität“, „soziale Teilhabe“, „Exazerbationen“, „Reduktion des zukünftigen Krankheitsrisikos: COPD-bedingte Hospitalisierung“ und „Lebensqualität“ wurden am häufigsten als „kritisch“ bewertet. Für diese sowie für die Angaben zur Sicherheit fand eine Extraktion der Ergebnisse statt.

## 7 Formulierung von Empfehlungen

Die Empfehlungsgrade wurden durch die Leitlinienautor\*innen im Rahmen eines formalen Konsensverfahrens vergeben (siehe Kapitel 8 Entwicklung und Konsentierung). Dabei wurden die folgenden Kriterien für die klinische Beurteilung vorgegeben [7,9,26]:

- die klinische Relevanz der Studienendpunkte (Outcome), Präzision des Effektschätzers und Effektstärken;
- die Konsistenz der Studienergebnisse;
- die Abwägung von potentiell Nutzen und Schaden (Verhältnis von erwünschten und unerwünschten Effekten);
- die Anwendbarkeit der Evidenz auf die Patientenzielgruppen der NVL (Direktheit);
- die Angemessenheit der Vergleichsintervention;
- das Risiko für Publikationsbias;
- die Präferenzen der Patient\*innen;
- die Umsetzbarkeit im klinischen Alltag und in verschiedenen Versorgungssettings/Sektoren;
- ethische, rechtliche sowie ökonomische Erwägungen.

Die Graduierung der Empfehlungen im NVL-Verfahren entspricht den in Tabelle 3 dargestellten Symbolen. Zunächst bestimmt die Qualität der Evidenz den Empfehlungsgrad. Eine mittlere Evidenzstärke führt demnach zu einem mittleren Empfehlungsgrad. Aufgrund der oben genannten Kriterien, insbesondere der Relevanz der Endpunkte und Effektstärken für die Patient\*innen, kann es jedoch zu einem begründeten Auf- oder Abwerten der Empfehlungsstärke gegenüber dem Evidenzgrad kommen. Die Gründe für ein Auf- oder Abwerten werden im Hintergrundtext dargelegt. Empfehlungen sollten möglichst klar und eindeutig, handlungsorientiert und leicht verständlich formuliert sein. Vereinfacht drücken im Ergebnis die Empfehlungsgrade folgende Gesamteinschätzung aus:

- Bei starken Empfehlungen (soll) sind sich die Leitlinienautor\*innen in ihrer Einschätzung sicher. Starke Empfehlungen drücken aus, dass die wünschenswerten Folgen mit hoher Wahrscheinlichkeit mögliche unerwünschte Effekte in Bezug auf patientenrelevante Endpunkte überwiegen.
- Bei abgeschwächten Empfehlungen (sollte) sind sich die Leitlinienautor\*innen in ihrer Einschätzung weniger sicher.
- Bei offenen Empfehlungen (kann) sind sich die Leitlinienautor\*innen nicht sicher. Offene Empfehlungen drücken eine Handlungsoption in Unsicherheit aus.

Empfehlungen für Versorgungsabläufe und Entscheidungsprozesse mit verschiedenen Handlungsoptionen werden als klinische Algorithmen dargestellt [27].

**Tabelle 3: Schema zur Graduierung von NVL-Empfehlungen, modifiziert nach [7,9]**

Empfehlungsgrad	Beschreibung	Formulierung	Symbol
A	Starke Positiv-Empfehlung	Soll	↑↑↑
B	Abgeschwächte Positiv-Empfehlung	Sollte	↑
0	Offene Empfehlung	Kann	↔
B	Abgeschwächte Negativ-Empfehlung	Sollte nicht	↓
A	Starke Negativ-Empfehlung	Soll nicht	↓↓↓

## 8 Entwicklung und Konsentierung

### Entwicklung

Der Entwicklungsprozess der 2. Auflage der NVL COPD wurde durch das ÄZQ seit März 2017 organisiert. Nach Durchführung der strukturierten Recherche in der Cochrane-Datenbank (siehe Kapitel 6 Auswahl und Bewertung der Evidenz) wurde die identifizierte aggregierte Evidenz bewertet, extrahiert und den jeweiligen Kapiteln der NVL COPD zugeordnet.

Folgende Kapitel wurden in den Arbeitsgruppen diskutiert und komplett überarbeitet:

- Definition und Epidemiologie;
- Diagnostik und Monitoring;
- Tabakentwöhnung;
- Nicht-medikamentöse Therapie;
- Medikamentöse Therapie;
- Medizinische Rehabilitation;
- Versorgungskoordination.

Zwischen April 2018 und Januar 2020 wurden die Empfehlungen und Hintergrundtexte der NVL in mehreren Telefonkonferenzen der Arbeitsgruppen (siehe Tabelle 4) diskutiert und erarbeitet. Die in den Arbeitsgruppen vorbereiteten Empfehlungen und Algorithmen wurden in der Konsensuskonferenz im Februar 2020 formal konsentiert. Im März und April 2020 wurde im Nachgang zur Konsensuskonferenz das Kapitel „Atmungsunterstützende Maßnahmen bei chronisch respiratorischer Insuffizienz“ in zwei weiteren Telefonkonferenzen (siehe Tabelle 4) erarbeitet und im elektronischen Abstimmungsverfahren konsentiert. Die Hintergrundtexte zu den Kapiteln wurden im schriftlichen Umlaufverfahren abgestimmt.

**Tabelle 4: Verfahren der Arbeitsgruppen, 2. Auflage**

Arbeitsgruppe	Diskussion der Empfehlungen und Hintergrundtexte
Diagnostik (inklusive Definition und Epidemiologie)	6 Telefonkonferenzen
Unterarbeitsgruppe: Aktualisierung Definition	1 Telefonkonferenz
Tabakentwöhnung	3 Telefonkonferenzen
Nicht-medikamentöse Therapie; Rehabilitation	4 Telefonkonferenzen
Unterarbeitsgruppe: Respiratorische Insuffizienz	2 Telefonkonferenzen
Medikamentöse Therapie	5 Telefonkonferenzen
Unterarbeitsgruppe: Darstellung Deeskalation	1 Telefonkonferenz
Versorgungskoordination	1 Telefonkonferenz



## Konsentierung

Die Empfehlungen und Abbildungen wurden in der Konsensuskonferenz (17.02.2020) sowie in einem formalisierten, schriftlichen Abstimmungsverfahren unter Anwendung der Delphi-Technik formal konsentiert. An den Abstimmungsprozessen nahmen die benannten Vertreter\*innen der an der Erstellung der NVL beteiligten Fachgesellschaften teil. Jeder Fachgesellschaft stand im Abstimmungsverfahren jeweils eine Stimme zur Verfügung.

Bei der Konsensuskonferenz wurden die Empfehlungen mit Hilfe eines nominalen Gruppenprozesses von Frau Schaefer und Frau Vader moderiert. Enthaltungen aufgrund eines Interessenkonfliktes sind im Anhang 1.4 dokumentiert. Der Ablauf des nominalen Gruppenprozesses gestaltete sich wie folgt:

- Präsentation der zu konsentierenden Inhalte;
- Gelegenheit zu Rückfragen zum methodischen Vorgehen/inhaltlichen Verständnis;
- Notiz von Stellungnahmen (jeder Teilnehmer für sich);
- Registrierung der Stellungnahmen im Einzel-/Umlaufverfahren;
- Klarstellung und Begründung alternativer Vorschläge;
- Abstimmung über Erstentwurf und alle Alternativen.

Wenn notwendig:

- Feststellung von Diskussionspunkten und Dissens;
- Debattieren und Diskutieren;
- endgültige Abstimmung.

Das elektronisch basierte, formalisierte, schriftliche Abstimmungsverfahren unter Anwendung der Delphi-Technik wurde wie folgt durchgeführt:

- Präsentation der zu konsentierenden Empfehlungen und Abbildungen in einer schriftlichen Umfrage;
- schriftliche Abstimmung der Empfehlungen/Abbildungen.

Nach der Konsensuskonferenz wurde eine zusätzliche schriftliche Abstimmung durchgeführt. Es wurden die neu erarbeiteten Empfehlungen des Kapitels „Atmungsunterstützende Maßnahmen bei chronisch respiratorischer Insuffizienz“ schriftlich abgestimmt. Außerdem wurde eine neue Empfehlung zum Diagnostik-Algorithmus (aus Konsistenzgründen) sowie die Darstellung der medikamentösen Deeskalation im Algorithmus „Medikamentöse Langzeitbehandlung“ und als neue Empfehlung abgestimmt.

Mit den oben beschriebenen Vorgehensweisen wurde zur Formulierung aller Empfehlungen ein Konsens erreicht. Gemäß dem Methodenreport NVL [8] stehen den Mitgliedern der Leitliniengruppe bei Nichterreichen eines Konsenses verschiedene Optionen, wie z. B. das Einbringen eines Sondervotums zur Verfügung.

**Tabelle 5: Feststellung der Konsensstärke**

Klassifikation der Konsensstärke	
starker Konsens	Zustimmung von > 95% der Teilnehmer*innen
Konsens	Zustimmung von > 75-95% der Teilnehmer*innen
mehrheitliche Zustimmung	Zustimmung von > 50-75% der Teilnehmer*innen
kein Konsens	Zustimmung von < 50% der Teilnehmer*innen

Alle Texte, Tabellen, Abbildungen und Patientenblätter wurden während der Erstellung der Leitlinie in der Leitliniengruppe abgestimmt. Die Vorstände aller beteiligten Fachgesellschaften und Organisationen werden vor der Veröffentlichung der NVL um Zustimmung gebeten und im Impressum als Mitherausgeber aufgeführt.

## 9 Externe Begutachtung

Nach Fertigstellung der inhaltlichen Arbeiten an der 2. Auflage der NVL wurde die Konsultationsfassung auf der Internetseite des NVL-Programms ([www.leitlinien.de](http://www.leitlinien.de)) öffentlich zugänglich für sechs Wochen (vom 08.10.2020 bis 19.11.2020) zur Kommentierung bereitgestellt. Der Beginn dieses externen Begutachtungsverfahrens wurde auf den Internetseiten des ÄZQ und über eine Pressemitteilung an Presseverteiler bekanntgegeben.

Eingehende Kommentare wurden durch das ÄZQ gesammelt, aufbereitet und an die Leitliniengruppe weitergeleitet. In einer Telefonkonferenz am 18.01.2021 und im schriftlichen Umlauf wurden die eingegangenen Kommentare diskutiert und daraus resultierende Änderungen beraten. Inhaltliche Änderungen an den Empfehlungen ergaben sich nicht. Eingegangene Kommentare und entsprechende Beschlüsse mit ihren jeweiligen Begründungen sind im Anhang zu finden. Literatur, die daraufhin ergänzend in die Leitlinie aufgenommen wurde, ist bei der Recherchestrategie bzw. in den Evidenztabelle der jeweiligen Kapitel zu finden.

## 10 Redaktionelle Unabhängigkeit

Die Erstellung der NVL COPD erfolgt in redaktioneller Unabhängigkeit von den finanzierenden Trägern des NVL-Programms. Diese finanzieren die Koordination und methodische Unterstützung der Entwicklung der NVL. Die im Rahmen der Treffen anfallenden Reisekosten werden von den beteiligten Fachgesellschaften/Organisationen getragen, die Leitlinienautor\*innen arbeiten ehrenamtlich und ohne Honorar.

Bei der Erstellung der NVL COPD kommen folgende schützende Faktoren zur Anwendung, die den Einfluss möglicher Interessenkonflikte reduzieren:

- unabhängige Koordination der Leitlinie (ÄZQ);
- unabhängige Moderation (AWMF, ÄZQ);
- unabhängige Leitung von Arbeitsgruppen (ÄZQ);
- Evidenzaufbereitung durch Methodikerinnen (ÄZQ);
- Diskussion der Interessenerklärung und des Umgangs mit Interessenkonflikten in der Auftaktsitzung und Konsensuskonferenz;
- multidisziplinäre Leitliniengruppe, bei Abstimmungen hat jede Fachgesellschaft/Organisation eine Stimme;
- strukturierter Konsensprozess;
- festgeschriebene Leitlinienmethodik (von der Evidenz zur Empfehlung bzw. ein strukturiertes Vorgehen bei rein konsensbasierten Empfehlungen).

### Umgang mit Interessenkonflikten

Die Mitglieder der Leitliniengruppe haben etwaige Interessen im Zusammenhang mit der Erstellung der NVL COPD zu Beginn schriftlich erklärt und vor der Konsensuskonferenz aktualisiert (Formular siehe Anhang 1.1). Diese sind im Anhang 1.2 tabellarisch zusammengefasst. Die vollständigen Erklärungen sind im ÄZQ hinterlegt. Interessenkonflikte (IK) wurden im Rahmen der Diskussion der Leitliniengruppe sowohl in der Auftaktsitzung als auch in der Konsensuskonferenz offen thematisiert. Dabei fand die von der AWMF empfohlene Vorgehensweise zum Umgang mit Interessenkonflikten Anwendung [7,9,28]. Vor der Konsensuskonferenz wurden die IK von einem Gremium bewertet (CS/ÄZQ und MN/AWMF). Den Teilnehmenden der Konsensuskonferenz lagen während der Konferenz Listen vor, auf denen vermerkt war, wie die Interessenkonflikte der einzelnen Teilnehmer durch AWMF und ÄZQ bewertet wurden, siehe auch Anhang 1.3. Ausschlüsse aus der Leitliniengruppe wurden als nicht erforderlich angesehen.

Hatte eine Expertin beziehungsweise ein Experte im aktuellen oder in einem der drei vorausgegangenen Jahre Honorare von der Industrie für Vorträge, Berater- oder Gutachtertätigkeit oder Forschungsvorhaben angegeben, auch wenn diese keinen Themenbezug zur Leitlinie haben, jedoch insbesondere bei Verbindungen zu Herstellern oder Firmen, die Medikamente zur Tabakentwöhnung bzw. Bronchodilatoren und/oder Inhalationsgeräte herstellen, wurden die Interessen als „moderat“ eingeschätzt mit der Folge der Enthaltung bei themenbezogenen Abstimmungen.

Enthaltungen bei empfehlungsrelevanten Interessenkonflikten bei nicht-finanziellen Kategorien wurden nahegelegt. Wenn bezahlte Vortragstätigkeit einen geringen Finanzrahmen von 1 000 € insgesamt nicht überschritt und keine weiteren finanziellen Verbindungen vorlagen, wurde dies als geringer IK bewertet. In diesem Falle wurden gemäß AWMF-Regel Enthaltungen nicht als erforderlich angesehen.

Lag bei dem oder der Erstbenannten der Fachgesellschaft ein Interessenkonflikt vor, wurde die Empfehlung vom jeweiligen Vertreter – sofern anwesend und ohne Interessenkonflikte – abgestimmt.

Enthaltungen aufgrund eines Interessenkonfliktes in der Konsensuskonferenz und in der elektronischen Abstimmung sind im Anhang 1.4 dokumentiert.

## 11 Gültigkeit und Aktualisierung

### Gültigkeitsdauer und Fortschreibung

Die 2. Auflage der NVL COPD wurde am 25. Juni 2021 durch die Träger des NVL-Programms verabschiedet. Die Gültigkeit der NVL ist in der aktuellen Fassung der Leitlinie festgelegt. Eine fünfjährige Überarbeitung und Herausgabe – gemessen ab dem Zeitraum der schriftlichen Publikation – wird angestrebt.

### Verantwortlichkeit für die Aktualisierung

Für die Aktualisierung ist die NVL-Redaktion im ÄZQ verantwortlich. Im Falle neuer relevanter Erkenntnisse, welche die Überarbeitung der NVL erforderlich machen, erfolgt eine kurzfristige Aktualisierung und Information der Öffentlichkeit über die Internetseite des Programms für Nationale Versorgungsleitlinien ([www.leitlinien.de/copd](http://www.leitlinien.de/copd)) und die Internetseite des Leitlinienregisters der AWMF ([www.awmf.org/leitlinien/detail/II/nvl-003.html](http://www.awmf.org/leitlinien/detail/II/nvl-003.html)).

### Änderungsprotokoll

Notwendige Korrekturen, Änderungen oder redaktionelle Überarbeitungen an den konsentierten und im Internet veröffentlichten Texten werden im Impressum der Langfassung protokolliert. Um Änderungen transparent und nachvollziehbar zu machen, stehen im Archiv auf der Internetseite alle Versionen der NVL zur Verfügung: [www.leitlinien.de/nvl/copd/archiv](http://www.leitlinien.de/nvl/copd/archiv).

## 12 Anwendung und Verbreitung

### 12.1 Materialien und Formate

#### Langfassung

Die Langfassung wird als Druckversion (PDF-Format) herausgegeben und kann auf den Internetseiten des NVL-Programms kostenlos heruntergeladen werden. Zusätzlich steht sie dort auch im html-Format zur Verfügung. Hierdurch ist die NVL auf mobilen Endgeräten sehr gut lesbar. Die Empfehlungen werden als Übersicht dargestellt, so dass der Nutzer von der Empfehlung zum Hintergrundtext und weiter zur Evidenz navigieren kann. Technisch bedingt kann die Darstellung der html-Version von der PDF-Version abweichen – die Inhalte bleiben die gleichen.

#### Kurzfassung

Die Kurzfassung besteht aus den Empfehlungen, wichtigen Tabellen und den Algorithmen der Langfassung. Nach der Veröffentlichung der Langfassung wird sie redaktionell im ÄZQ erstellt und ist als Druckversion auf den Internetseiten des NVL-Programms frei verfügbar.

#### Flyer und Foliensatz

Zur besseren Verbreitung und Information von Ärzten wurde ein DIN-A5-Flyer mit den wichtigsten Änderungen und Kernbotschaften der NVL erstellt. Der Flyer kann kostengünstig in großem Umfang gedruckt und z. B. bei Kongressen oder Aktionstagen der Fachgesellschaften verteilt werden. Ergänzend wurde ein Foliensatz erstellt. Dieser kann für Vorträge und Präsentationen der Leitlinienautor\*innen auf Kongressen und/oder Veranstaltungen adaptiert und genutzt bzw. kostenlos von den Internetseiten heruntergeladen werden.

## Patientenblätter

Zur Implementierung der Empfehlungen der NVL bei spezifischen Entscheidungs- oder Informationssituationen wurden Patientenblätter erstellt. Diese sollen behandelnde Ärzt\*innen bei der Beratung der Patient\*innen unterstützen und zur gemeinsamen Entscheidungsfindung (Shared-Decision-Making) beitragen.

Themen für spezifische Entscheidungs- oder Informationssituationen wurden während des gesamten Leitlinienprozess gesammelt. Dabei wurden folgende Kriterien (modifiziert nach GKE-Manual der AWMF [29]) angewendet:

- Hinweise auf ein Versorgungsproblem;
- Umsetzbarkeit in der Praxis, Möglichkeit der Beeinflussung in der Praxis;
- geringes Risiko für Fehlsteuerung;
- erhöhter Kommunikationsbedarf mit Patient\*innen.

Zu diesen Themen wurden passende Patientenblätter gemäß den Anforderungen der „Guten Praxis Gesundheitsinformation“ [30] entwickelt. Die Patientenblätter wurden mit der Leitliniengruppe abgestimmt und werden als integraler Bestandteil der NVL COPD veröffentlicht. Evidenzgrundlage ist die Evidenzaufbereitung der NVL COPD (siehe Tabelle 6: Evidenzgrundlage der Patientenblätter).

**Tabelle 6: Evidenzgrundlage der Patientenblätter**

<b>COPD: Information für Angehörige</b>	<b>Literatur</b>
Tabelle 5: Risikofaktoren für die Entwicklung einer COPD	[31]
Empfehlung 3-1	[32,33]
Empfehlung 5-1 und Abbildung 4: Medikamentöse Langzeitbehandlung	[34–51]
Empfehlungen 5-4 - 5-7	[52–55], Expert*innenkonsens
Empfehlungen 4-1 - 4-9; 6-3	[56–88]
Empfehlungen 4-15; 4-18	Expert*innenkonsens
<b>COPD: Meine wichtigsten Medikamente</b>	<b>Literatur</b>
Empfehlung 5-1 und Abbildung 4: Medikamentöse Langzeitbehandlung	[34–51]
Empfehlungen 5-4 - 5-7	[52–55]
Empfehlung 5-8	[89–91]
<b>COPD: Warum Bewegung wichtig ist</b>	<b>Literatur</b>
Empfehlungen 4-1- 4-5; 6-3	[56–68]
<b>COPD: Brauche ich besondere Impfungen?</b>	<b>Literatur</b>
Empfehlung 5-9	[92–94]
<b>COPD: Spray, Pulver oder Vernebler – Welche Unterschiede gibt es?</b>	<b>Literatur</b>
Empfehlungen 5-4; 5-7; 7-11	Expert*innenkonsens
<b>COPD: Was tun bei unbekanntem Inhalier-Gerät</b>	<b>Literatur</b>
Empfehlungen 5-6; 7-9 - 7-11	[53–55]; Expert*innenkonsens

<b>COPD: Brauche ich Kortison?</b>	<b>Literatur</b>
Empfehlung 5-1 und Abbildung 4: Medikamentöse Langzeitbehandlung	[39–50,95–99]
<b>COPD: Warum alltägliche und seelische Belastungen wichtig werden können</b>	<b>Literatur</b>
Punkt 2.5.2 Angst und Depression	[100–103]
Punkt 4.7.1 Psychosomatische Einschätzung	[104–106]
<b>COPD: Warum Rauchstopp wichtig ist</b>	<b>Literatur</b>
Tabelle 5: Risikofaktoren für die Entwicklung einer COPD	[31] [31]
Empfehlung 3-1	[17,32,33,107,108]; Expert*innenkonsens
Empfehlungen 3-3; 3-4	[15,109]; Expert*innenkonsens
<b>COPD: Soll ich an einer Schulung teilnehmen?</b>	<b>Literatur</b>
Empfehlung 4-10	[110,111]
Empfehlung 4-11	[13]; Expert*innenkonsens

### Patientenleitlinie

Im Anschluss an die Veröffentlichung der Langfassung wird die Patientenleitlinie COPD aktualisiert. Die Patientenleitlinie übersetzt die ärztliche Leitlinie in eine allgemeinverständliche Sprache und stellt umfassend alles Wesentliche zum Krankheitsbild COPD dar. Die Patientenleitlinie wird vom ÄZQ mit dem Patientenvertreter und Mitgliedern der Leitliniengruppe gemäß einer festgeschriebenen Methodik (siehe [www.patienten-information.de/medien/methodik/erstellung-pll-mr-nvl-ol-2aufl-vers1.pdf](http://www.patienten-information.de/medien/methodik/erstellung-pll-mr-nvl-ol-2aufl-vers1.pdf)) erstellt und auf den Seiten des ÄZQ veröffentlicht ([www.leitlinien.de/copd](http://www.leitlinien.de/copd) bzw. [www.patienten-information.de/uebersicht/copd](http://www.patienten-information.de/uebersicht/copd)).

### Kurzinformationen

Im Anschluss an die Veröffentlichung der Langfassung wird die Kurzinformation für Patient\*innen aktualisiert. In der Kurzinformation werden die wichtigsten Informationen zum Krankheitsbild übersichtlich auf zwei DIN-A4-Seiten zusammengefasst. Die Kurzinformationen werden im ÄZQ nach einer festgeschriebenen Methodik (siehe [www.patienten-information.de/medien/methodik/aezq-kip-patienten-methodik-auf3.pdf](http://www.patienten-information.de/medien/methodik/aezq-kip-patienten-methodik-auf3.pdf)) erstellt und in den Sprachen Deutsch, Englisch, Französisch, Spanisch, Russisch, Türkisch und Arabisch herausgegeben ([www.leitlinien.de/copd](http://www.leitlinien.de/copd) bzw. [www.patienten-information.de/uebersicht/copd](http://www.patienten-information.de/uebersicht/copd)).

## 12.2 Implementierung und Öffentlichkeitsarbeit

Zur Verbreitung und Implementierung gibt es folgende Maßnahmen:

- Verbreitung über die Publikationsorgane und Kongressveranstaltungen der kooperierenden Fachgesellschaften und Organisationen (z. B. Verteilung der Flyer bei Kongressen);
- Informationen an Einrichtungen der gemeinsamen Selbstverwaltung und an Berufsorganisationen;
- Integration der NVL-Inhalte in bestehende Qualitätsmanagementsysteme, z. B. QEP® ([www.kbv.de/qep](http://www.kbv.de/qep)) oder KTQ® ([www.ktq.de](http://www.ktq.de));
- Unterstützung der Verbreitung der Patientenleitlinie durch die Patient\*innenorganisationen ([www.patienten-information.de/ueber-uns/wie-wir-arbeiten#selbsthilfe](http://www.patienten-information.de/ueber-uns/wie-wir-arbeiten#selbsthilfe)).

## 13 Evaluation

Eine Evaluation der NVL soll im Hinblick auf die Ziele des NVL-Programms erfolgen:

- Verbreitung von evidenzbasierten und formal konsentierten ärztlichen Empfehlungen zu versorgungsbereichsübergreifenden Vorgehensweisen für spezielle Erkrankungen;
- Verbreitung von NVL-basierten Qualitätsindikatoren, Patientenleitlinien und weiteren Patientenmaterialien;
- möglichst flächendeckende Implementierung der NVL-Empfehlungen;
- Berücksichtigung von NVL-Empfehlungen durch insbesondere strukturierte Behandlungsprogramme (DMP) sowie durch Verträge zur Integrierten Versorgung (IV);
- Berücksichtigung von NVL-Empfehlungen in der ärztlichen Aus-, Fort- und Weiterbildung und in Qualitätsmanagementsystemen.

## Tabellenverzeichnis

Tabelle 1: Vertreter*innen der Fachgesellschaften/Organisationen .....	7
Tabelle 2: Methodik, Redaktion und Moderation .....	11
Tabelle 3: Schema zur Graduierung von NVL-Empfehlungen, modifiziert nach [7,9] .....	15
Tabelle 4: Verfahren der Arbeitsgruppen, 2. Auflage .....	15
Tabelle 5: Feststellung der Konsensstärke.....	16
Tabelle 6: Evidenzgrundlage der Patientenblätter.....	19

## Anhang

### Anhang 1 Darstellung von Interessenkonflikten

#### Anhang 1.1 Formular zur Darlegung von Interessenkonflikten



### Erklärung von Interessen

NVL COPD

zu Händen

Ärztliches Zentrum für Qualität in der Medizin (ÄZQ)

#### Vorbemerkung

Die Erklärung von Interessen durch alle Mitglieder der Leitliniengruppe ist Voraussetzung für die Mitarbeit an einer NVL. Die Erklärung wird zu Beginn der Arbeit an der Leitlinie abgegeben und ggf. vor der Konsensfindung erneuert. In der Erklärung sollen alle Interessen aufgeführt werden - unabhängig davon, ob der/die Erklärende selbst darin einen thematischen Bezug zur Leitlinie oder einen Interessenkonflikt sieht. Die Erklärung betrifft das laufende Jahr und die drei Kalenderjahre davor. Die Leitliniengruppe diskutiert die abgegebenen Erklärungen dahingehend, bei welchen Fragestellungen der Leitlinie das professionelle Urteilsvermögen eines Mitglieds durch sekundäre Interessen beeinflusst sein könnte. Die Leitliniengruppe bewertet die erklärten Interessen und vereinbart Vorgehensweisen für den Umgang mit Interessenkonflikten.

Die Originale der Erklärungen verbleiben im ÄZQ. Die Inhalte der Erklärungen werden (ausgenommen die Höhe der Zuwendungen) im Leitlinienreport veröffentlicht. Ergänzend werden die Ergebnisse der Diskussion in der Leitliniengruppe zum Umgang mit Interessenkonflikten dargelegt.

#### Informationen zur Datenerhebung gemäß Artikel 13 DSGVO

Das ÄZQ erhebt Ihre Daten zum Zweck des o.g. Leitlinienvorhabens sowie zur Erfüllung des Methodenreports des NVL-Programms und des AWMF-Regelwerks. Die Datenerhebung und Datenverarbeitung sind für die Durchführung des Leitlinienvorhabens erforderlich und beruhen auf Artikel 6 Abs. 1 b) DSGVO. Eine Weitergabe der Daten an Dritte findet nur zum Zweck der Erfüllung des Methodenreports des NVL-Programms bzw. des AWMF Regelwerks statt. Die Daten werden gelöscht, sobald sie für den Zweck ihrer Verarbeitung nicht mehr erforderlich sind. Sie sind berechtigt, Auskunft der im Rahmen des Leitlinienvorhabens über Sie gespeicherten Daten zu beantragen sowie bei Unrichtigkeit der Daten die Berichtigung oder bei unzulässiger Datenspeicherung die Löschung der Daten zu fordern.





NVL COPD  
Erklärung von Interessen



<b>Name/Anschrift (Stempel)</b>	
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### 1 Direkte finanzielle Interessen

Haben Sie oder die Einrichtung, für die Sie tätig sind innerhalb des laufenden Jahres oder der 3 Kalenderjahre davor Zuwendungen erhalten von Unternehmen der Gesundheitswirtschaft (z. B. Arzneimittelindustrie, Medizinprodukteindustrie), industriellen Interessenverbänden, kommerziell orientierten Auftragsinstituten, Versicherungen/ Versicherungsträgern oder von öffentlichen Geldgebern (z. B. Ministerien), Körperschaften/Einrichtungen der Selbstverwaltung, Stiftungen, oder anderen Geldgebern?

Angaben zu den direkten finanziellen Interessen der Institution, für die Sie tätig sind, sind nur dann erforderlich, falls Sie persönlich verantwortlich für die Verwendung der Zuwendung sind.

Machen Sie bitte in folgender Tabelle zu allen zutreffenden Aspekten konkrete Angaben.

Art der Beziehung/ Tätigkeit	Name des Kooperationspartners	Zeitraum der Beziehung/Tätigkeit (MM.JJ-MM.JJ)	Themenbezug zur Leitlinie, z. B. Arzneimittel, Technologie etc.	Art der Zuwendung (Honorar, Drittmittel, geldwerte Vorteile*, Verkaufslizenz)	Höhe der Zuwendung† (< 1 000 €, < 10 000 €, < 50 000 €, < 100 000 €, > 100 000 €)	Empfänger (persönlich/ institutionell)
Berater-/ Gutachter-tätigkeit						

\* geldwerte Vorteile sind z. B. Personal- oder Sachmittel; Reisekosten, Teilnahmegebühren, Bewirtung im Rahmen von Veranstaltungen

† Die Angaben beziehen sich auf die Gesamtsumme über den angegebenen Zeitraum. Diese Angaben werden vertraulich behandelt und nicht veröffentlicht.

NVL COPD  
Erklärung von Interessen



Art der Beziehung/ Tätigkeit	Name des Kooperationspartners	Zeitraum der Beziehung/Tätigkeit (MM.JJ-MM.JJ)	Themenbezug zur Leitlinie, z. B. Arzneimittel, Technologie etc.	Art der Zuwendung (Honorar, Drittmittel, geldwerte Vorteile, Verkaufslizenz)	Höhe der Zuwendung <sup>†</sup> (< 1 000 €, < 10 000 €, < 50 000 €, < 100 000 €, > 100 000 €)	Empfänger (persönlich/ institutionell)
Mitarbeit in einem Wissenschaftlichen Beirat (advisory board)						
Vortrags-/oder Schulungs-tätigkeit						
Forschungsvorhaben/ Durchführung klinischer Studien						
Eigentümerinteressen (Patent, Urheberrecht, Aktienbesitz)						

\* Angaben zu Mischfonds sind nicht erforderlich

NVL COPD  
Erklärung von Interessen



## 2 Indirekte Interessen

Hier werden persönliche Beziehungen zu Interessenverbänden im Gesundheitswesen, „intellektuelle“, akademische und wissenschaftliche Interessen oder Standpunkte sowie Schwerpunkte klinischer Tätigkeiten/Einkommensquellen erfasst (innerhalb des laufenden Jahres oder der 3 Kalenderjahre davor). Hierunter fallen auch solche, die indirekt mit finanziellen Interessen verbunden sein können.

- Sind oder waren Sie in Wissenschaftlichen Fachgesellschaften, Berufsverbänden, Institutionen der Selbstverwaltung, Patientenselbsthilfegruppen, Verbraucherververtretungen oder anderen Verbänden aktiv? Wenn ja, in welcher Funktion?
- Können Sie Schwerpunkte Ihrer wissenschaftlichen und /oder klinischen Tätigkeiten benennen? Fühlen Sie sich bestimmten „Schulen“ zugehörig?
- Waren Sie an der inhaltlichen Gestaltung von Fortbildungen federführend beteiligt?
- Haben Sie enge persönliche Beziehungen zu einem Vertretungsberechtigten eines Unternehmens der Gesundheitswirtschaft?

Machen Sie bitte in folgender Tabelle zu allen zutreffenden Aspekten konkrete Angaben.

Art der Beziehung/ Tätigkeit	Namen/Schwerpunkte (bitte konkret benennen)	Zeitraum der Beziehung/Tätigkeit (MM.JJ-MM.JJ)	Themenbezug zur Leitlinie (Ja/Nein)
Mitgliedschaft/Funktion in Interessenverbänden			
Schwerpunkte wissen- schaftlicher Tätigkeiten, Pu- blikationen			

NVL COPD  
Erklärung von Interessen



Art der Beziehung/ Tätigkeit	Namen/Schwerpunkte (bitte konkret benennen)	Zeitraum der Beziehung/Tätigkeit (MM.JJ-MM.JJ)	Themenbezug zur Leitlinie (Ja/Nein)
Schwerpunkte klinischer Tätigkeiten			
Federführende Beteiligung an Fortbildungen/ Ausbildungsinstituten			
Enge persönliche Beziehungen zu einem Vertretungsberechtigten eines Unternehmens der Gesundheitswirtschaft			

### 3 Sonstige Interessen

Sehen Sie andere Aspekte oder Umstände, die von Dritten als einschränkend in Bezug auf Ihre Objektivität oder Unabhängigkeit wahrgenommen werden könnten?	
---	--

NVL COPD  
Erklärung von Interessen



#### 4 Arbeitgeber/Funktion

	Arbeitgeber/Institution	Position/Funktion in der Institution
Gegenwärtig		
Frühere Arbeitgeber im Zeitraum der Erklärung		

Ich erkläre hiermit nach bestem Wissen und Gewissen, dass ich alle mir derzeit bekannten Umstände aufgeführt habe, die gegebenenfalls zu einem persönlichen Interessenkonflikt bei der Erstellung der Leitlinie führen können. Ich erkläre weiterhin, dass ich die Angaben zur Höhe der Zuwendungen anderer Mitglieder in der Leitliniengruppe absolut vertraulich behandeln werde. Ich bin darüber informiert, dass alle Angaben (außer der Höhe der Zuwendungen) im Leitlinienreport der NVL veröffentlicht werden.

\_\_\_\_\_ Datum

\_\_\_\_\_ Unterschrift

Anhang 1.2 Übersicht Interessenkonflikterklärungen

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
	Berater-/Gutachtertätigkeit	Mitarbeit in einem Wissenschaftlichen Beirat (advisory board)	Vortrags-/ oder Schultätigkeit	Forschungsvorhaben/Durchführung klinischer Studien	Eigentümerinteressen (Patent, Urheberrecht, Aktienbesitz)	Mitgliedschaft/Funktion in Interessenverbänden	Schwerpunkte wissenschaftlicher Tätigkeiten, Publikationen	Schwerpunkte klinischer Tätigkeiten	Federführende Beteiligung an Fortbildungen /Ausbildungsinstituten	Enge persönliche Beziehungen zu einem Vertretungsberechtigten eines Unternehmens der Gesundheitswirtschaft	Sehen Sie andere Aspekte oder Umstände, die von Dritten als einschränkend in Bezug auf Ihre Objektivität oder Unabhängigkeit wahrgenommen werden könnten?	Gegenwärtiger Arbeitgeber und Funktion	Frühere Arbeitgeber und Funktion (im Zeitraum der Erklärung)
<b>Andreas, Prof. Dr. med. Stefan</b>	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Deutsche Forschungsgemeinschaft	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Boehringer; kontinuierlich; Honorar; persönlich - GSK; kontinuierlich; Honorar; persönlich - Novartis; kontinuierlich; Honorar; persönlich	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - AstraZeneca; 2017; Honorar; persönlich - Boehringer Ingelheim; kontinuierlich; Honorar ; persönlich - Chiesi; 2017; Honorar; persönlich - GSK; kontinuierlich; Honorar; persönlich - Novartis; kontinuierlich; Honorar; persönlich - Roche; kontinuierlich; Honorar; persönlich	Keine	Keine	<b>Themenbezug zur Leitlinie:</b> - Deutsche Gesellschaft Pneumologie; kontinuierlich - Lungentiftung; kontinuierlich - Deut. Gesell Schlafmed.; kontinuierlich - Hess. Onkologiegesellschaft; kontinuierlich - Aktionsbündnis Nichtrauchererschutz; kontinuierlich  Marburger Bund; kontinuierlich - Fellow DZL (Deutsches Zentrum Lungenforschung)	<b>Themenbezug zur Leitlinie:</b> - COPD; kontinuierlich - Kardiopulmonale Interaktion	- Pneumologie - COPD - Kardiopulmonale Interaktion	- Vorlesungen Universitätsmedizin Göttingen	Keine	Keine	Lungenfachklinik Immenhausen und Universitätsmedizin Göttingen; Ärztlicher Leiter	
<b>Batra, Prof. Dr. Anil</b>	Keine	Keine	<b>Themenbezug zur Leitlinie (Tabakentwöhnung):</b> - Forum f. Med. Fortbildungen; 2016-2019; Honorar; persönlich  <b>Themenbezug zur Leitlinie</b>	<b>Themenbezug zur Leitlinie (Studie zur Tabakentwöhnung):</b> - Deutsche Krebs-hilfe; 2016-2019; Drittmit-tel; Institution	Keine	<b>Themenbezug zur Leitlinie:</b> - Wissenschaftliche Aktionskreis Tabakentwöhnung(WAT) e. V.; schon vor 2016 - DG-Sucht; schon vor 2016 - DG-Suchtmedizin; schon vor	<b>Themenbezug zur Leitlinie:</b> - Tabakentwöhnung; schon vor 2016 - Grundlage der Tabakabhängigkeit; schon vor 2016 - Ganz allgemein: Suchtforschung und	<b>Themenbezug zur Leitlinie:</b> - Leitung der Sektion Suchtmedizin und Suchtforschung; seit 2008	<b>Themenbezug zur Leitlinie:</b> - Curriculum Tabakabhängigkeit der Bundesärztekammer; schon vor 2016 - Curriculum Verhaltenstherapie; schon vor 2016	Keine	"Klageinitiative Tabakentwöhnung": Finanzierung der Tabakentwöhnung soll von Kassen übernommen werden; Eigenes Raucherentwöhnung	Universitätsklinik Tübingen; Stellvertreter der Ärztlicher Direktor	

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13	
Art	Direkt					Indirekt								
			<p><b>(Curriculum Tabak):</b> - Ärztekammern; 2016-2019; Honorar; persönlich - Wissenstransfer; 2016-2018; Honorar; persönlich - Deutsche Psychologen Akademie; 2016-2019; Honorar; persönlich</p>	<p><b>Themenbezug zur Leitlinie (Entwicklung IRIS Beratungsplattform Tabak):</b> - BZgA; 2016-2019; Drittmittel; Institution</p> <p><b>Themenbezug zur Leitlinie (Entwicklung CSI Beratungsplattform Tabak):</b> - BMBF; 2016-2019; Drittmittel; Institution</p>		2016 - DGPPN; schon vor 2016	Suchttherapie; schon vor 2016					nungsprogramm "Nicht-raucherin 6 Wochen" mit Schulungen von Teilnehmern und eigenem Manual		
<b>Bausewein, Prof. Dr. med. Claudia, PhD, MSc</b>	<p><b>Themenbezug zur Leitlinie (S3 LL Palliativmedizin):</b> - Deutsche Krebshilfe; seit 2012; Drittmittel; institutionell</p>	Keine	<p><b>Themenbezug zur Leitlinie:</b> - Thema: Atemnot; Bayer Healthcare; 10/2015; Honorar; persönlich - Thema: Fortbildungen zu S3 LL Palliativmedizin; Nationale Gesundheitsakademie; seit 2015; Honorar; persönlich - diverse Themen; diverse Hospizvereine, Krankenhäuser; seit 2012; Honorar; persönlich - Thema: Palliativmedizin bei Lungenerkrankungen; Med Update GmbH; 2016; Honorar; persönlich</p>	<p><b>Themenbezug zur Leitlinie:</b> - <b>Thema:</b> Atemnot; BMBF (2x); seit 2014; Forschungsförderung; institutionell - Thema: Arzneimittelinformation; Dr. August und Anniesmüllerstiftung; Forschungsförderung; institutionell - Thema: Komplexität in der Palliativmedizin; Dt. Stifterverband; seit 2014; Forschungsförderung; institutionell - Mitwirkung an einer EU-geförderten Arzneimittelstudie zur Testung von Mirtazapin bei Atemnot (Förderung von 2019-2022)</p>	Keine	<p><b>Themenbezug zur Leitlinie:</b> - Deutsche Gesellschaft für Palliativmedizin für Palliativmedizin, Co-Leitung der S3 LL Palliativmedizin für Patienten mit nicht heilbaren Krebserkrankungen; seit 2012 - Deutsche Gesellschaft für Palliativmedizin, Sprecherin der AG LL; seit 2006</p> <p><b>Kein Themenbezug zur Leitlinie:</b> - Deutsche Gesellschaft für Palliativmedizin, Sprecherin der Landesvertretung Bayern; seit 2014; Schriftführerin, seit 2018</p>	<p><b>Themenbezug zur Leitlinie:</b> - Palliativmedizin für Patienten mit nicht-onkologischen Erkrankungen; seit 2005 - Management von Atemnot bei Patienten mit fortgeschrittenen Erkrankungen; seit 2005</p>	<p><b>Themenbezug zur Leitlinie:</b> - Palliativmedizinische Versorgung von Patienten mit fortgeschrittenen malignen und nicht-malignen Erkrankungen; seit 20 Jahren</p>	<p><b>Kein Themenbezug zur Leitlinie:</b> - Leiterin der Christophorus Akademie für Palliativmedizin, Palliativpflege und Hospizarbeit der Klinik für Palliativmedizin; seit 2012 - Leitung von Kursen zum Erwerb der Zusatzbezeichnung Palliativmedizin und anderen Fortbildungen zu Palliativmedizin; seit 2012</p>	Keine	Keine	Klinikum der Universität München; Klinikdirektorin, Lehrstuhlinhaberin	Keine	

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
<b>Críe, Prof. Dr. med. C.-P.</b>	Keine	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Chiesi; seit 2015; Honorar; persönlich - Böhringer; seit 2015; Honorar; persönlich - Novartis; seit 2015; Honorar; persönlich	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Berlin-Chemie; seit 2015; Honorar; persönlich - Böhringer; seit 2015; Honorar; persönlich - Novartis; seit 2015; Honorar; persönlich <b>Themenbezug zur Leitlinie (Diagnostik):</b> - Chiesi; 2017; Honorar; persönlich - TEVA; 2016-2017; Honorar; persönlich <b>Themenbezug zur Leitlinie (Beatmung):</b> - Res-Med; 2015-2017; Honorar; persönlich	Keine	Keine	<b>Themenbezug zur Leitlinie:</b> - Deutsche Atemwegsliga; Vorsitzender - Deutsche Gesellschaft für Pneumologie + Beatmungsmedizin; Mitglied - Deutsche interdisziplinäre Gesellschaft für außerklinische Beatmung; Mitglied	<b>Themenbezug zur Leitlinie:</b> - Mitglied der Leitlinien-gruppe der Atemwegsliga und DGB zu den Leitlinien Asthma und COPD	<b>Kein Themenbezug zur Leitlinie:</b> - Chefarzt einer pneumolog. Abteilung	Keine	Keine	Keine	Evangelisches Krankenhaus Göttingen-Weende; ärztliche Tätigkeiten	Keine
<b>Dalhoff, Prof. Dr. med. Klaus</b>	Keine	Keine	<b>Themenbezug zur Leitlinie:</b> - Thema: Antibiotika; Bayer-Vital; 10/2017; Honorar; persönlich - Thema: Allergische Alveolitis; Gilead; 12/2015; Honorar; institutionell <b>Themenbezug zur Leitlinie (Impfungen):</b> - Novartis; 11/2014; Honorar; persönlich - Pfizer; 05/2014; Honorar; persönlich	<b>Themenbezug zur Leitlinie:</b> - Thema: Pneumol. Onkologie/Infektologie; Multicenterstudien als Leiter des Studienzentrums der eigenen Klinik; Keine persönliche Zuwendung	Keine	<b>Themenbezug zur Leitlinie:</b> - DGP - AkdÄ - ERS (Eur Respir Society) - ATS (Am Thoracic Society) <b>Kein Themenbezug zur Leitlinie:</b> - DGIM - DGI	<b>Kein Themenbezug zur Leitlinie:</b> - Pneumonie - Deutsches Zentrum für Lungenforschung (DZL)	- Pneumologie - Infektologie	Keine	Keine	Keine	UKSH; Stv. Klinikdirektor	



Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
de Roux, Dr. med. Andrés		<b>Themenbezug zur Leitlinie:</b> - Boehringer; 2016; COPD; Honorar; persönlich	<b>Themenbezug zur Leitlinie:</b> - Mundipharma; 2016; Produkte Pneumologie; Honorar; persönlich - Astra; 2016; COPD; Honorar; persönlich - Novartis; 2015; COPD; Honorar; persönlich - Berlin Chemie; 2015+2016; Asthma, COPD; Honorar; persönlich - Bayer; 2016; Bronchieksten; Honorar; persönlich	<b>Themenbezug zur Leitlinie:</b> - Bayer; seit 2010; Finanzierung des Prognosisregisters; Drittmittel; Prognosis, Bronchieksten, Register ( ich bin Mitglied der Steuerungsgruppe, Anträge wurden über die MHH Hannover gestellt)	Keine	<b>Kein Themenbezug zur Leitlinie:</b> - Vorstandmitglied im BdP; 2017-2018 - Vorsitzender des LvBB (Berlin-Brandenburg); seit 2/18 - Berufsverbandsvorsitzender der Berlin-Brandenburger Pneumologen e. V.; seit 2016 KV - Berlin; Mitglied der Vertreterversammlung, seit 2018	<b>Themenbezug zur Leitlinie:</b> - Schutimpfungen, COPD; seit 1999 - Brochieksten (PROGNOSIS REGISTER); 2017-2020	<b>Themenbezug zur Leitlinie:</b> - Lungenfacharzt in der Niederlassung; seit 2008	<b>Themenbezug zur Leitlinie:</b> - Qualitätszirkel der Berliner Pneumologen; seit 2016	Keine	Keine	Praxisinhaber; Chef	Keine
Dreher, Michael Prof. Dr. med.	Keine	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Böhringer; seit 2014; Honorar; persönlich - Novartis; seit 2016; Honorar; persönlich <b>Themenbezug zur Leitlinie (Beatmung):</b> - Res-Med; seit 2013; Honorar; persönlich - Respirationics; seit 2013; Honorar; persönlich	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Böhringer; seit 2013; Honorar; persönlich - Novartis; seit 2013; Honorar; persönlich - Chiesi; seit 2017; Honorar; persönlich <b>Themenbezug zur Leitlinie (Beatmung):</b> - Res-Med; seit 2010; Honorar; persönlich - Respirationics; seit 2010; Honorar; persönlich	<b>Themenbezug zur Leitlinie (Beatmung):</b> - Res-Med; 2015-2017; Drittmittel; institutionell	Keine	<b>Themenbezug zur Leitlinie:</b> - DGP, Vertreter der DGp in der FERS; seit 2015 - Vorstandsmitglied der DIGAB; 2013-2017 - Secretary der Group 2.02 der ERS - Chair der Group 2.02 der ERS	<b>Themenbezug zur Leitlinie:</b> - Nichtinvasive Beatmung; seit 2005 - Pathophysiologie der COPD; seit 2005 - Inhalationstechnik bei COPD; seit 2017	Keine	Keine	Keine	Keine	Uniklinik RWTH Aachen; Leiter der Sektion Pneumologie	Universitätsklinikum Freiburg; Assistenz-, Fach- und Oberarzt der Abteilung für Pneumologie
Eggeling, Dr. med. Stephan	Keine	Keine	Keine	Keine	Keine	Keine	Keine	Keine	<b>Kein Themenbezug zur Leitlinie:</b> - Leitlinie Pneumothorax D6 TH; 2016 - 2018	Keine	Keine	Vivantes GmbH; Chef- arzt Klinik Für Thoraxchirurgie	Keine

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13	
Art	Direkt					Indirekt								
Freitag, Christiane, B.A.	Keine	Keine	Keine	Keine	Keine	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Deutsche Gesellschaft für Pflegewissenschaft, Mitglied; 08.2017 bis auf weiteres</li> </ul> <p><b>Kein Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- DRK Hamm OV Bockum-Hövel, Gemeinschaft Bockum-Hövel; 09.1989 bis auf weiteres</li> <li>- Ausbilder Sanitätsdienst/ Erste Hilfe im DRK KV Hamm; 04.2014 bis auf weiteres</li> <li>- Medizinproduktbeauftragte/ Hygienebeauftragte im DRK OV Bockum Hövel; 10.2011 bis auf weiteres</li> <li>- Rettungssanitäterin im DRK; 07.2007 bis auf weiteres</li> </ul>	Keine	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Gesundheits- u. Krankenpflegerin im UKM Herz-u. Thoraxchirurgie; 05.2001- bis auf weiteres</li> <li>- QMB Pflege Herz-Thoraxchirurgie UKM; 03.2012 bis auf weiteres</li> </ul> <p><b>Kein Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Medizinproduktbeauftragte Pflege Herz-u. Thoraxchirurgie UKM; 01.2002 bis auf weiteres</li> </ul>	Keine	Keine	Keine	Keine	Universitätsklinikum Münster, Department für Herz- Thoraxchirurgie; Stellv. Stationsleitung	
Freitag, Prof. Dr. med. Michael, MPH	Keine	<p><b>Themenbezug zur Leitlinie (Krankenversicherung):</b></p> <ul style="list-style-type: none"> <li>- DAK Gesundheit; 2007-aktuell; Honorar; persönlich</li> </ul>	<p><b>Themenbezug zur Leitlinie (Fortbildung):</b></p> <ul style="list-style-type: none"> <li>- Ärztekammer Niedersachsen; 2015-aktuell; Honorar; persönlich</li> </ul>	<p><b>Kein Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- G-BA (Innovationsfonds); 07/2017-aktuell; Drittmittel; institutionell</li> </ul>	Keine	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Mitglied der Ständigen Leitlinienkommission der DEGAM; seit 2007</li> <li>- Mitglied beim Deutschen Hausärzteverband</li> </ul>	- Borreliose, Diabetes, Multimorbidität	- Allgemeinmedizin/Primärversorgung	Keine	Keine	Keine	Carl von Ossietzky-Universität Oldenburg (seit 02/2015); Universitätsprofessor für Allgemeinmedizin	Universitätsklinikum Jena (bis 01/2015); Wiss. Mitarbeiter	
Frohnhofen, PD Dr. med. Helmut	Keine	<p><b>Themenbezug zur Leitlinie (Osteoporose):</b></p> <ul style="list-style-type: none"> <li>- Amgen; seit 2012; Honorar;</li> </ul>	<p><b>Themenbezug zur Leitlinie (Osteoporose):</b></p> <ul style="list-style-type: none"> <li>- Amgen; seit 2012; Honorar;</li> </ul>	Keine	Bayer AG; persönlich	Keine	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Schlafstörungen; Schlafapnoe; Demenz;</li> </ul>	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Leitender Krankenhausarzt; 1999</li> </ul>	Keine	Keine	Keine	Alfried-Krupp-Krankenhaus, Essen; Abteilungsarzt Altersmedizin	Kliniken Essen Mitte; Direktor Zentrum für Altersmedizin	

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
		persönlich - Heel; 2017; Honorar; persönlich	persönlich - Lilly; 2017; Honorar; persönlich				COPD im Alter; seit 2007						
<b>Gogol, Dr. med. Manfred</b>	<b>Kein Themenbezug zur Leitlinie:</b> - 7. Altenberichts-kommission; 2015-16; Honorar; persönlich - AOK Baden-Württemberg; 2014-16; Honorar; persönlich - IQTiQ; 2017; Honorar; persönlich - IQWiG; 2014-16; Honorar; persönlich - Commonwealth Fund; 2017; Honorar; persönlich	Keine	<b>Themenbezug zur Leitlinie:</b> - Novartis 3 x; 2015-16; Honorar; persönlich  <b>Kein Themenbezug zur Leitlinie:</b> - Pfizer 5 x; 2014-17; Honorar; persönlich - Astellas 1 x; 2016; Honorar; persönlich - Osuka 1 x; 2015; Honorar; persönlich - BMS; 2017; Honorar; persönlich	<b>Themenbezug zur Leitlinie:</b> - COSYCO-NET; 2014-17; Drittmittel; institutionell	Keine	<b>Themenbezug zur Leitlinie:</b> - Mitglied DGP und ERS; fortlaufend - Mitglied DGG, DGGG, DGIM, BDI, AGS, BGS, GSA, AAA, AAAS; fortlaufend  <b>Kein Themenbezug zur Leitlinie:</b> - Schatzmeister AWMF; 05/17 - Ich war Delegierter für die Geriatrie in der S3-LL Demenzen sowie Teilnehmer der Gründungssitzung des Steuerkreises der geplanten LL Eingeschränkte Einwilligungsfähigkeit 2016; 2014-16 - Ich bin Treasurer in der Fachgesellschaft Geriatric Medicines Society (GMS). - Ich bin Vice chair der Special Interest Group WE-SHARE (The World Explores Space Health and Aging Research) der Gerontological Society of America (GSA); fortlaufend - Ich bin Fellow	<b>Themenbezug zur Leitlinie:</b> - Geriatrie und Gerontologie; fortlaufend - COPD; fortlaufend  <b>Kein Themenbezug zur Leitlinie:</b> - Gemeinsam Klug Entscheiden; fortlaufend - Kognition; fortlaufend	<b>Themenbezug zur Leitlinie:</b> - Chefarzt; bis 30.06.2017 (s. "Früherer Arbeitgeber")	Keine	Keine	Keine	Seit 01.07.2017 freiberufliche Tätigkeit in Form von Gutachter-tätigkeit für Gerichte und Schlichtungsstelle für Arzthauptpflichtfragen.	Bis 30.06.2017 Chefarzt der Klinik für Geriatrie am Krankenhaus Lindenbrunn, 31863 Coppenbrügge; Chefarzt

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13	
Art	Direkt					Indirekt								
						der GSA seit 2016. - Ich bin Mitglied der Special Interest Group Geroscience der Gerontological Society of America (GSA); seit 2015 - Ich bin Mitglied der Special Interest Group Geroscience der American Geriatrics Society (AGS); seit 2016. - Ich bin Mitglied der Specialinterest Group Healthy Aging der AGS; seit 2017. - Ich bin Mitglied des Herausbergremiums der Zeitschrift für Gerontologie und Geriatrie (Z Gerontol Geriatr); seit 2010/11. - Ich bin Mitglied des Herausbergremiums der Zeitschrift European Geriatric Medicine (Eur Geriatr Med). - Ich war Präsident der Deutschen Gesellschaft für Gerontologie und Geriatrie (DGGG); bis 09/2014 - Ich bin Delegierter der Deutschen Gesellschaft für Gerontologie								

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13		
Art	Direkt					Indirekt									
						und Geriatrie (DGGG) für die AWMF; seit ca.2004 - Ich bin Stellvertretender Vorsitzender der Alzheimer-Gesellschaft Hameln-Pyrmont und Niedersachsen. - Ich war Mandatsträger für die Deutsche Gesellschaft für Geriatrie (OGG) und die Deutsche Gesellschaft für Gerontologie und Geriatrie (OGGG) bei der BÄK für die Novellierung der GOÄ. - Ich bin Mitglied der Kommission Gemeinsam Klug Entscheiden der AWMF. Ich bin Mitglied der Kommission Klug Entscheiden der DGIM für die Geriatrie. - Ich Mitglied im International Choosing Wisely Roundable seit 2014 und vertrete dort mit D. Klemperer Deutschland. - Ich bin Mitglied des Medikamenten-Bewertungs-Board FORTA (Fit for The Aged).									

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
<b>Groneberg, Prof. Dr. David</b>	Keine	<p><b>Themenbezug zur Leitlinie (Editor):</b></p> <ul style="list-style-type: none"> <li>- Springer Verlag; 2015-2018; Honorar; Groneberg</li> <li>- Journal of Occupational Medicine; 2016-2018; Honorar; Groneberg</li> </ul> <p><b>Themenbezug zur Leitlinie (Beirat):</b></p> <ul style="list-style-type: none"> <li>- Europäische Forschungsvereinigung; 2015-2018; Aufwandsentschädigung; Groneberg</li> </ul>	Kein Themenbezug zur Leitlinie: - Landesärztekammer Hessen; 2015-2018; Groneberg	Kein Themenbezug zur Leitlinie: - UBS Optimus Foundation; 2016; Drittmittel; Goethe-Universität - Bundesministerium für Bildung und Forschung; 2017; Drittmittel; Goethe-Universität - Berufsgenossenschaft Gesundheit; 2015-2018; Drittmittel; Goethe-Universität	Kein Themenbezug zur Leitlinie: - Europäischer Sozialfond; 2015; Drittmittel; Goethe-Universität - Europäische Forschungsvereinigung; 2015-2017; Drittmittel; Goethe-Universität	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Deutsche Gesellschaft für Arbeitsmedizin und Umweltmedizin; 2015-2018</li> <li>- Deutsche Gesellschaft für Nikotin und Tabakforschung; 2014-2018</li> </ul>	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Arbeitsmedizin, Umweltmedizin, Pneumologie, Allergologie; 2015-2018</li> <li>- Versorgungsforschung, Public Health; 2014-2018</li> </ul>	Keine	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Landesärztekammer Hessen - Weiterbildung Arbeitsmedizin</li> </ul>	Keine	Keine	Goethe-Universität Frankfurt am Main, Institut für Arbeitsmedizin, Sozialmedizin, Umweltmedizin; Direktor	
<b>Hellmann, Dr. Andreas</b>	<p><b>Themenbezug zur Leitlinie (Mitglied VV, Ausschüsse):</b></p> <ul style="list-style-type: none"> <li>- KBV; permanent; Entschädigungen; persönlich</li> <li>- KVB; permanent; Entschädigungen; persönlich</li> <li>- Thema: Delegierter Ärztetag; BLÄK; permanent; Entschädigungen; persönlich</li> <li>- Thema: Vorstand Akademie, Delegierter Ärztetag; BÄK; permanent; Entschädigungen; persönlich</li> <li>- Thema: ...; medInfo; permanent; Honorar; persönlich</li> </ul>	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Thema: Versorgungsforschung; WIN-PNEU; permanent; Entschädigung, Praxisausfall; persönlich</li> <li>- Thema: advisory board; Dänisches Konsulat; 25.2.2015; Honorar</li> </ul>	<p><b>Themenbezug zur Leitlinie (Schulung von MFA bez. Allergologe):</b></p> <ul style="list-style-type: none"> <li>- Allergopharma; 25.02.2017; Honorar; persönlich</li> <li>- Allergopharma; 10.06.2017 Honorar; persönlich</li> <li>- Allergopharma; 15.07.2017; Honorar; persönlich</li> </ul> <p><b>Themenbezug zur Leitlinie (Vortrag):</b></p> <ul style="list-style-type: none"> <li>- Novartis; 01.02.2015; persönlich</li> </ul>	<p><b>Themenbezug zur Leitlinie (Daccord Studie):</b></p> <ul style="list-style-type: none"> <li>- Institut für Lungenforschung; 2017; Honorar; Praxis</li> </ul>	Keine	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Berufsverband der Pneumologen Bayern, Ehrenvorsitz; permanent</li> <li>- Deutsche Gesellschaft für Pneumologie, Mitglied; permanent</li> <li>- DFFP, stellv. Vorsitzender; permanent</li> <li>- Pneumomed e.G., Vorstand; permanent</li> <li>- Kein Themenbezug zur Leitlinie:</li> <li>- BD Internisten, Mitglied; permanent</li> <li>- Bundesverband der Belegärzte, stellv. Vorsitz; permanent</li> </ul>	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Versorgungsforschung; permanent</li> </ul>	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Praxis; permanent</li> </ul>	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Pneumologische Schlaglichter; 2015-2017</li> <li>- Pneumologische Praxistage; 2015-2017</li> </ul>	Keine	Keine	selbstständig, Praxis; Praxisleiter	

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
<b>Heister, Dr. med. Elisabeth</b>	keine, aber angestellt bei DRV - RLP; seit 01.12.2017; Gutachter-Ärztin	Keine	<b>Themenbezug zur Leitlinie: (Innere Medizin; Ergotherapie; Ergotherapie):</b> - Lehrfähigkeit; seit 2000; Dozentenonorar; persönlich	Keine	Keine	- Akademie für Ethik in der Medizin; Mitglied - DGNR Deutsche Gesellschaft für Neuro. Reha.; Mitglied - DGG Deutsche Gesellschaft für Geriatrie; Mitglied - BDI Bund Deutscher Internisten; Mitglied - Berufsverband der Ärzte für Physikalische u. Rehabilitative Medizin; Mitglied	Keine	-Neurologische Frührehabilitation; seit 1998 bis 11/2017 -Stat. Reha, Neurologie, Innere Medizin, Orthopädie, 1990-1998	- Klinisches Ethik Komitee / AK Ethik, Westpfalz-Klinikum GmbH; 2000 bis 11/2017	Keine	Keine	Westpfalz-Klinikum GmbH bis 30.11.2017; Fachärztin ab 01.12.2017 DRV Rheinland Pfalz; Gutachterärztin	-Univ. Freiburg, Institut für Geschichte der Medizin; 1987-1990; wissenschaftliche Angestellte - LVA Baden; Stationsärztin; 1990-1998
<b>Hepner, Prof. Dr. med. Hans Jürgen</b>	Keine	<b>Kein Themenbezug zur Leitlinie:</b> - Pfizer Pharma; 07.16-01.17; Honorar; institutionell	<b>Kein Themenbezug zur Leitlinie:</b> - Pfizer Pharma; 2014-2017; Honorar; institutionell - Bayer Healthcare; 2014-2017; Honorar; institutionell - Sanofi Pharma; 2014-2017; Honorar; institutionell - Omnicell; 05.2015; Honorar; institutionell	<b>Kein Themenbezug zur Leitlinie:</b> - Robert-Bosch-Stiftung; 08.15-02.17; Studien-geld; institutionell	Keine	<b>Themenbezug zur Leitlinie:</b> - Deutsche Gesellschaft für Geriatrie; 01.07 bis heute	<b>Themenbezug zur Leitlinie:</b> - Infektion, Sepsis, Beatmung, in der Geriatrie; bis heute	<b>Themenbezug zur Leitlinie:</b> - Geriatrie; bis heute	Keine	Keine	Keine	Helios Klinikum Schwelm; Chef- arzt Universität Witten/Herdecke; Lehrstuhlinhaber Geriatrie	
<b>Hering, Dr. med. Thomas</b>	<b>Themenbezug zur Leitlinie (COPD/Asthma):</b> - Berlin-Chemie; laufend; Honorar; persönlich  <b>Themenbezug zur Leitlinie (Asthma):</b> - GSK; 2019;	<b>Themenbezug zur Leitlinie (Asthma):</b> - Sanofi; 2018-2019; Honorar; persönlich  <b>Themenbezug zur Leitlinie (COPD):</b> - GSK; 2019; Honorar; persönlich	<b>Themenbezug zur Leitlinie (COPD/Asthma):</b> - Berlin-Chemie; laufend; Honorar; persönlich	Keine	Keine	<b>Themenbezug zur Leitlinie:</b> - Bundesverband der Pneumologen (BdP); Beauftragter für die Tabak-Entwöhnung; laufend - WAT (Wissenschaftlicher Aktionskreis Ta-	<b>Themenbezug zur Leitlinie:</b> - Tabak-Risiken und Tabakentwöhnung - Asthma und COPD	<b>Themenbezug zur Leitlinie:</b> - Lungenfacharzt in eigener Praxis	Keine	Keine	Keine	eigene Praxis; Leitung	Keine

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
	Honorar; persönlich - Sanofi; laufend; Honorar; persönlich  <b>Themenbezug zur Leitlinie (Tabakabhängigkeit):</b> - Pfizer; laufend; Honorar; persönlich					bakentwöhnung); Delegierter des BdP; laufend							
<b>Heußel, Prof. Dr. med. Claus Peter</b>	- Pfizer; 2008-2014 - Boehringer Ingelheim; 2010-2014 - Novartis; 2010, 2012, 2014 - Gilead; 2011-2015 - Intermune; 2013-2014 - Fresenius; 2013, 2014	Keine	- Gilead; 2008-2014 - MSD; 2009-2014 - Pfizer; 2010-2014 - Intermune; 2011-2014 - Novartis; 2013-2016 - Basilea; 2015, 2016 - Bayer; 2016	- Siemens; 2012-2014 - Pfizer; 2012-2014 - Boehringer Ingelheim; 2014 - Deutsches Lungenforschungszentrum	- Aktienbesitz in der Medizinindustrie: GSK Patent: Method and Device For Representing the Microstructure of the Lungs. IPC8 Class: AA61B5055FI, PAN: 20080208038, Inventors: W Schreiber, U Wolf, AW Scholz, CP Heussel	- Mitglied im Deutschen Lungenforschungszentrum - Mitglied in der Arbeitsgemeinschaft Thoraxdiagnostik in der deutschen Röntgengesellschaft: - Leitlinien: Lungenkarzinom, Mesotheliom, COPD, Screening Lungenkarzinom, CT und MR-Bildgebung des Thorax, Pneumonie, HAP - Berater für E-CIL-3, ECCMID, E-ORTC/MSG - Guideline for diagnosis of infections in immunocompromized hosts - Gründungsmitglied der Arbeitsgemeinschaft Infektionen der Hämatologie/ Onkologie der DGHO - Guideline for diagnosis of in-	Mitherausgeber „Medizinische Klinik, Intensivmedizin und Notfallmedizin“, Dr. Dietrich Steinkopff (Springer Verlag)	Keine	Keine	Keine	Keine	Thoraxklinik am Universitätsklinikum Heidelberg Röntgenstraße 1 69126 Heidelberg; Chefarzt der Diagnostischen und Interventionellen Radiologie mit Nuklearmedizin	



Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
						fections in immunocompromized hosts - Fakultätsmitglied der European Society of Thoracic Radiology (ESTI) - Fakultätsmitglied der European Respiratory Society (ERS) - Mitglied der EIBALL (European Imaging Biomarkers Alliance)							
<b>Kauczor, Prof. Dr. med. Hans-Ulrich</b>	Keine	Keine	<b>Themenbezug zur Leitlinie (Technologie):</b> - Siemens, Philips; 2014-2017; Honorar; persönlich - Boehringer Ingelheim; 2014-2017; Honorar; persönlich - Glaxo SmithKline; 2014-2017; Honorar; persönlich - Novartis; 2014-2017; Honorar; persönlich - AstraZeneca; 2014-2017; Honorar; persönlich  <b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Bracco; 2016; Honorar; persönlich	<b>Themenbezug zur Leitlinie:</b> - Thema: Technologie; Siemens; 2014-2017; Drittmittel, geldwerte Vorteile; institutionell - Thema: Arzneimittel; Bayer; 2014-2017; geldwerte Vorteile; institutionell	Keine	<b>Kein Themenbezug zur Leitlinie:</b> - Deutsche Röntgengesellschaft; 2014-2017 - Europäische Röntgengesellschaft; 2014-2017	<b>Themenbezug zur Leitlinie:</b> - Thoraxradiologie; 2014-2017	<b>Kein Themenbezug zur Leitlinie:</b> - Onkoradiologie; 2014-2017	Keine	Keine	Keine	Universitätsklinik Heidelberg, Land Baden-Württemberg; Ärztlicher Direktor	
<b>Kaufmann, Jan</b>	Keine	Keine	<b>Kein Themenbezug zur Leitlinie:</b> - Hochschule Fresenius;	Keine	Keine	Themenbezug zur Leitlinie: - AG-Atemphysiotherapie/	<b>Themenbezug zur Leitlinie:</b> - Körperliches Training und	<b>Themenbezug zur Leitlinie:</b> - Rehabilitation bei pneumolo-	<b>Themenbezug zur Leitlinie:</b> - Fortbildungsreihe "Atemphysiotherapie"	Keine	Keine	Therapie- und Rehabilitationszentrum Baumgarten am Ochsenzoll GmbH,	Atem-Reha GmbH, Jungestr.10, 20535

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13	
Art	Direkt					Indirekt								
			01/2014-heute; Honorar; persönlich			Deutscher Verband für Physiotherapie (ZVK) e. V.; 01/2010-heute - Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin e. V.; 01/2006-heute - Beisitz im Vorstand der "AG Lungensport in Deutschland e. V."  Kein Themenbezug zur Leitlinie: - Buteyko Deutschland - Arbeitsgemeinschaft von AtemlehrerInnen und Förderern e. V.; 04/2011-heute	Atemphysiotherapie bei pneumologischen Erkrankungen	gischen Erkrankungen; 01/2003-heute	der AG-Atemphysiotherapie; 01/2015-heute				Langenhorner Chaussee 623, 22419 Hamburg	Hamburg; Leitender Physiotherapeut  RehaCentrum Hamburg, Martinstr. 66, 20251 Hamburg
<b>Klose, Dr. Petra, M.A.</b>	Keine	Keine	Keine	Keine	Keine	<b>evtl. Themenbezug zur Leitlinie:</b> - Gesellschaft für Phytotherapie	<b>Kein Themenbezug zur Leitlinie:</b> - Naturheilkundliche Forschung	Keine	Keine	Keine	Keine	Kliniken Essen-Mitte		
<b>Knoll, Dr. med. Katrin</b>	Keine	Keine	<b>Kein Themenbezug zur Leitlinie:</b> - Akademie des EGZB; Vortrag und Tutorentätigkeit; Honorar für Vortrag; persönlich <b>Teilweise Themenbezug zur Leitlinie:</b> - Berlin Chemie 2019 (1x); Vortrag "Diabetes im Alter"; Honorar; persönlich	Keine	Keine	<b>Kein Themenbezug zur Leitlinie:</b> - Mitglied im Marburger Bund (passiv); seit 2004 - Mitglied der DGGG (passiv); seit 2017 - Mitglied im Berufsverband Deutscher Internisten (BDI), passiv; seit 2016	Keine	<b>teilweise Themenbezug zur Leitlinie:</b> - geriatrische, frührehabilitative Komplexbehandlung; seit 2016	Keine	Keine	Keine	Vivantes Humboldt Klinikum; Innere Medizin - Geriatrie; Chefärztin	Ev. Geriatriezentrum Berlin; Oberärztin	

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
<b>Köhler, Dr. med. Michael</b>	Keine	Keine	Keine	Keine	Keine	<b>Themenbezug zur Leitlinie:</b> - Deutsche Patientenliga Atemwegserkrankungen e. V. - DPLA; seit 2010 Vorsitzender - Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin e. V.; seit ca. 25 Jahren Mitglied - Deutsche Atemwegsliga e. V.; seit ca. 30 Jahren Mitglied - Deutsche Lungenstiftung e. V.; seit ca. 25 Jahren Mitglied - AG Lungensport in Deutschland e. V.; seit ca. 30 Jahren Mitglied - Deutscher Lungentag e. V.; seit ca. 20 Jahren Mitglied	<b>Themenbezug zur Leitlinie:</b> - Deutsche Sauerstoffliga und Beatmungsmedizin LOT e. V.; seit c.. 10 Jahren Mitglied und seit 2017 Besitzer - Redaktionsleiter der Patientenzeitschrift "Luftpost"; seit Ende 2014	Keine	Keine	Keine	Keine	Sascha Piprek, SP Medienservice, Köln; Redaktionsleiter der "Luftpost"	
<b>Kotz, Univ.-Prof. Dr. Daniel, PhD, MSc, MPH</b>	Keine	Keine	Keine	<b>Themenbezug zur Leitlinie:</b> - Bundesministerium für Gesundheit; 03.2019-02.2022; Thema: DERBA-II Studie: Repräsentative Befragung der deutschen Bevölkerung zum Konsum von Tabak	Keine	<b>Themenbezug zur Leitlinie:</b> - Society for Research on Nicotine and Tobacco (SRNT); Vorstandsmitglied und aktueller Präsident; seit 09.2017 - WAT; Mitglied; seit 03.2019	<b>Themenbezug zur Leitlinie:</b> - Leiter des Schwerpunkts Suchtforschung und klinische Epidemiologie am Institut für Allgemeinmedizin, Medizinische Fakultät der Heinrich-Heine-Universität Düsseldorf; seit 12.2014 - Senior Editor	Keine	Keine	Keine	Keine	Heinrich-Heine-Universität Düsseldorf; Professor für Allgemeinmedizin mit Schwerpunkt Suchtforschung und klinische Epidemiologie	Keine

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13	
Art	Direkt					Indirekt								
				<p>und E-Inhalationsprodukten (DRKS00011322); Drittmittel; institutionell - Bundesministerium für Gesundheit; 03.2017-02.2020; Drittmittel; Thema: ABC-II Studie: Randomisierter kontrollierter Trial zum Training von Hausärzten in der leitliniengerechten Kurzberatung zur Tabakentwöhnung (DRKS00012786); institutionell - European Union Horizon 2020 (HCO-06-2015); 11.2015-11.2019; Thema: Tobacco cessation within tuberculosis programmes: a "real world" solution for countries with dual burden of diseases (IS-RCTN43811467); Drittmittel; institutionell - Ministerium für Innovation, Wissenschaft und Forschung des Landes Nordrhein Westfalen; 12.2014-12.2019; Thema: Forschungsprogramm mit verschiedenen Projekten zu</p>				<p>der Fachzeitschrift Addiction; seit 2016</p>						

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
				Tabakrauchen, Tabakentwöhnung und Nutzung von E-Zigaretten (NRW Rückkehrprogramm); Drittmittel; institutionell									
<b>Kraus, Prof. Dr. med. Thomas</b>	<b>Themenbezug zur Leitlinie (Berufskrankheit):</b> - Sozialgerichte BG'n; 03/15 - a.w.; Honorar; persönlich	Keine	<b>Themenbezug zur Leitlinie (COPD als Berufskrankheit):</b> - DGUV; 03/15 - a.w.; Honorar/Reisekosten; persönlich	Keine	Keine	<b>Themenbezug zur Leitlinie:</b> - DGAUM / Wissen. Fachgesellschaft; 03/15 - a.w.	<b>Themenbezug zur Leitlinie:</b> - berufsbedingte Atemwegserkrankung; 03/15 - a.w.	<b>Themenbezug zur Leitlinie:</b> - berufsbedingte Atemwegserkrankung; - a.w.	Keine	Keine	Keine	Uniklinikum RWTH Aachen; Direktor des Instituts für Arbeits-, Sozial- und Umweltmedizin	
<b>Lange, PD Dr. med. Tobias J.</b>	<b>Themenbezug zur Leitlinie:</b> - Actelion; Wiss-Komitee einer klin. Studie; seit 03.2018; Honorar; institutionell	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - GSK; 12.2015; Honorar; persönlich - Actelion; 03.2015-02.2020; Honorar; persönlich - Acceleron; 07.19; Honorar; persönlich	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Actelion; 03.2015-02.2020; Honorar; persönlich - Bayer; 03.2015-03.2018; Honorar; persönlich - MSD; 03.2015-02.2020; Honorar; persönlich - Pfizer; 03.2015-10.2017; Honorar; persönlich - OMT; 11.2018; Honorar; persönlich <b>Themenbezug zur Leitlinie (Antikoagulantien):</b> - BMS; 07.2019; Honorar; persönlich	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Actelion; 03.2015-02.2020; Drittmittel; institutionell - Bayer; 03.2015-03.2018; Drittmittel; institutionell - Pfizer; 03.2015-01.2020; Drittmittel; institutionell - Acceleron; 06.18-06.21; Drittmittel; institutionell	Keine	<b>Themenbezug zur Leitlinie:</b> - Mitglied der Deutschen Gesellschaft für Kardiologie, aktuell Sprecher AG25; seit 03.2015 - Mitglied der Deutschen Gesellschaft für Pneumologie und Beatmungsmedizin; seit 03.2015 - Mitglied der European Respiratory Society (ERS); seit 03.2015 <b>kein Themenbezug zur Leitlinie:</b> - Mitglied im HERMES examination committee der ERS; seit 03.2015	<b>Kein Themenbezug zur Leitlinie:</b> - Publikationen zur Diagnostik und Therapie der pulmonalen Hypertonie; seit 03.2015	<b>Themenbezug zur Leitlinie:</b> - Leitung Spezialambulanz für Pulmonale Hypertonie am UKR; 03.2015-02.2020 - Internistische Intensivmedizin; 10.2018-03.2020	<b>Themenbezug zur Leitlinie:</b> - Mitgestaltung von Fortbildungen im Rahmen der Kongresse von DGK und DGP; seit 03.2015	Keine	nein	Universitätsklinikum Regensburg Klinik für Innere Medizin II; Oberarzt Bereich Pneumologie	nein
<b>Langhorst, Prof. Dr. med. Jost</b>	<b>Themenbezug zur Leitlinie (Expertenrunden):</b> - Steigerwald Arzneimittel;	Keine	<b>Themenbezug zur Leitlinie (Integrative Therapien bei CED):</b> - Falk Foundation; 1-2015 -	<b>Themenbezug zur Leitlinie:</b> - Thema: Literaturrecherche für Metaanalysen und Leitlinienvorbereitung;	Keine	<b>Themenbezug zur Leitlinie:</b> - Leitlinienbeauftragter der Gesellschaft für Phytotherapie; 1-2015 - 12-	<b>Themenbezug zur Leitlinie:</b> - Phytotherapie - Naturheilkunde und komplementäre Medizin	<b>Themenbezug zur Leitlinie:</b> - Lehrstuhl für Naturheilkunde - Integrative Medizin - Integrative	<b>Themenbezug zur Leitlinie:</b> - Naturheilverfahren	Keine	Keine	Prof. Dr. med. Jost Langhorst Leitender Arzt Integrative Gastroenterologie Naturheilkunde	

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13		
Art	Direkt					Indirekt									
	<p>07-2016; Honorar; persönlich - Repha GmbH; 01-2015 - 6.2017; Honorar; persönlich - Ferring Arzneimittel; 02-2017- 06-2017; Honorar; persönlich</p> <p><b>Themenbezug zur Leitlinie (Schriftleitung ZPT):</b> - Medizinverlage Stuttgart; 01-2015-12.2017; Honorar; persönlich</p>		<p>12-2017; Honorar; persönlich - MSD Shap&amp;Dohme; 8-2016; Honorar; persönlich</p> <p><b>Themenbezug zur Leitlinie: (Phytotherapie bei CED und RDS)</b> - Repha GmbH; 1-2015 - 12-2017; Honorar ; persönlich</p> <p><b>Themenbezug zur Leitlinie (Integrative Therapie des RDS):</b> - Ardeypharm; 2015; Honorar; persönlich</p> <p><b>Themenbezug zur Leitlinie (Integrative Therapie des Pankreas-Ca):</b> - Celgene GmbH; 5-2017; Honorar; persönlich</p> <p><b>Themenbezug zur Leitlinie (Phytotherapie bei Husten):</b> - Dr. Wilmar Schwabe Arzneimittel; 9-2017; Honorar; persönlich</p>	<p>Rut-und Klaus Bahlsen-Stiftung; 1-2015 - 12-2017; Forschungsgrant; institutionell - Thema: PET/MRT bei CED; Eli and Edythe L. Broad Foundation Medical Research Program und die Crohn's Colitis Foundation of America (CCFA); 1-2016 - 12-2017; Forschungsgrant; institutionell - Thema: Lebensstil und Krankheitsaktivität bei Colitis ulcerosa – eine randomisiert kontrollierte Studie zum Einfluss von Stressreduktion und Lebensstilmodifikation und Kurzkettigen Fettsäuren bei Colitis ulcerosa - Einfluss eines pflanzlichen Kombinationspräparats aus Myrrhe, Kaffeekohle und Kamillenblütenextrakt im Vergleich zum Goldstandard Mesalazin auf den Verlauf von kurzkettigen Fettsäuren in Remission und akutem Schub; Karl und Veronica Carstens-Stiftung; 1-2016 -</p>			<p>2017 - Leitlinienbeauftragter der Deutschen Gesellschaft für Naturheilkunde; 1-2015 - 12-2017 - Deutsche Schmerzgesellschaft; 1-2015 - 12-2017 - Deutsches Kollegium für Psychosomatische Medizin; 1-2015 - 12-2017 Kein Themenbezug zur Leitlinie: - Sprecher der AG Psychosomatik in der Gastroenterologie der Deutsche Gesellschaft für Gastroenterologie; 9-2017 - 12-2017 - Deutsche Gesellschaft für Neurogastroenterologie und Motilität; 1-2015 - 12-2017</p>	<p>- Mind-Body-Verfahren Kein Themenbezug zur Leitlinie: - Gastroenterologie</p>	Gastroenterologie					<p>und Integrative Medizin Kliniken Essen-Mitte Knappschafts Krankenhaus Am Deimelsberg 34 a 45276 Essen; Leitender Arzt</p>	

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13	
Art	Direkt					Indirekt								
				12-2017; Forschungsgrant; institutionell  <b>Kein Themenbezug zur Leitlinie:</b> - Thema: TSST bei Colitis ulcerosa; Raßfeld-Stiftung; 2016; Forschungsgrant; institutionell - Thema: Lebensstil bei Colitis ulcerosa; Dr. Heinz Horst Deichmann Stiftung; 2015; Forschungsgrant; institutionell - Thema: Phytotherapie Colitis ulcerosa; Steigerwald Arzneimittelwerke GmbH; 2015; Forschungsgrant; institutionell - Thema: Lecithin Colitis ulcerosa; Falk Foundation; 01/2015-12/2017; Forschungsgrant; institutionell - Thema: fäkale Biomarker; TechLab; 01/2015-12/2017; Forschungsgrant; institutionell - Thema: Phytotherapie RDS); Dr. Wilmar Schwabe; 01/2016-										

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
				12/2017; Forschungsgrant; institutionell									
<b>Martin, Dr. phil. nat. Eric</b>	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Astra Zeneca; Experten-Workshop zu "Asthma Zero"; 2019</li> </ul> <p><b>Kein Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Sanofi Aventis; Thema: Einsatz von Laxanzien in der Selbstmedikation; seit 09/19</li> </ul>	<p><b>Kein Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Bundesapothekerkammer; seit 1999 fortlaufend; Aufwandsentschädigung; persönlich</li> <li>- Förderinitiative pharm. Betreuung; 2007-2016; Keine; persönlich</li> <li>- Bayer; Akad. F. Klin. Pharmazie; 2007-2016; Reisekosten; persönlich</li> </ul>	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Thema: Asthma im Kindesalter gemeinsam mit Kinderpneumologen, Keine Mitsprache des Auftraggebers bei Inhalen.; Consilium-Infectopharm; 11/2014-04/2017; Honorar; persönlich</li> <li>- Vorträge für Kammern, Hochschulen, Fachgesellschaften</li> <li>- Berlin Chemie; drei Vorträge: "Pharmakodynamische und pharmakokinetische Unterschiede inhalativer Glukokortikoide", Inhalative Therapie (2019/20)</li> </ul>	Keine	<p>Aktien der Stada AG (von bisheriger Inhaberin der Apotheke im Zuge des Erwerbs der Apotheke übernommen); Die Stada AG (Standard-Arzneimittel Deutscher Apotheker) war früher eine Genossenschaft und der Erwerb von Genossenschaftsanleihen, später Aktien, Voraussetzung für die Konfektionieren von Eigenspezialitäten (= kein Interessenkonflikt).</p>	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Mitglied der Arzneimittelkommission der Dt. Apotheker AMK; seit 2007</li> </ul> <p><b>Kein Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Mitglied des wissenschaftlichen Beirats der Bundesapothekerkammer (Tätigkeitsschwerpunkt Planung und Konzeptionierung der produktneutralen Pharmakon-Kongresse der BAK); 1999-2019</li> <li>- Mitglied des wissenschaftlichen Beirats der Förderinitiative Pharmaz. Betreuung; 2007-2016</li> <li>- Mitglied des wissenschaftlichen Beirats der Bayer. Akademie für Klin. Pharmazie; 2007-2016</li> </ul>	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Pharmazeutische Betreuung von Patienten mit Asthma bronchiale bzw. COPD</li> </ul> <p><b>Kein Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Pharmazeutische Betreuung von Patienten mit Typ-2-Diabetes</li> </ul>	Keine (im Berichtszeitraum lediglich eine Studienteilnahme als Interventionsapotheke (Typ-2-Diabetes); 07/2017 ff)	<p><b>Kein Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Als Mitglied des Wissenschaftlichen Beirats der Bundesapothekerkammer mitverantwortlich für die inhaltliche Gestaltung der jährlichen Pharmakon-Kongresse in Schladming / Meran (produktneutral, kein Firmensponsoring); laufend</li> </ul>	Keine	Keine	Selbstständig; Leiter der Hubertus-Apotheke, Luitpoldstraße 31, 97828 Marktheidenfeld	
<b>Mühlig, Prof. Dr. Stephan</b>	Keine	Keine	<p><b>Themenbezug zur Leitlinie (Tabakentwöhnung):</b></p> <ul style="list-style-type: none"> <li>- Pfizer; 2017-2019; Vortrag + Tagung; persönlich</li> </ul>	<p><b>Themenbezug zur Leitlinie (Tabak+ COPD):</b></p> <ul style="list-style-type: none"> <li>- AOKPLUS; 2015-2020; Drittmittel; institutionell</li> </ul> <p><b>Themenbezug zur Leitlinie</b></p>	Keine	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Wissenschaftlicher Aktionskreis Tabak (WAT); seit 2015</li> <li>- Deutsche Gesellschaft für Suchtforschung und -therapie</li> </ul>	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Tabakforschung; seit 2002</li> <li>- Publikationen zum Rauchen + COPD; seit 2002</li> </ul> <p><b>Kein Themenbezug zur Leitlinie:</b></p>	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Tabakentwöhnung; seit 2004</li> <li>- Raucherambulanz Chemnitz; seit 2007</li> </ul> <p><b>Kein Themenbezug zur Leitlinie:</b></p>	<p><b>Themenbezug zur Leitlinie:</b></p> <ul style="list-style-type: none"> <li>- Train-the-Trainer-Seminare u.a. von Kammern; seit 2012</li> </ul> <p><b>Kein Themenbezug zur Leitlinie:</b></p>	Keine	Keine	TU Chemnitz; PHA-TUC; Professur für Klinische Psychologie und Psychotherapie; Klinischer Direktor, Geschäftsführer	vor 2007



Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
				(Tabakentwöhnung): Deutsche; 2018-2020; Drittmittel; institutionell		(DGS); seit 2010 - Editor Zeitschrift SUCHT; seit 2018 - Psych. Psychotherapeut mit Fachkunde Verhaltenstherapie; seit 2014 - Fortbildungen für PT- und Ärztekammer; seit 2014  <b>Kein Themenbezug zur Leitlinie:</b> - Deutsche Gesellschaft für Psychologie; seit 2000		- Psychotherapie; seit 2014	- TUCed; seit 2007				
<b>Nehls, Dr. med. Wiebke</b>	Keine	Keine	<b>Themenbezug zur Leitlinie (Palliativversorgung):</b> - mission lebenshaus gGmbH; 01/15-10/17; Honorar; institutionell - Wannsee Akademie; 01/15 - 12/16; Honorar; institutionell - Thema: Palliativversorgung COPD; Pneumo Update; 11/16; Honorar; institutionell	Keine	Keine	<b>Themenbezug zur Leitlinie:</b> - Deutsche Gesellschaft für Palliativversorgung; Vorstandstätigkeit; ab 07/14 bis aktuell - Deutsche Gesellschaft für Pneumologie; seit 2009	<b>Themenbezug zur Leitlinie:</b> - Kommunikation; 2014-2016 - Palliativversorgung; 2014-2017	<b>Themenbezug zur Leitlinie:</b> - Palliativmedizin in der Pneumologie; seit 2008	Keine	Keine	Keine	HELIOS Klinikum Emil von Behring, Klinik für Pneumologie; Oberärztin, Bereichsleitung Palliativmedizin	
<b>Neumann, Prof. Dr. med. Andreas</b>	Keine	Keine	Keine	Keine	Keine	<b>Themenbezug zur Leitlinie:</b> - Deutsche Gesellschaft für HNO Heilkunde, KHC  <b>Kein Themenbezug zur Leitlinie:</b>	<b>Themenbezug zur Leitlinie:</b> - Septum- Nasenhöhlenchirurgie  implantierbare Hörsysteme	<b>Themenbezug zur Leitlinie:</b> - Nebenhöhlenchirurgie - Septumdefektverschluss  <b>Kein Themenbezug zur Leitlinie:</b> - rekonstruktive	<b>Kein Themenbezug zur Leitlinie:</b> - Neusser HNO-Kolloquium - Präsident westdeutscher HNO-Kongress 2019	Keine	Keine	Städtische Kliniken Neuss Klinik für Hals-Nasen-Ohrenheilkunde; seit 9 Jahren Chefarzt	

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
						- Deutsch-Spanische HNO-Gesellschaft; > 20 Jahre - Deutsche Gesellschaft für Biomaterialien		Mittelohrchirurgie					
<b>Nilius, Prof. Dr. med. Georg</b>	<b>Themenbezug zur Leitlinie (Kontrolle von Krankenhausbehandlungen):</b> - Qualitätssicherung, Pneumonie Landesarztekammer; fortlaufend; Reisekosten; persönlich	Keine	<b>Themenbezug zur Leitlinie (Ärztliche Weiterbildung):</b> - Akademie für ärztliche Fortbildung; fortlaufend; Honorar; persönlich - Boehringer; 05/2017; Honorar; Klinik	<b>Themenbezug zur Leitlinie:</b> - Thema: Beatmung/Nasale High flow Therapie; Studie COPO und Hyperkapnie; fortlaufend; Honorar; Klinik - Thema: Grundlagenforschung; Biomarker bei COPD/Bayer; seit 3/2017; Drittmittel; Klinik - Thema: Geräteentwicklung; CPAP/Algorithmen zur Therapiesteuerung/Löwenstein; fortlaufend; Drittmittel; Klinik	Keine	<b>Themenbezug zur Leitlinie:</b> - DGP; fortlaufend - DGSM; fortlaufend - ERS; fortlaufend - ATS; fortlaufend	<b>Themenbezug zur Leitlinie:</b> - Beatmungstherapie/Atmungsunterstützung bei respiratorischer Insuffizienz und Schlaf-Apnoe; fortlaufend	<b>Themenbezug zur Leitlinie:</b> - Chefarzt HELIOS Klinik Hagen-Ambrock; Fachgruppenleiter der HELIOS Kliniken für Pneumologie /Thoraxchirurgie; fortlaufend	<b>Themenbezug zur Leitlinie:</b> - Akademie für ärztliche Weiterbildung Westfalen-Lippe; fortlaufend	Keine	Keine	HELIOS-Klinik Hagen-Ambrock GmbH; Chefarzt	
<b>Nothacker, Dr. med. Monika</b>	<b>Kein Themenbezug zur Leitlinie:</b> - Thema: Medizinisch Fachliche Beratung Frühe Nutzenbewertung Pertuzumab; IQWiG; Oktober 2015; Honorar; persönlich - Thema: Methodische Beratung planungsrelevante Indikatoren; IQTIG; Januar-Juni 2016; Honorar; persönlich	Keine	<b>Themenbezug zur Leitlinie:</b> - Thema: Maximale Medizin – Optimal?; 4. Vortrag Berliner UG 2017; Honorar; persönlich Kein Themenbezug zur Leitlinie: - Thema: EbM und Leitlinien; 1. Dozentin: QM-Kurs Ärztekammer Niedersachsen; 2/2016 2/2017; Honorar; persönlich	<b>Kein Themenbezug zur Leitlinie:</b> - Thema: Drittmittel im Rahmen des Leitlinienprogramms Onkologie; Deutsche Krebshilfe; Gesamter Zeitraum; Drittmittel; institutionell - Thema: Forschungsprojekt leitlinienbasierte QI; DFG; 7/2016-6/2018; Drittmittel; institutionell	Keine	- Deutsches Netzwerk Evidenzbasierte Medizin: Sprecherin Fachbereich Leitlinien; Gesamter Zeitraum - Deutsche Krebsgesellschaft: einfache Mitgliedschaft	- Publikationen zu Leitlinien und zu Gemeinsam Klug Entscheiden; Gesamter Zeitraum	Keine	Keine	Keine	Keine	Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e. V. (AWMF); Wiss. Mitarbeiterin, Stellvertr. Leitlinien des AMWF-Instituts für Medizinisches Wissensmanagement	s.o.

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
			- Thema: Wahlpflichtfach: EbM und Leitlinien; 2.Dozentin: Berlin School of Public Health; 2013-2016 jeweils 4 Termine; Honorar; persönlich										
<b>Nowak, Prof. Dr. med. Dennis</b>	<b>Themenbezug zur Leitlinie (Aspekt Berufskrankheiten):</b> - Gutachtertätigkeit für Unfallversicherungsträger und Sozialgerichte; laufend; Honorare; persönlich, Mitarbeiterbeteiligung und Abführung an Klinikum	<b>Themenbezug zur Leitlinie (Rauchentwöhnung):</b> - Pfizer; laufend; Honorare, Reisekosten; persönlich	<b>Themenbezug zur Leitlinie (Begutachtung, Medikation):</b> - Berlin Chemie, Pfizer, Mundipharma, Boehringer, MedUpdate; laufend; Honorare, Reisekosten; persönlich	<b>Themenbezug zur Leitlinie (Forschung über Berufskrankheiten):</b> - DGUV; laufend; Drittmittel; institutionell	- nur Mischfonds	<b>Themenbezug zur Leitlinie:</b> - DGAUM; laufend - DGP; laufend	<b>Themenbezug zur Leitlinie:</b> - Arbeits- und umweltbedingte Atemwegs- und Lungenkrankheiten; laufend	<b>Themenbezug zur Leitlinie:</b> - Berufskrankheiten, Prävention, Asthma, COPD; laufend	<b>Themenbezug zur Leitlinie:</b> - zahlreiche Fortbildungsveranstaltungen zu o.g. Themen; laufend	Keine	Keine	Klinikum der Universität München, Institut und Poliklinik für Arbeits-, Sozial- und Umweltmedizin; Direktor	
<b>Ritz, Prof. Dr. Thomas</b>	<b>Themenbezug zur Leitlinie:</b> - 11/16-12/16; Breathing training for asthma; Honorar; persönlich - Editor-in-Chief, Biological Psychology (Elsevier)	<b>Themenbezug zur Leitlinie:</b> - Mitglied des Komitees fuer die S2k-Leitlinie zur Diagnostik und Therapie von Patienten mit Asthma, 2015-2021	Keine	<b>Themenbezug zur Leitlinie:</b> - National Institutes of Health; 9/15-8/18; A Wearable Asthma Trigger Monitoring System with integrated physiological monitor; Gehalt; persönlich, institutionell - National Institutes of Health; 7/18-8/18; The Dallas Asthma Brain an Cognition Study; persönlich, institutionell - National Institutes of Health; 7/18-8/18; Reward Sesivity	<b>Themenbezug zur Leitlinie:</b> - U.S. 10,942,174 B2 (approved 03/09/21); Title: "Calcium Binding Protein, Spermatid Specific 1, as a Biomarker for Diagnosis or Treatment of Stress"; Anteile; persönlich	<b>Kein Themenbezug zur Leitlinie:</b> - America Psychosomatic Society; 2001-2008 - International Society for the Advancement of Respiratory Psychophysiology; 1996-2008 - Society for Psychophysiological Research; 1993-2008	<b>Themenbezug zur Leitlinie:</b> - Psychophysiologie und Verhaltensmedizin von Atemwegserkrankungen; 2015-2021	Keine	Keine	Keine	Keine	Southern Methodist University (SMU), Department of Psychology; Professor, Forschung und Lehre	Keine

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
				as a Mechanism of Positive Affect Treatment; persönlich, institutionell									
<b>Schaefer, Corinna, M.A.</b>	Keine	Keine	Keine	Keine	Keine	<b>Kein Themenbezug zur Leitlinie:</b> - DNEbM; Fachbereiche Leitlinien und Patienteninformation	Keine	Keine	Keine	Keine	Keine	Keine	Ärztliches Zentrum für Qualität in der Medizin; Stv. Leitung; Abteilungsleitung EbM/Leitlinien und Patienteninformation
<b>Schäfer, Prof. Dr. med. Harald</b>	Keine	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Boehringer Ingelheim; 5/2015-10/2017; Honorar; persönlich	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Novartis; 2/2015-10/2017; Honorar; persönlich - AstraZeneca; 4/2015; Honorar; persönlich - Boehringer; 5/2015-10/2017; Honorar; persönlich - Berlin Chemie; 07-09/2014; Honorar; persönlich	Keine	Keine	Keine	Keine	<b>Themenbezug zur Leitlinie:</b> - Pneumologie; seit 1995	<b>Themenbezug zur Leitlinie:</b> - Veranstaltung von Fortbildungsveranstaltungen zum Thema Pneumologie; seit 1996	Keine	Keine		SHG Kliniken Völklingen; Chefarzt und Ärztlicher Direktor
<b>Schneider, Univ.-Prof. Dr. med. Antonius</b>	<b>Themenbezug zur Leitlinie:</b> - Thema: Lungenfunktionsdiagnostik; medinfo GmbH; 01/17 - bis jetzt; Honorar; persönlich - Thema: Qualitätsindikatoren QISA; AOK Bundesverband; 2016-2017; Honorar; persönlich - Thema: DMP Asthma/COPD; G-BA; 2004-bis jetzt; Honorar	Keine	<b>Themenbezug zur Leitlinie (DMP Asthma/COPD):</b> - Kassenärztliche Vereinigung Bayerns; 2012-12/15; Honorar; persönlich	Ganshorn (Hersteller von Spirometern und Boddylethmographen); 01.02.2018; Drittmittel; Mit dem Projekt soll ein neuartiges Spirometer evaluiert werden, das in der Lage ist, mit arbeitsunabhängig Atemwegsobstruktionen zu detek-	Keine	<b>Themenbezug zur Leitlinie:</b> - Deutsche Gesellschaft für Allgemeinmedizin (DEGAM); 2003 bis jetzt - Sprecher der Selektion Forschung, ständige Leitlinienkommission (SKL); jetzt	<b>Themenbezug zur Leitlinie:</b> - Zahlreiche; siehe <a href="http://www.am.med.tu-muenchen.de">www.am.med.tu-muenchen.de</a> (TU München); bis jetzt	<b>Themenbezug zur Leitlinie:</b> - Allgemeinmedizin/Hausarztpraxis; bis jetzt	Keine	Keine	Keine		Kliniken rechts der Isar / TU München; Direktion Institut für Allgemeinmedizin

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
	(Aufwandsent-schädigung); persönlich			tieren (Diag-nostische Stu-die).									
<b>Schüler, Sa-bine</b>	Keine	Keine	Keine	Keine	Keine	<b>Kein Themen-bezug zur Leitlinie:</b> - Berlin-Brandenburgische Gesellschaft für Herz- und Kreislauferkrankungen e. V. (BBGK e. V.)	<b>Themenbezug zur Leitlinie:</b> - methodische und Berichts-qualität diag-nostischer Ge-nauigkeitsstu-dien im Rah-men der Pro-motion; seit 2011	Keine	Keine	Keine	Keine	Ärztliches Zent-rum für Qualität in der Medizin (ÄZQ) Straße des 17. Juni 106-108 10623 Berlin; Wissenschaftliche Mitarbeite-rin	01/2016 - 12/2016: Bezirks-samt Neukölln; Gesundheitsamt; Assistenzärztin im Bereich Hygi-ene und Umwelt-medin 11/2012 - 04/2014: Medical Park Berlin Hum-boldtstraße; As-sistenzärztin in der Abteilung Or-thopädie und Un-fallchirurgie
<b>Schultz, Dr.med. Kon-rad</b>	Keine	<b>Themenbezug zur Leitlinie (allg. Pneumo-logie inklusive Arzneimittel):</b> - Boehringer; 2014-2015; Ho-norar; persöhn-lich - Berlin Che-mie; seit 2014; Honorar; persöhnlich <b>Themenbezug zur Leitlinie (Alpha-1-AT-Center):</b> - Grifols 2014-2015; Honorar; persönlich <b>Themenbezug zur Leitlinie (Rehabilita-tion):</b> - Novartis; 2014; Honorar; persönlich <b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Mundipharma;	<b>Themenbezug zur Leitlinie (Rehabilitation + Arzneimittel):</b> - Berlin Che-mie, seit 2014; Honorar; persöhnlich - Novartis; seit 2014; Honorar; persönlich - AstraZeneca; 2014 und 2016; Honorar; persöhnlich <b>Themenbezug zur Leitlinie (Rehabilita-tion):</b> - Mundipharma; 2014-2015; Ho-norar; persöhn-lich - Boehringer; seit 2014; Ho-norar; persöhn-lich <b>Themenbezug zur Leitlinie (Pneum. Diag-nostik):</b> - BdP; seit	<b>Themenbezug zur Leitlinie (Asthma, COPD):</b> - DRV Bayern Süd; seit 2014; Drittmittel; insti-tutionell	Keine	<b>Themenbezug zur Leitlinie:</b> Fachgesell-schaften - DGP; >20 Jahre - ERS; >15 Jahre - DGPMR; >20 Jahre - DGRW; seit 2014 - DGAKI; seit 2014 Berufsver-bände - BdP; seit 2008 - BDI; > 20 Jahre - BV der Reha-bilitationsärzte Deutschlands; seit 2008	<b>Themenbezug zur Leitlinie:</b> - Asthma, COPD, nicht-medikamen-töse Therapie, Rehabilitation; seit 2014	- Allgemeine Pneumologie - Innere Medi-zin - Rehabilitation - Sozialmedizin	<b>Themenbezug zur Leitlinie:</b> - Durchführung von DMP-Kur-sen zu Asthma/COPD	Keine	Keine	Klinik Bad Rei-chenhall der DRV Bayern Süd; Medizini-scher Direktor	

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
		2014; Honorar; persönlich	2014; Honorar; persönlich										
Schulz, Prof. Dr. rer. nat. Martin	Kein Themenbezug zur Leitlinie: - Gerichtsgutachten; 09/2015-09/2019; Gutachten MASGF Brandenburg; Aufwandsentschädigung; persönlich	Keine	Themenbezug zur Leitlinie (Arzneimittel*): - LAKs/LAVs; 09/2015-08/2017; Honorar; persönlich - BVKA; 2016; Honorar; persönlich - MSD; 10/2017; Honorar; persönlich *nicht im Bereich COPD  Kein Themenbezug zur Leitlinie: - Schwabe; 10/2017; Vortragshonorar; persönlich - Novartis; 10/2017; Posterhonorar; persönlich - DGK; 05/2019; Vortragshonorar - DHKT; 01/2020; Vortragshonorar - Sanofi; 01/2020; Vortragshonorar	Themenbezug zur Leitlinie (Medikationsplan): - BMG; 2015-2017; Drittmittel; institutionell	Keine	Kein Themenbezug zur Leitlinie: - Vorsitzender der Arzneimittelkommission der Deutschen Apotheker (AMK); 2009 - Mitglied DNEbM; kontinuierlich - DPhG; kontinuierlich - DGPT; kontinuierlich - ESCP; kontinuierlich - ASCPT; kontinuierlich - ACCPharm; kontinuierlich - ACCPharmacol; kontinuierlich - ISPE; kontinuierlich - ISOP; kontinuierlich - APhA; kontinuierlich - ESC/DGK; kontinuierlich - DDG; kontinuierlich	Kein Themenbezug zur Leitlinie: - Evidenzbasierte Medizin und Pharmazie (= Schule); > 10 Jahre - Therapie-treue; > 10 Jahre - AM-Versorgung; > 10 Jahre - AMTS; > 10 Jahre - Pharmakoepidemiologie; > 10 Jahre	Keine	Keine	Keine	Keine	ABDA-Bundesvereinigung Deutscher Apothekerverbände e. V., BAK, DAV; Geschäftsführer Arzneimittel	
Simon, Prof. Dr. phil. Alfred	Kein Themenbezug zur Leitlinie: - Nds. Ministerium für Wissenschaft und Kultur; jährlich (seit 1996); Institutionelle Förderung der Geschäftsstelle der Akademie für Ethik in der Medizin; institutionell	Kein Themenbezug zur Leitlinie: - Mitglied des Ausschusses für ethische und medizinisch-juristische Grundsatzzfragen der Bundesärztekammer* - Sprecher der Arbeitsgruppe	Kein Themenbezug zur Leitlinie: - Dozententätigkeit* im Rahmen von Weiterbildungskursen zu Palliativmedizin / Palliativ Care für Ärzte, Pflegendende und Vertreter anderer Gesundheitsberufe, u.a. für	Keine	Keine	Themenbezug zur Leitlinie: - Mitglied der Akademie für Ethik in der Medizin (AEM); kontinuierlich - Mitglied der Deutschen Gesellschaft für Palliativmedizin; kontinuierlich	Themenbezug zur Leitlinie: - Ethische Aspekte medizinischer Entscheidungen am Lebensende; kontinuierlich - Patientenautonomie, Patientenverfügung, Gesundheitliche Vorausplanung; kontinuierlich	Keine	Kein Themenbezug zur Leitlinie: - Mitveranstalter des Fernlehrgang „Berater/in für Ethik im Gesundheitswesen“ am cekib, Klinikum Nürnberg; kontinuierlich - Mitveranstalter des Qualifi-	Keine	Keine	Akademie für Ethik in der Medizin; Geschäftsführer	Universitätsklinikum Münster (jeweils im Wintersemester); Lehrstuhlvertretung



Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
		Ethik des Deutschen Verbandes für Ergotherapie* * Tätigkeit erfolgt ehrenamtlich bzw. im Rahmen meiner beruflichen Tätigkeit als Geschäftsführer der Akademie für Ethik in der Medizin	Honorar*; persönlich - PalliativNetz Pein; Honorar*; persönlich - Palliativnetz Wolfsburg; Honorar*; persönlich - Städtisches Klinikum Braunschweig; Honorar*; persönlich - Universitätsklinikum Münster; Honorar*; persönlich - Vitos Akademie Gießen; Honorar*; persönlich - Vitos Rheingau; Honorar*; persönlich * Dozenten honorare entsprechend den Honorarordnungen der Landesärztekammer für Weiterbildungen (bzw. orientieren sich daran)										
<b>Storre, Jan Prof. Dr. med.</b>	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Böhlinger Ingelheim; 01.2014-04.2018; Honorar; persönlich  <b>Themenbezug zur Leitlinie (technischen Hilfsmittel):</b> - Breas Medical AB; 01.2014-12.2019; Honorar; persönlich	Keine	<b>Themenbezug zur Leitlinie (techn. Hilfsmittel):</b> - Fischer & Paykel Healthcare; 01.2014-03.2018; Honorar; persönlich - Heinen & Löwenstein und Weinmann; 01.2014-03.2018; Honorar; persönlich - SenTec AG und Keller Medical; 01.2014-03.2018; Honorar; persönlich	<b>Themenbezug zur Leitlinie (techn. Hilfsmittel):</b> - Weinmann GmbH und Vivisol Deutschland; 2013-2015; Drittmittel; institutionell (Köln) - VitalAire GmbH; 2015-2017; institutionell (Köln) - Heinen & Löwenstein und Vivisol; 2015-2017; institutionell (Köln)	Keine	<b>Themenbezug zur Leitlinie:</b> - Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin; >10 Jahre - European Respiratory Society; >10 Jahre - Deutsche interdisziplinäre Gesellschaft für außerklinische Beatmung; >10 Jahre - Deutsche Gesellschaft für	<b>Themenbezug zur Leitlinie:</b> - Forschungstätigkeiten Beatmungsmedizin, Lebensqualität bei respiratorischer Insuffizienz, Monitoring des Gasaustausches u.a.; >10 Jahre	<b>Themenbezug zur Leitlinie:</b> - siehe unten Institutionen, Lungenklinik/ - Fachklinik; seit 2011	<b>Themenbezug zur Leitlinie:</b> - Lehrauftrag an der Albert-Ludwigsuniversität Freiburg i. Br., Schwerpunkt Pneumologie; seit 2011 - Ausbildung als leitender Arzt in den u.g. Positionen, Schwerpunkt Pneumologie; seit 2011	Keine	Keine	Pneumologie Solln Praxis für Lungen- und Bronchialheilkunde, Innere Medizin und Schlafmedizin; eigene Praxis	Lungenklinik Köln-Merheim, Kliniken der Stadt Köln gGmbH, Köln; Asklepios Fachklinik Abteilung für Intensiv-, Schlaf- und Beatmungsmedizin Gauting GmbH Robert-Koch-Allee 2 82131 Gauting bis 09/2019



Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
			- VitalAire, Vivosol; 01.2014-03.2018; Honorar; persönlich - ResMed; 01.2014-03.2018; Honorar; persönlich - Linde und WKM; 01.2014-03.2018; Honorar; persönlich										
<b>Vader, Isabell MPH</b> (ausgeschieden 01/2021, Stand 01/2021)	Keine	Keine	Keine	Keine	Keine	<b>Kein Themenbezug zur Leitlinie:</b> - Mitglied Marburger Bund; seit 12/2012	Keine	Keine	Keine	Keine	Keine	ÄZQ; wissenschaftliche Mitarbeiterin	05/2015-10/2015: Technische Universität Berlin, Fachgebiet Management im Gesundheitswesen (drittmittelfinanziert durch BMBF);  09/2013-09/2014: Evangelisches Krankenhaus Königin Elisabeth Herzberge Berlin
<b>Vogelmeier, Prof. Dr. C.</b>	Keine	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Almirall; 2015; Honorar; persönlich - AstraZeneca; aktuell; Honorar; persönlich - Boehringer Ingelheim; aktuell; Honorar; persönlich - Chiesi; aktuell; Honorar; persönlich - Grifols; aktuell; Honorar; persönlich - Novartis; aktuell; Honorar; persönlich - CSL Behring; aktuell; Honorar; persönlich	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Almirall; 2015; Honorar; persönlich - AstraZeneca; aktuell; Honorar; persönlich - Boehringer Ingelheim; aktuell; Honorar; persönlich - Chiesi; aktuell; Honorar; persönlich - Grifols; aktuell; Honorar; persönlich - Mundipharma; 12.2016; Honorar; persönlich - Novartis; aktuell; Honorar; persönlich - Takeda; 2015;	<b>Kein Themenbezug zur Leitlinie:</b> - AstraZeneca; aktuell; institutionell - Boehringer; aktuell; institutionell - Grifols; aktuell; institutionell - GlaxoSmithKline; aktuell; institutionell - Novartis; aktuell; institutionell - Teva; aktuell; institutionell - Bundesministerium für Bildung und Forschung; aktuell;	Keine	<b>Themenbezug zur Leitlinie:</b> - Präsident der DGP; 2009-2011 - Mitglied/Sprecher des Science Committee der GOLD; seit 2009  <b>Kein Themenbezug zur Leitlinie:</b> - Vorsitzender der Deutschen Lungenstiftung; seit 2015	<b>Themenbezug zur Leitlinie:</b> - COPD; aktuell	<b>Themenbezug zur Leitlinie:</b> - COPD; aktuell	Keine	nicht vorhanden	Nein!	Philips-Universität Marburg und UKGM, Standort Marburg; Professor für Innere Medizin und Direktor der Klinik für Innere Medizin mit Schwerpunkt Pneumologie, Intensiv- und Schlafmedizin, UKGM, Standort Marburg	Keine

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
		- Berlin Chemie / Menarini; persönlich	Honorar; persönlich - Berlin Chemie/ Menarini; Honorar; persönlich - CSL Behring; Honorar; persönlich	Drittmittel; institutionell									
<b>Watz, PD Dr. med. Henrik</b>	<b>Themenbezug zur Leitlinie:</b> - GSK; seit 2016; Honorar; persönlich - AstraZeneca; seit 2013; Honorar; persönlich -Boehr. Ingelheim; seit 2013; Honorar; persönlich - Novartis; seit 2017; Honorar; persönlich - BerlinChemie; seit 2017; Honorar; persönlich -CHIESI; seit 2017; Honorar; persönlich	<b>Themenbezug zur Leitlinie:</b> - GSK; seit 2014; Honorar; persönlich - AstraZeneca; seit 2014; Honorar; persönlich -Boehr. Ingelheim; seit 2016; Honorar; persönlich -CHIESI; seit 2019; Honorar; persönlich	<b>Themenbezug zur Leitlinie:</b> -Boehr. Ingelheim; seit 2013; Honorar; persönlich - Chiesi; seit 2016; Honorar; persönlich - AstraZeneca; seit 2013; Honorar; persönlich - Novartis; seit 2013; Honorar; persönlich - Berlin Chemie; seit 2014; Honorar; persönlich	<b>Themenbezug zur Leitlinie:</b> - AstraZeneca; seit 2013; Honorar; institutionell - Chiesi; seit 2013; Honorar; institutionell - GSK; seit 2013; Honorar; institutionell	<b>Themenbezug zur Leitlinie:</b> -Boehr. Ingelheim; seit 2013; Honorar; institutionell - Novartis; seit 2013; Honorar; institutionell - Takeda; seit 2013; Honorar; persönlich	<b>Themenbezug zur Leitlinie:</b> - Co-Autor der COPD-Leitlinie der DGP und Atemwegsliga; seit Dez 2015 Kein Themenbezug zur Leitlinie: - Mitglied wissenschaftlicher Fachgesellschaften (DGP, ATS, ERS); seit 2008 - Mitglied DGIM; seit 2003	<b>Themenbezug zur Leitlinie:</b> - COPD und Asthma; > 100 Publikationen; seit 2005	<b>Themenbezug zur Leitlinie:</b> - Internist und Pneumologe; seit 2008	<b>Themenbezug zur Leitlinie:</b> - diverse Fortbildungsveranstaltungen für Allgemeinmediziner; seit 2008 - diverse Fortbildungsveranstaltungen für Pneumologen; seit 2008 - Herausgeber COPD Buch; 2017 - ERS task force chair Körperliche Aktivität COPD; 2014	Keine	Keine	Pneumologisches Forschungsinstitut an der Lungen-Clinic Großhansdorf; Arzt und Geschäftsführer	
<b>Weber, PD Dr. Cora</b>	<b>Kein Themenbezug zur Leitlinie:</b> - Bayer; 02/2017-02/2019; Pain Endometriosis; Honorar; institutionell	Keine	<b>Kein Themenbezug zur Leitlinie:</b> - Bayer; 17.06.2017; Psychokardiologie; Honorar; institutionell (Klinik Konto) - 38. BNK Jahrestagung; Vortrag - Servier Telefonhörer-Aktion 15.03.2018; Depression Telefonberatung; Honorar; persönlich	Keine	Keine	<b>Themenbezug zur Leitlinie:</b> - American Psychosomatic Society; seit 2004 - Deutsches Kollegium für Psychosomatische Medizin DKPM e. V.; seit 2002 - Deutsche Gesellschaft für Psychosomatische Medizin und Ärztliche Psychotherapie e. V.; seit 2002 - Bundesverband der Fachärzte für Psychosomatische	Psychokardiologie, Herzratenvariabilität, Salzsensitivität, Bluthochdruckregulation, Schmerz, inter-nistische Psychosomatik	<b>Themenbezug zur Leitlinie:</b> - Psychosomatische Medizin und Psychotherapie, Chefärztin der Fachabteilung innere Medizin (Fachärztin/ i.R. psychosomat. Medizin); seit 1.1.18	<b>Themenbezug zur Leitlinie:</b> - Psychokardiologie, Dozentin Dt. Gesellschaft für Kardiologie, Curriculum Psychosomatische Grundversorgung - Akademie für psychosom. Medizin und Psychotherapie, Berlin Dozentin; seit 2012	Keine	nein	Medizin und Psychotherapie Oberhavelklinik Henningsdorf; Chefärztin seit 1.1.2018	Park-Klinik Sophie Charlotte, Abt. Psychosomatik; Chefärztin v. 1.8.2014-31.12.2017

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
						Medizin und Psychotherapie e. V., Wiss. Beirat; seit 2014 - Dt. Gesellschaft für Kardiologie-Herz- u. Kreislauforschung e. V.; seit 2017							
<b>Weber, Dr. Michael</b>	Keine	<b>Themenbezug zur Leitlinie (Allergie):</b> - Bencard Allergie GmbH; 2015; Honorar; persönlich	<b>Themenbezug zur Leitlinie (Medikamente):</b> - Novartis; 2015-2019; Honorar; persönlich - Boehringer; 2015-2019; Honorar; persönlich - Glaxo; 2015-2019; Honorar; persönlich - Astra; 2015-2016; Honorar; persönlich - MedInfo; 2015-2019; Honorar; persönlich	<b>Kein Themenbezug zur Leitlinie (MS-Medikament):</b> - Novartis; 2015-2018	Keine	<b>Themenbezug zur Leitlinie:</b> - Berufsverband der Pneumologen Bundesverband; -2017 - Berufsverband der Pneumologen Bayern; -2018 - Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin; -2018 - Deutsche Forschungsgruppe Pneumologie in der Primärversorgung e. V. (DFPP); -2018	Keine	<b>Themenbezug zur Leitlinie:</b> - Niedergelassener Pneumologe in eigener Praxis; 1992-2018	Keine	Keine	Keine	Keine	Keine
<b>Welte, Prof. Dr. med. Tobias</b>	Keine	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Boehringer; 2017-2020; persönlich - AstraZeneca; 2017-2020; persönlich - GSK; 2017-2020; - Novartis; 2017-2020; persönlich	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - AstraZeneca; 2017-2020; persönlich - Berlin-Chemie; 2019; persönlich - Boehringer; 2017-2020; persönlich - GSK; 2017-2020; persönlich - Novartis; 2017-2020; persönlich	<b>Themenbezug zur Leitlinie (Arzneimittel):</b> - Novartis; 2017-2019; institutionell - GSK; 2018-2020; institutionell - AstraZeneca; 2017-2020; institutionell	Keine	<b>Themenbezug zur Leitlinie:</b> - President of the European Respiratory Society; 2018/19 - President of the Forum of Internal Respiratory Society; 2019 - Präsident der Deutschen Gesellschaft für Pneumologie; 2013-2015 <b>Themenbezug zur Leitlinie</b>	<b>Themenbezug zur Leitlinie:</b> - Lungentransplantation; seit 1990 - Asthma + COPD; seit 1985 <b>Themenbezug zur Leitlinie (bedingt):</b> - pulmonale Infektionen einschließlich Pneumonie und Sepsis; seit 1985 - Intensivmedizin, vor allem	<b>Themenbezug zur Leitlinie:</b> - akute und chronische Infektionen; seit 1985 - Lungen- und Bronchialerkrankungen; seit 1985	<b>Themenbezug zur Leitlinie:</b> -Hannover Biomedical Research School; seit 2004	Keine	Keine	Medizinische Hochschule Hannover; Klinikdirektor Pneumologie Senatsmitglied	

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
						<p><b>(bedingt):</b> - Präsident der Paul Ehrlich Gesellschaft; 2018-2020 - Präsident der Deutschen Sepsis Gesellschaft; 2009-2013 - Präsident der Deutschen Gesellschaft für internistische Intensivmedizin; 2008-2010</p>	Beatmung; seit 1985						
<b>Welter, PD Dr. med. Stefan</b>	Keine	Keine	<p><b>Themenbezug zur Leitlinie (Technologie):</b> - KLS-Martin; 01.2014-12.2017; Honorar und Reisekostenerstattung; persönlich - Johnson u. Johnson; 01.2016-03.2018; Reisekostenerstattung und Fortbildungshospitation; persönlich - MedExpert; 01.2015-10.2017; Honorar und Reisekostenerstattung; persönlich - Gore; 01.2015-03.2018; Honorar und Reisekostenerstattung; persönlich</p>	Keine	Keine	<p><b>Themenbezug zur Leitlinie:</b> - DGT; seit ca. 2006 - DGP; seit 2017 - ESTS; seit 2008</p> <p><b>Kein Themenbezug zur Leitlinie:</b> - BDC; seit ca. 2001 - DHV; seit 2015</p>	<p><b>Themenbezug zur Leitlinie:</b> - Lungenmetastasen Chirurgie - Management von Komplikationen</p>	<p><b>Themenbezug zur Leitlinie:</b> - operative Lungenreduktion; 01.2008-03.2018 Kein Themenbezug zur Leitlinie: - onkologische Chirurgie der Lunge - septische Chirurgie</p>	Keine	Keine	Keine	Lungenklinik Heuer, Theodor-Funccius-Str.1, 58675 Heuer; Chefarzt der Thoraxchirurgie	Ruhrlandklinik, Tüschener Weg 40, 45239 Essen; Ltd. OA Thoraxchirurgie
<b>Worth, Prof. Dr. med. Heinrich</b>	Themenbezug zur Leitlinie (Arzneimittel): - AstraZeneca; 07/2017-jetzt;	Themenbezug zur Leitlinie (Arzneimittel): - AstraZeneca; 2016; Honorar;	Themenbezug zur Leitlinie (Arzneimittel): - Novartis; ca. 5 Jahre; Honorar;	Themenbezug zur Leitlinie (DACCORD-Studie): - Novartis; ca. 5	Keine	Themenbezug zur Leitlinie: - Deutsche Atemwegsliga; ca. 30 Jahre	Themenbezug zur Leitlinie: - Kardiopulmonale Interaktionen,	Themenbezug zur Leitlinie: - Pneumologie; ca 25 Jahre - Asthma,	Themenbezug zur Leitlinie: - Patientenschulung Asthma,	Keine	Keine	Praxis-Kooperation Dr. Bily/Kellermann/Fürth;	Chefarzt, Med. Klinik 1, Klinikum Fürth; bis 31.12.2014

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13		
Art	Direkt					Indirekt									
	Honorar; persönlich - Klosterfrau; ca. 2008-jetzt; Honorar; persönlich - Chiesi; Honorar; persönlich; - GSK; Honorar; persönlich; - Novartis; Honorar; persönlich; - Omron; Honorar; persönlich;  - DMP Asthma/COPD; Reisekosten	persönlich - Klosterfrau; ca. 5 Jahre; Honorar; persönlich - BerlinChemie; ca. 5 Jahre; Honorar; persönlich - Chiesi; Honorar; persönlich  <b>Themenbezug zur Leitlinie (COPD):</b> - Novartis; ca. 5 Jahre; Honorar; persönlich	persönlich - BerlinChemie; ca. 5 Jahre; Honorar; persönlich - Klosterfrau; ca. 5 Jahre; Honorar; persönlich - AstraZeneca; ca. 2 Jahre; Honorar; persönlich - Almirall; ca. 2 Jahre; Honorar; persönlich	Jahre; Honorar; persönlich			- Deutsche Gesellschaft für Pneumologie; ca. 30 Jahre - AG Lungensport in Deutschland; ca. 15 Jahre - Deutsche Gesellschaft für Innere Medizin; ca. 30 Jahre		COPD, Asthma, Patientenschulung, Lungensport; ca. 35 Jahre		COPD, Lungenembolie		COPD; ca. 20 Jahre		Kooperationspartner


**Externe Expertin ohne Stimmberechtigung, 2. Auflage**

Nr.	1	2	3	4	5	6	7	8	9	10	11	12	13
Art	Direkt					Indirekt							
	Berater-/Gutachter-tätigkeit	Mitarbeit in einem Wissenschaftlichen Beirat (advisory board)	Vortrags-/oder Schulungstätigkeit	Forschungsvorhaben/Durchführung klinischer Studien	Eigentümerinteressen (Patent, Urheberrecht, Aktienbesitz)	Mitgliedschaft/Funktion in Interessenverbänden	Schwerpunkte wissenschaftlicher Tätigkeiten, Publikationen	Schwerpunkte klinischer Tätigkeiten	Federführende Beteiligung an Fortbildungen /Ausbildungsinstituten	Enge persönliche Beziehungen zu einem Vertretungsberechtigten eines Unternehmens der Gesundheitswirtschaft	Sehen Sie andere Aspekte oder Umstände, die von Dritten als einschränkend in Bezug auf Ihre Objektivität oder Unabhängigkeit wahrgenommen werden könnten?	Gegenwärtiger Arbeitgeber und Funktion	Frühere Arbeitgeber und Funktion (im Zeitraum der Erklärung)
Meiling, Claudia	Keine	Keine	Keine	Keine	Keine	Keine	Keine	Keine	Keine	Keine	Keine	Deutscher Verband der Ergotherapeuten (DVE); seit 2011; Referentin für Standards und Qualität	Keine

### Anhang 1.3 Stimmenthaltungen bei der Konsensuskonferenz, 2. Auflage

Vor der Konsensuskonferenz waren die Interessenkonflikte der Teilnehmer\*innen durch AWMF und ÄZQ (Frau Dr. Nothacker und Frau Schaefer) bewertet worden. Enthaltungen waren bei moderaten IK unabhängig vom Themenzug zur Leitlinie beschlossen worden. Jede Fachgesellschaft hatte eine Stimme. Waren mehrere Expert\*innen für eine Fachgesellschaft benannt und hatte nur einer/eine einen IK angegeben, so konnte eine andere Vertreterin/ ein anderer Vertreter das Stimmrecht für die Fachgesellschaft wahrnehmen. Folgende Liste lag bei der Konsensuskonferenz als Tischvorlage aus:

NVL COPD  
Interessenkonflikte



## 1 Grundlage:

Bewertung der IK-Formulare durch Frau Dr. Nothacker und Frau Schaefer am 10.02.2020; abgeglichen am 12.02.2020. Es wurden Interessen des laufenden Jahres sowie der letzten drei Jahre (2017-2019) eingeschätzt.

- Als „gering“ bewertet wurden Gesamt-Vortragseinkünfte < 1000 €.
- Verbindungen zu Herstellern/Firmen, die Medikamente (zur Tabakentwöhnung; ~~Strochodilatoren~~) und Inhalationsgeräte herstellen, wurden als „moderat“ eingestuft, auch wenn diese keinen Themenbezug zur Leitlinie haben; Folge: Enthaltung bei themenbezogenen Abstimmungen.

## 2 Enthaltungen: Diagnostik (Algorithmus, CT)

Nr.	Experten	Fachgesellschaft
1	<del>Kauczor</del> Prof. Dr. med. Hans-Ulrich	DRG

## 3 Enthaltungen: Medikamentöse Therapie (Algorithmus)

Nr.	Experten	Fachgesellschaft
1	Andreas, Prof. Dr. med. Stefan	DEGIM
2	Criée, Prof. Dr. med. Carl-Peter	Dt. Atemwegsliga
3	Dreher, Prof. Dr. med. Michael	DIGAB
4	Hellmann, Dr. med. Andreas	DFPP
5	Hering, Dr. med. Thomas	DFPP
6	Heußel, Prof. Dr. med. Claus Peter	DRG
7	<del>Kauczor</del> Prof. Dr. med. Hans-Ulrich	DRG
8	Nowak, Prof. Dr. med. Dennis	DGAUM
9	Schäfer, Prof. Dr. med. Harald	<del>ÄkdÄ</del>
10	Schultz, Dr. med. Konrad	DGPMD/DGRW
11	Schulz, Prof. Dr. <del>Dr.</del> nat. Martin	AMK
12	Storre, Prof. Dr. med. Jan H.	DIGAB
13	Vogelmeier, Prof. Dr. med. Claus F.	DGIIN
14	<del>Watz</del> PD Dr. med. Henrik	DGP
15	Weber, Dr. med. Michael	DFPP
16	Welte, Prof. Dr. med. Tobias	DGIIN
17	Worth, Prof. Dr. med. Heinrich	DGP

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1



#### 4 Enthaltungen: Tabakentwöhnung (Algorithmus; Empfehlung 5-4 kombinierte Therapie)

Nr.	Experten	Fachgesellschaft
1	Gogol, Dr. med. Manfred	DGGG
2	Heppner, Prof. Dr. med. Hans Jürgen	DGG
3	Hering, Dr. med. Thomas	DFPP
4	Lange, PD Dr. med. Tobias J.	DGK
5	Mühlig, Prof. Dr. Stephan	DGPs
6	Nowak, Prof. Dr. med. Dennis	DGAUM



## Anhang 1.4 Übersicht: Stimmenthaltungen aufgrund Interessenkonflikt

### Stimmenthaltungen bei der Konsensuskonferenz aufgrund IK

Empfehlung/Statement (Nummerierung siehe Konsultationsfassung)	Anzahl Enthaltungen aufgrund von Interessenkonflikten
3-2 + Abbildung 3 (Algorithmus Tabakentwöhnung)	3
3-4	2
5-1 + Abbildung 4 (Medikamentöse Langzeitbehandlung)	8

### Stimmenthaltungen: elektronische Abstimmung nach der Konsensuskonferenz

Empfehlung/Statement (Nummerierung siehe Konsultationsfassung)	Anzahl Enthaltungen aufgrund von Interessenkonflikten
4-18	1
4-19	1

## Anhang 2 Endpunktgraduierung

### Sammlung der Endpunkte in der Auftaktsitzung

- Gesamtmortalität
- krankheitsspezifische Mortalität
- Morbidität
  - Symptomatik: Atemnot, Husten und Auswurf
  - Mobilität/Funktionalität
  - soziale Teilhabe
  - Erwerbsfähigkeit
  - Exazerbationen
  - Reduktion des zukünftigen Krankheitsrisikos
    - Lungenfunktion
    - Gesamt-Hospitalisierung
    - COPD-bedingte Hospitalisierung
  - therapiebedingte Morbidität
- Lebensqualität
- Krankheitsbewältigung

## Anhang 3 Recherchestrategien

### Anhang 3.1 Leitlinien

#### Recherchestrategie

Die strukturierte Leitlinienrecherche wurde vom 22.02.2017 bis 22.03.2017 durchgeführt. Es wurden Leitlinien zu COPD gesucht. Recherchestrategie und -vokabular richteten sich nach den Möglichkeiten der jeweiligen Recherchequelle, wurden entsprechend modifiziert und sind nachfolgend dargelegt. Die Suche umfasste Dokumente in deutscher und englischer Sprache.

#### Leitliniendatenbanken

#### Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)

Leitliniensuche unter [www.awmf.org/leitlinien/leitlinien-suche.html](http://www.awmf.org/leitlinien/leitlinien-suche.html), keine weiteren Filter.

Suche nach „COPD“, „Chronisch obstruktive Lungenerkrankung“, „Chronisch obstruktive Atemwegserkrankung“, „Chronische Atemwegserkrankung“, „Chronisch obstruktive Bronchitis“, „Chronische Bronchitis“.

### Guidelines International Network (G-I-N)

Leitliniensuche unter [www.g-i-n.net/library/international-guidelines-library](http://www.g-i-n.net/library/international-guidelines-library).

Suche nach: „COPD“, „chronic obstructive pulmonary disease“, „chronic obstructive lung disease“, „chronic obstructive airway disease“, „chronic bronchitis“, „COLD“.

### National Guideline Clearinghouse (NGC)

Leitliniensuche unter [www.guideline.gov](http://www.guideline.gov).

Suche nach: „chronic obstructive pulmonary disease“ (die Suche nach „chronic obstructive lung disease“ und „chronic obstructive airway disease“ war zusätzlich nicht notwendig, da in der Suche nur Einzelwörter gesucht werden und die Ergebnisse somit bereits in der oberen Suche „chronic obstructive pulmonary disease“ gefunden wurden), „chronic bronchitis“, „COAD“, „COPD“, „COLD“.

### National Institute for Health and Clinical Excellence (NICE)

Leitliniensuche unter [www.nice.org.uk](http://www.nice.org.uk), über „guidance“, filter by type: NICE guidelines; clinical guidelines, public guidelines.

Suche nach: „COPD“, „COLD“, „COAD“, „chronic obstructive pulmonary disease“, „chronic obstructive lung disease“, „chronic obstructive airway disease“, „chronic bronchitis“.

### Scottish Intercollegiate Guidelines Network (SIGN)

Sichtung der Liste „Guidelines“ published by topic „respiratory medicine“ unter [www.sign.ac.uk](http://www.sign.ac.uk)

### Institute for Clinical Systems Improvement (ICSI)

Leitliniensuche unter [www.icsi.org](http://www.icsi.org) über „guidelines and more“, „Search by keywords“

Suche nach: „COPD“, „COAD“, „COLD“, „chronic obstructive pulmonary disease“, „chronic obstructive lung disease“, „chronic obstructive airway disease“, „chronic bronchitis“.

### Deutsche Gesellschaft für Allgemeinmedizin (DEGAM), DE

Sichtung der Leitlinien unter [www.degam.de/degam-leitlinien-379.html](http://www.degam.de/degam-leitlinien-379.html)

### Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ), DE

Leitliniensuche unter [www.akdae.de](http://www.akdae.de) über die Suchfunktion mit Eingrenzung: Arzneimitteltherapie/Therapieempfehlungen.

Suche nach: „COPD“, „Chronisch obstruktive Lungenerkrankung“, „Chronisch obstruktive Atemwegserkrankung“, „Chronische Atemwegserkrankung“, „Chronisch obstruktive Bronchitis“, „Chronische Bronchitis“.

### National Health and Medical Research Council (NHMRC), AUS

Gesucht wurde unter „Guidelines & Publication“ auf der Seite des NHMRC ([www.nhmrc.gov.au/](http://www.nhmrc.gov.au/)) und im Australian Clinical Practice Guidelines Portal ([www.clinicalguidelines.gov.au/](http://www.clinicalguidelines.gov.au/)).

Leitliniensuche unter [www.nhmrc.gov.au/](http://www.nhmrc.gov.au/), „filter by keyword“.

Suche nach: „COPD“, „COAD“, „COLD“, „chronic obstructive pulmonary disease“, „chronic obstructive lung disease“, „chronic obstructive airway disease“, „chronic bronchitis“.

Leitliniensuche im „guideline portal search“ über „Free text search“ unter [www.clinicalguidelines.gov.au/](http://www.clinicalguidelines.gov.au/)

Suche nach: „COPD“, „COAD“, „COLD“, „chronic obstructive pulmonary disease“, „chronic obstructive lung disease“, „chronic obstructive airway disease“, „obstructive“.

### Tripdatabase (UK)

Leitliniensuche unter [www.tripdatabase.com/](http://www.tripdatabase.com/), Filter: „guidelines“

Suche nach: „COPD“, „chronic obstructive pulmonary disease“, „chronic obstructive pulmonary chronic obstructive lung copd“.

**World Health Organization (WHO) (International)**

Leitliniensuche unter [www.euro.who.int/de](http://www.euro.who.int/de) über den Pfad: „health topic“: „chronic respiratory diseases“: „publications“.

**DynaMed Plus (USA)**

Leitliniensuche unter [www.dynamed.com/home](http://www.dynamed.com/home), Eingrenzung: „Guidelines and Resources“ und „Keine Reviews“.

Suche nach: „COPD“.

Die Suchbegriffe "chronic obstructive pulmonary disease", "chronic obstructive lung disease", "chronic obstructive airway disease" und "COAD" sind innerhalb der Dynamed-Suchfunktion auf das Suchwort "COPD" verlinkt und führten zu simultanen Suchergebnissen wie bei o.g. Strategie („COPD“).

Suche nach: „COLD“.

**Fachspezifische Anbieterorganisationen****European Respiratory Society (ERS) (EU)**

Sichtung der Leitlinien auf [www.ersnet.org/research/published-guidelines](http://www.ersnet.org/research/published-guidelines). Sortiert nach Topic: COPD;

Suche ohne Einschränkungen nach „COPD“.

**Deutsche Atemwegsliga (DE)**

Leitliniensuche auf [www.atemwegsliga.de/empfehlungen-positions-papiere.html](http://www.atemwegsliga.de/empfehlungen-positions-papiere.html), keine weiteren Einschränkungen möglich.

**Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin (DGP) (DE)**

Leitliniensuche auf [www.pneumologie.de/publikationen/leitlinien/](http://www.pneumologie.de/publikationen/leitlinien/), keine weiteren Einschränkungen möglich.

**Schweizerische Gesellschaft für Pneumologie, CH**

Leitliniensuche auf [www.pneumo.ch/](http://www.pneumo.ch/), über „Informationen für Fachpersonen“.

**American Association for Respiratory Care (AARC) (US)**

Leitliniensuche auf [www.aarc.org/resources/clinical-resources/clinical-practice-guidelines](http://www.aarc.org/resources/clinical-resources/clinical-practice-guidelines), keine weiteren Einschränkungen möglich.

**American College of Chest Physicians (ACCP) (US)**

Leitliniensuche auf [www.chestnet.org/Guidelines-and-Resources/CHEST-Guideline-Topic-Areas/Airway-Disorders](http://www.chestnet.org/Guidelines-and-Resources/CHEST-Guideline-Topic-Areas/Airway-Disorders), keine weiteren Einschränkungen möglich.

**National Heart, Lung, and Blood Institute (NHLBI) (US)**

Leitliniensuche auf [www.nhlbi.nih.gov/health-pro/guidelines/current](http://www.nhlbi.nih.gov/health-pro/guidelines/current) und <https://www.nhlbi.nih.gov/health-pro/guidelines/archive>, keine weiteren Einschränkungen möglich.

**Australian Lung Foundation (AUS)**

Leitliniensuche auf [lungfoundation.com.au/health-professionals/guidelines/](http://lungfoundation.com.au/health-professionals/guidelines/).

**British Thoracic Society (BTS), UK**

Leitliniensuche auf [www.brit-thoracic.org.uk/standards-of-care/guidelines](http://www.brit-thoracic.org.uk/standards-of-care/guidelines) über „Disease/Condition: COPD“

**Canadian Thoracic Society (CTS) (CA)**

Leitliniensuche auf [www.respiratoryguidelines.org/](http://www.respiratoryguidelines.org/) über „COPD: Guidelines and Standards“

**Thoracic Society of Australia & New Zealand (TSANZ) (AUS, NZ)**

Leitliniensuche auf [www.thoracic.org.au/journal/search](http://www.thoracic.org.au/journal/search).

Suche nach „keyword: guideline, category: COPD“.

Suche nach „keywords: COPD, sort by relevance“,

**Global Initiative for chronic obstructive lung disease (GOLD) (US, WHO) (INT)**

Leitliniensuche auf [goldcopd.org](http://goldcopd.org) über GOLD Reports.

Identifizierte Leitlinien

**Eingeschlossenen Leitlinien**

Titel Suchergebnis	Land	Kommentar	DELBI Domäne 3	DELBI Domäne 6
NICE: Chronic obstructive pulmonary disease in over 16s: diagnosis and management (update) 2010	UK	Quelleitlinie	85%	50%
NICE: Chronic obstructive pulmonary disease in over 16s: diagnosis and management – NICE guideline 2018	UK	Quelleitlinie	85%	75%
Global Initiative for Chronic Obstructive Lung Disease (GOLD) global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (Report 2018)	INT	Quelleitlinie, international	38%	50%
Global Initiative for Chronic Obstructive Lung Disease (GOLD) global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (Report 2020)	INT	Quelleitlinie, international	40%	42%
S2k-Leitlinie zur Diagnostik und Therapie von Patienten mit chronisch obstruktiver Bronchitis und Lungenemphysem (COPD)	DE	Referenzleitlinie	S2k	
Spirometrie	DE	Referenzleitlinie	S2k	
Tabakentwöhnung bei COPD	DE	Referenzleitlinie	S3	
Husten	DE	Referenzleitlinie	S3	
Tabakkonsum (Rauchen), abhängiger und schädlicher: Screening, Diagnostik und Behandlung	DE	Referenzleitlinie	S3	
Nichtinvasive und invasive Beatmung als Therapie der chronischen respiratorischen Insuffizienz	DE	Referenzleitlinie	S2k	
Langzeit-Sauerstofftherapie	DE	Referenzleitlinie, aktuell in Revision; selektiv eingebracht	S2k	
Nicht erholsamer Schlaf /Schlafstörungen - Schlafbezogene Atmungsstörungen	DE	Referenzleitlinie	S3	
Hausärztliche Leitlinie Multimedikation	DE	Referenzleitlinie	S2e	
Prolongiertes Weaning	DE	Referenzleitlinie	S2k	
Akuter und chronischer Husten, Diagnostik und Therapie von erwachsenen Patienten	DE	Referenzleitlinie	S2k	
Palliativmedizin für Patienten mit einer nicht heilbaren Krebserkrankung	DE	zurückgestellte Referenzleitlinie; für Kapitel Palliativmedizin, 3. Auflage NVL COPD		

Titel Suchergebnis	Land	Kommentar	DELBI Domäne 3	DELBI Domäne 6
Nichtinvasive Beatmung als Therapie der akuten respiratorischen Insuffizienz	DE	zurückgestellte Referenzleitlinie; für Kapitel Exazerbation, 3. Auflage NVL COPD	S3	
VA/DoD clinical practice guideline for the management of chronic obstructive pulmonary disease.	USA	Suche max. bis 2015, E für Diagnostik-Kapitel	65%	25%
Management of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline	EU/ USA	zurückgestellt; evtl. für Kapitel Exazerbationen, 3. Auflage NVL COPD	67%	25%
Prevention of COPD exacerbations: a European Respiratory Society/American Thoracic Society guideline	EU/ USA	zurückgestellt; evtl. für Kapitel Exazerbationen, 3. Auflage NVL COPD	63%	25%

#### Ausgeschlossene Leitlinien

Titel Suchergebnis	Land	A	Kommentar
Prevention of Acute Exacerbations of COPD: American College of Chest Physicians and Canadian Thoracic Society Guideline	USA/ CA	A4	Literaturrecherche bis 2013 durchgeführt.
Global Initiative for Chronic Obstructive Lung Disease (GOLD) global strategy on diagnosis, management, and prevention of COPD (Report 2017)	INT	A4	Aktualisierte Version verfügbar.
Institute for Clinical Systems Improvement (ICSI) Health Care Guideline: Diagnosis and Management of Chronic Obstructive Pulmonary Disease (COPD)	USA	A3	keine LL; behandelt andere Forschungsfragen.
National Institute for Health and Clinical Excellence (NICE) guideline on management of COPD in adults in primary and secondary care; Update 2012	UK	A4	Aktualisierte Version verfügbar.
Diagnosis and Pharmacotherapy of Stable Chronic Obstructive Pulmonary Disease: The Finnish Guidelines	FIN	A2	Methodische Bewertung nicht möglich; nur Auszug in Englisch verfügbar (MiniReview); Langfassung der Leitlinie nur in Finnisch.
The COPD X Plan: Australian and New Zealand Guidelines for the management of Chronic Obstructive Pulmonary Disease 2016	AUS	A7	Methodische Qualität AGREE II, Domäne 3: 10%.
Chronic Obstructive Pulmonary Disease (COPD): Diagnosis and Management	CA	A7	Methodische Qualität AGREE II, Domäne 3: 8%.
Clinical practice guideline for the treatment of patients with chronic obstructive pulmonary disease (COPD)	ESP	A3	Kein Diagnostik-Kapitel; methodische Begleitdokumente nur in Spanisch.
Diagnosis and Management of Chronic Obstructive Pulmonary Disease: The Swiss Guidelines	CHE	A7	Methodische Qualität Domäne 3: 8%; Domäne 6: 0%.
Lagerungstherapie und Frühmobilisation zur Prophylaxe oder Therapie von pulmonalen Funktionsstörungen	DE	A3	zu speziell für NVL.
Pneumonie, ambulant erworben, Behandlung und Prävention von erwachsenen Patienten	DE	A3	nicht COPD-relevant.

Titel Suchergebnis	Land	A	Kommentar
Epidemiologie, Diagnostik und Therapie erwachsener Patienten mit nosokomialer Pneumonie	DE	A3	zu speziell für NVL
Therapieempfehlungen der Arzneimittelkommission der deutschen Ärzteschaft 3. Auflage 2013 Atemwegsinfektionen	DE	A5	keine Leitlinie
Lungenzintigraphie	DE	A3	zu speziell für NVL
Legende der Ausschlussgründe: A1: Dopplung, A2: Sprache, A3: thematisch nicht passend, A4: Gültigkeit/ Veröffentlichungsdatum, A5: keine Leitlinie, A6: nicht erhältlich; A7: Qualität			

## Anhang 3.2 Cochrane Reviews bis 2017

### PICO-Fragestellung

Population: COPD

Intervention: keine Einschränkung

Vergleich: keine Einschränkung

Endpunkte: keine Einschränkung

Studientyp: Cochrane Reviews (Systematische Übersichtsarbeiten und Metaanalysen) und Protokolle

### Begründung für die Recherche

Ziel war es, qualitativ hochwertige systematische Übersichtsarbeiten für die Aktualisierung der NVL COPD, 2. Auflage zu identifizieren.

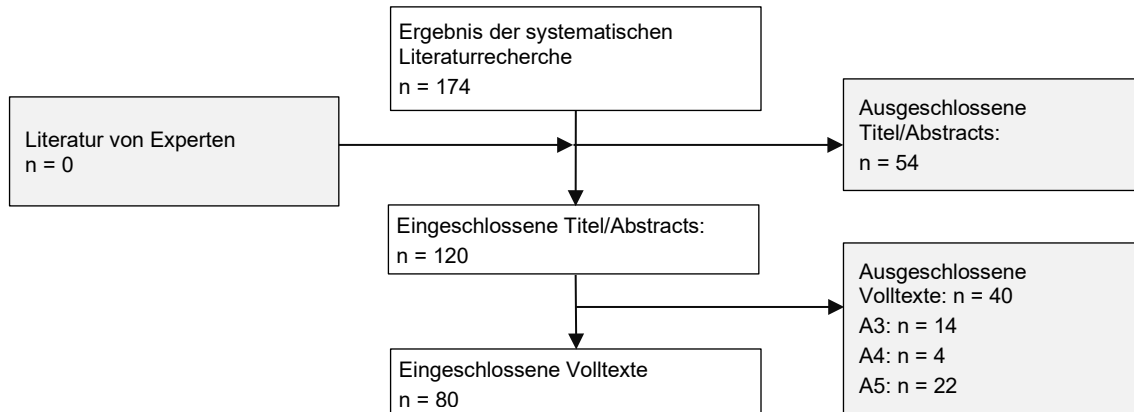
### Recherchestrategien

#### Datenbanken der Cochrane Library (4. September 2017)

Nr.	Suchfrage	Anzahl
#5	#1 or #2 or #3 or #4 in Cochrane Reviews (Reviews and Protocols)	174
#4	(obstruct*) near/3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*):ti (Word variations have been searched)	6172
#3	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	3428
#2	COAD:ti,ab,kw (Word variations have been searched)	48
#1	COPD:ti,ab,kw (Word variations have been searched)	10352
Cochrane Reviews		
•	Review	146
•	Protocol	28

**Anzahl der Treffer: 174**

Flussdiagramm:



Legende:

A3: andere Fragestellung

A4: abgelaufene Gültigkeit, neuere Version des Reviews bereits veröffentlicht

A5: Publikationstyp: Protokolle (vorläufig), Netzwerk-Metaanalyse

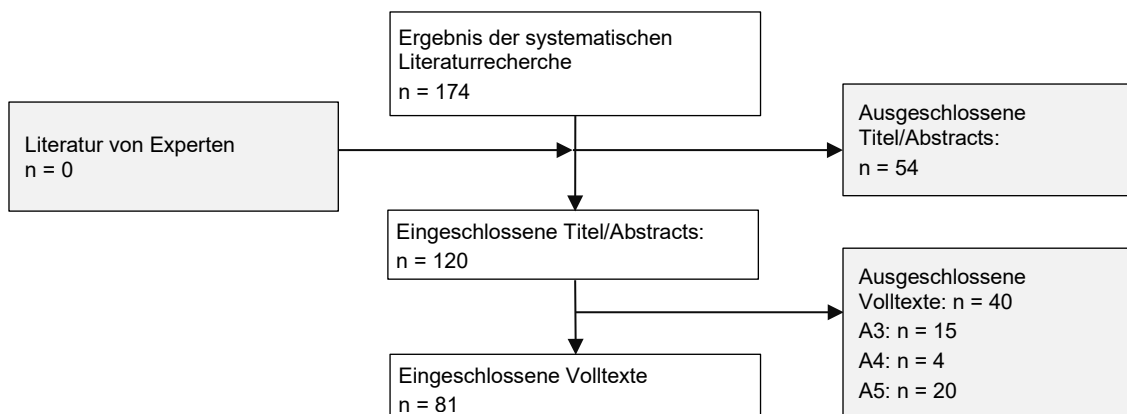
In der Literaturrecherche identifizierte und thematisch passende Protokolle wurden nach dem Volltext-Screening vorerst wieder als ausgeschlossen gekennzeichnet (n=21). Sobald diese als Reviews publiziert werden, wird erneut der Volltext geprüft, die AMSTAR-Bewertung durchgeführt und dementsprechend über Ein- bzw. Ausschluss entschieden.

Cochrane Reviews, welche sich inhaltlich mit Patient\*innen mit Bronchiektasen befassen, wurden A3 ausgeschlossen (n=13).

Cochrane Reviews 08/2018

Für die Arbeiten an den Kapiteln nichtmedikamentöse Therapie sowie Rehabilitation wurde der Publikationsstatus der zu diesen Themen passenden Protokolle (n=9) überprüft. 2 Reviews wurden mittlerweile veröffentlicht. Einer dieser Review [59] behandelt speziell Patient\*innen mit COPD, so dass ein bis dato vorläufig eingeschlossener Review [112], welcher COPD als Subgruppe untersuchte, nun ausgeschlossen werden konnte.

Flussdiagramm:



### Anhang 3.3 Cochrane Reviews 2017 – 2019

#### PICO-Fragestellung

**Population:** COPD

**Intervention:** keine Einschränkung

**Vergleich:** keine Einschränkung

**Endpunkte:** keine Einschränkung

**Studientyp:** Cochrane Reviews (Systematische Übersichtsarbeiten und Metaanalysen) und Protokolle

#### Begründung für die Recherche

Die im September 2017 durchgeführte Recherche zum Thema COPD in der Cochrane Library wurde wiederholt; eine Einschränkung des Suchzeitraumes von 09/2017 – 01/2019 wurde angewendet.

#### Recherchestrategie

##### Datenbanken der Cochrane Library (11. Januar 2019)

Komplettrecherche Update (Suchzeitraum 09/2017 – 01/2019):

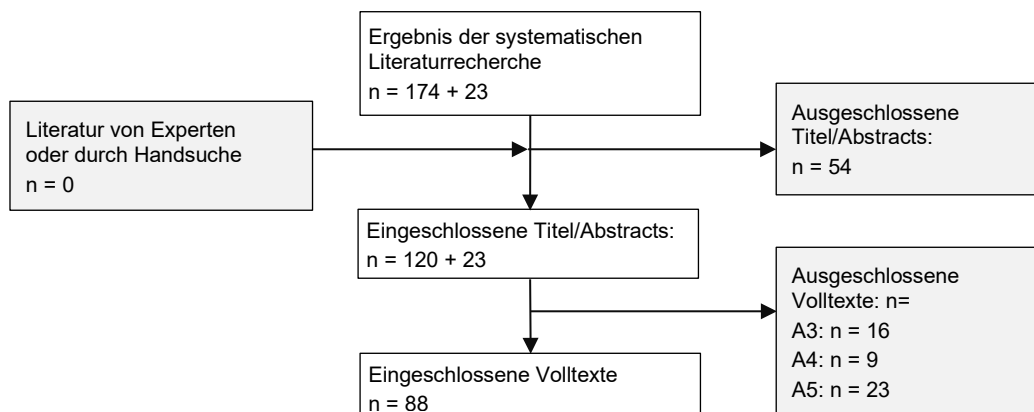
Nr.	Suchfrage	Anzahl
#5	<b>#1 or #2 or #3 or #4 with Cochrane Library publication date Between Sep 2017 and Jan 2019, in Cochrane Reviews, Cochrane Protocols</b>	<b>23</b>
#4	(obstruct*) near/3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*):ti (Word variations have been searched)	6074
#3	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4634
#2	(COAD):ti,ab,kw	63
#1	(COPD):ti,ab,kw	12057

Cochrane Reviews	
• Review	13
• Protocol	10

Für die n=13 identifizierten Reviews:

- 1/13 wurde neu gefunden, behandelt das Selbstmanagement bei Bronchiektasen und wird somit A3 ausgeschlossen.
- 7/13 sind publizierte Reviews, deren Protokolle in der 1. Recherche identifiziert wurden.
- 5/13 sind Update-Reviews, deren Vorgängerversionen ebenfalls bereits gefunden werden konnten.

#### Flussdiagramm:





## Anhang 3.4 Stellenwert der diagnostischen Verfahren

### PICO-Fragestellung

Population: Patient\*innen mit (Verdacht auf) COPD

Intervention: Spirometrie, DLCO, Bodyplethysmographie, Computertomographie

Vergleich: jegliche

Endpunkte: Testgüte; diagnostische Genauigkeit

Studientyp: Diagnostische Studien, systematische Übersichtsarbeiten

### Recherchestrategien

Der McMaster (2) –Filter für diagnostische Studien wurde in dieser Recherche angewendet.

#### Medline via Pubmed (www.pubmed.gov) (08.06.2018)

Nr.	Suchfrage	Anzahl
#21	Search ((#17 AND #19) NOT #20)	2057
#20	Search (#17 AND #18)	285
#19	Search (sensitiv*[Title/Abstract] OR sensitivity and specificity[MeSH Terms] OR (predictive[Title/Abstract] AND value*[Title/Abstract]) OR predictive value of tests[MeSH Term] OR accuracy*[Title/Abstract])	1830262
#18	Search systematic[sb]	365593
#17	Search (#7 AND #16)	15134
#16	Search (#8 OR #9 OR #11 OR #12 OR #13 OR #14 OR #15)	673350
#15	Search ((Computed OR Computerized OR "Computer Assisted" OR x-ray OR xray) AND tomography[tiab] OR CT[tiab] OR CT-scan OR "CAT scan" OR CAT-scan OR "Electron Beam Tomography" OR MDCT OR MSCT OR multi-detector OR "multi detector" OR multidetector OR multi-slice OR "multi slice" OR multislice	634520
#14	Search "Tomography, X-Ray Computed"[Mesh]	381065
#13	Search "Body plethysmography"[tiab] OR "Bodyplethysmography"[tiab]	1726
#12	Search "Plethysmography, Whole Body"[Mesh]	1800
#11	Search "lung diffusion"[tiab] OR "diffusion capacity" [tiab] OR "diffusing capacity"[tiab] OR "diffusion lung capacity" [tiab] OR "transfer factor" [tiab] OR "DLCO"[tiab] OR "TLCO"[tiab]	9206
#10	Search "Pulmonary Diffusing Capacity"[Mesh]	3675
#9	Search spirometr*[tiab]	19399
#8	Search "spirometry"[Mesh]	20552
#7	Search (#1 OR #2 OR #3 OR #4 OR #5 OR #6)	96369
#6	Search "Air trapping"[tiab] OR airtrapping[tiab]	1210
#5	Search COAD [tiab]	260
#4	Search COPD[tiab]	38713
#3	Search Emphysem*[tiab]	25581
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	48371
#1	Search ((chronic*[tiab] AND ((obstruct*[tiab] AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab])))	53298

**Anzahl der Treffer: Aggregierte Evidenz: 285; Diagnostische Studien: 2057**

## Datenbanken der Cochrane Library (08.06.2018)

Nr.	Suchfrage	Anzahl
<b>#43</b>	<b>#36 and #42 in Cochrane Reviews (Reviews and Protocols), Other Reviews, Trials and Technology Assessments</b>	<b>259</b>
#42	#37 or #38 or #39 or #40 or #41	85211
#41	(predictive and value*):ti,ab,kw (Word variations have been searched)	16587
#40	MeSH descriptor: [Predictive Value of Tests] explode all trees	7863
#39	accuracy*:ti,ab,kw (Word variations have been searched)	20958
#38	sensitiv*:ti,ab,kw (Word variations have been searched)	62756
#37	MeSH descriptor: [Sensitivity and Specificity] explode all trees	19485
#36	#9 and #35	2581
#35	#10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 #33 or #34	98092
#34	(MDCT or MSCT):ti,ab,kw	464
#33	(multi-detector or "multi detector" or multidetector or multi-slice or "multi slice" or multislice):ti,ab,kw (Word variations have been searched)	1159
#32	"Electron Beam Tomography":ti,ab,kw (Word variations have been searched)	34
#31	"CAT scan":ti,ab,kw (Word variations have been searched)	18
#30	CT-scan:ti,ab,kw (Word variations have been searched)	3444
#29	CT:ti,ab,kw	86283
#28	"Xray tomography":ti,ab,kw (Word variations have been searched)	0
#27	"x-ray tomography":ti,ab,kw (Word variations have been searched)	12
#26	"Computer Assisted tomography":ti,ab,kw (Word variations have been searched)	4897
#25	"Computerized tomography":ti,ab,kw (Word variations have been searched)	657
#24	"Computed tomography":ti,ab,kw (Word variations have been searched)	9682
#23	MeSH descriptor: [Tomography, X-Ray Computed] explode all trees	5664
#22	"Bodyplethysmography":ti,ab,kw (Word variations have been searched)	24
#21	"Body plethysmography":ti,ab,kw (Word variations have been searched)	229
#20	MeSH descriptor: [Plethysmography, Whole Body] explode all trees	95
#19	TLCO:ti,ab,kw	38
#18	DLCO:ti,ab,kw	376
#17	"transfer factor":ti,ab,kw (Word variations have been searched)	196
#16	"diffusion lung capacity":ti,ab,kw (Word variations have been searched)	6
#15	"diffusing capacity":ti,ab,kw (Word variations have been searched)	382
#14	"diffusion capacity":ti,ab,kw (Word variations have been searched)	360
#13	"lung diffusion":ti,ab,kw (Word variations have been searched)	289
#12	MeSH descriptor: [Pulmonary Diffusing Capacity] explode all trees	121
#11	spirometry:ti,ab,kw (Word variations have been searched)	4504
#10	MeSH descriptor: [Spirometry] explode all trees	1625
#9	#1 or #2 or #3 or #4 or #7 or #8	17799
#8	("air trapping" or airtrapping):ti,ab,kw (Word variations have been searched)	99
#7	(#6 and chronic*):ti,ab,kw	12332
#6	(#5 and obstruct*):ti,ab,kw	18192
#5	(pulmonary or lung* or airway* or airflow* or bronchi* or respirat*):ti,ab,kw (Word variations have been searched)	121055

Nr.	Suchfrage	Anzahl
#4	Emphysem*:ti,ab,kw (Word variations have been searched)	1228
#3	COAD:ti,ab,kw	51
#2	COPD:ti,ab,kw	12534
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	5044

Cochrane Reviews	
• Review	0
• Protocol	0
Other Reviews	1
Trials	258
Methods Studies	Nicht gesucht
Technology Assessment	0
Economic Evaluations	Nicht gesucht
Cochrane Groups	Nicht gesucht

Anzahl der Treffer: 259

### Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz	285	1	286
Diagnostische Studien/ Trials	2057	258	2315
<b>Gesamt</b>			<b>2601</b>

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

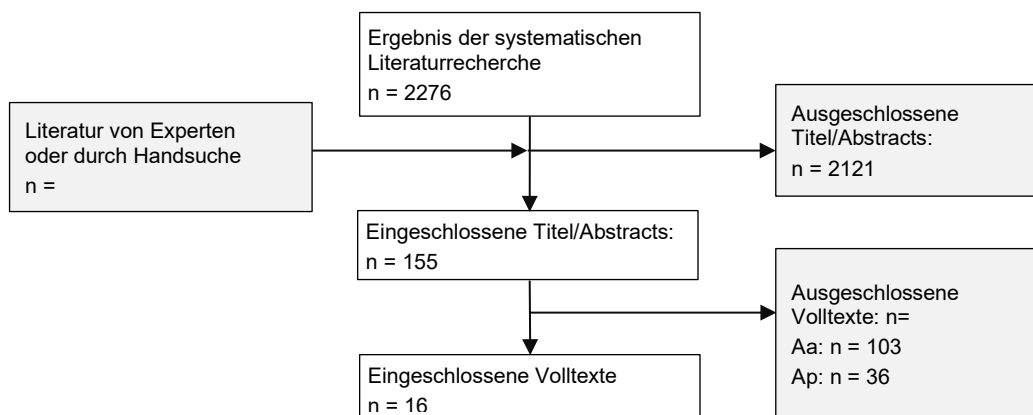
A1 (Dubletten): 137

A2 (nicht englisch/deutsch): 145

A3 (Conference Abstracts): 43

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 2276**

Flussdiagramm:



Aa: andere Fragestellung; Ap: Publikationstyp nicht passend

## Anhang 3.5 Über-/Unterdiagnose

### PICO-Fragestellung

Population: Patient\*innen mit COPD bzw. mit Verdacht auf COPD

Intervention: jegliche

Vergleich: jegliche

Endpunkte: Über- und Unterdiagnose

Studientyp: Kohortenstudien, systematische Übersichtsarbeiten, keine Eingrenzung des Suchzeitraumes

### Recherchestrategien

Gesucht wurde nach möglicher Über- bzw. Unterdiagnose einer COPD im Rahmen der verschiedenen diagnostischen Verfahren. Insbesondere die Nutzung verschiedener Referenzwerte soll näher beleuchtet werden. Der SIGN-Filter für Kohortenstudien wurde in dieser Recherche angewendet.

#### Medline via Pubmed ([www.pubmed.gov](http://www.pubmed.gov)) (06.06.2018)

Nr.	Suchfrage	Anzahl
#30	Search (((#23 AND #27) NOT (#28 OR #29))) - Beobachtungsstudien	927
#29	Search ((#23 AND #25) NOT #28) - RCTs	239
#28	Search (#23 AND #24) – aggregierte Evidenz	144
#27	Search (((((((("Case-Control Studies"[Mesh] OR "Cohort Studies"[Mesh])) OR "Cross-Sectional Studies"[Mesh]) OR ("Follow-Up Studies"[Mesh] OR ("follow-up" OR "follow up") AND (studies OR study)))))) OR ((longitudinal[tw] OR retrospective[tw] OR "cross-sectional"[tw] OR "cross sectional"[tw])) OR ("case control"[tw] OR (cohort[tw] AND analy*[tw])) OR "Observational Study"[pt]))	2767403
#25	Search (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic" [MeSH Terms:noexp] OR randomly [tiab] OR trial [ti])	1160741
#24	Search systematic[sb]	365316
#23	Search (#7 AND #22)	3149
#22	Search (#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21)	500488
#21	Search ((Accuracy[tiab] OR Inaccuracy[tiab] OR Inadequate[tiab] OR Improper[tiab] OR Incorrect[tiab] OR Imprecise[tiab] OR Erroneous[tiab]) AND diagnos*[tiab])	113990
#20	Search Validit*[tiab]	150189
#19	Search "False negative" [tiab]	25493
#18	Search Under-diagnos*[tiab]	2929
#17	Search Underdiagnos*[tiab]	7921
#16	Search "False positive" [tiab]	43517
#15	Search Overdetection[tiab]	95
#14	Search Mis-diagnos*[tiab]	183
#13	Search Misdiagnos*[tiab]	27986
#12	Search Overdiagnos*[tiab]	3431
#11	Search "diagnostic error"[tiab]	1239
#10	Search "Diagnostic Errors"[Mesh]	109206
#9	Search Overestim*[tiab]	33606
#8	Search Underestim*[tiab]	56642
#7	Search (#1 OR #2 OR #3 OR #4 OR #5 OR #6)	96331

Nr.	Suchfrage	Anzahl
#6	Search "Air trapping"[tiab] OR airtrapping[tiab]	1210
#5	Search COAD[tiab]	260
#4	Search COPD[tiab]	38687
#3	Search Emphysem*[tiab]	25576
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	48354
#1	Search ((chronic*[tiab]) AND ((obstruct*[tiab]) AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab])))	53267

**Anzahl der Treffer: aggregierte Evidenz: 144; RCTs 239; Beobachtungsstudien: 927**

**Datenbanken der Cochrane Library (06.06.2018)**

Nr.	Suchfrage	Anzahl
<b>#26</b>	<b>(#9 and #25) not "conference abstract":pt in Cochrane Reviews (Reviews and Protocols), Other Reviews, Trials, Methods Studies and Technology Assessments</b>	<b>357</b>
#25	#10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24	46333
#24	Overestimat*:ti,ab,kw (Word variations have been searched)	1797
#23	Underestimat*:ti,ab,kw (Word variations have been searched)	2268
#22	(#21 and diagnos*):ti,ab,kw (Word variations have been searched)	12801
#21	(Accuracy or Inaccuracy or Inadequate or Improper or Incorrect or Imprecise or Erroneous):ti,ab,kw (Word variations have been searched)	31255
#20	Validit*:ti,ab,kw (Word variations have been searched)	8866
#19	"False negative":ti,ab,kw (Word variations have been searched)	1554
#18	Under-diagnos*:ti,ab,kw (Word variations have been searched)	123
#17	Underdiagnos*:ti,ab,kw (Word variations have been searched)	196
#16	"False positive":ti,ab,kw (Word variations have been searched)	2414
#15	Overdetection:ti,ab,kw (Word variations have been searched)	20
#14	Mis-diagnos*:ti,ab,kw (Word variations have been searched)	3
#13	Misdiagnos*:ti,ab,kw (Word variations have been searched)	375
#12	Overdiagnos*:ti,ab,kw (Word variations have been searched)	221
#11	"diagnostic error*":ti,ab,kw (Word variations have been searched)	648
#10	MeSH descriptor: [Diagnostic Errors] explode all trees	3093
#9	#1 or #2 or #3 or #4 or #7 or #8	17788
#8	("air trapp*" or airtrapp*):ti,ab,kw (Word variations have been searched)	88
#7	(#6 and chronic*):ti,ab,kw	12332
#6	(#5 and obstruct*):ti,ab,kw	18192
#5	(pulmonary or lung* or airway* or airflow* or bronchi* or respirat*):ti,ab,kw (Word variations have been searched)	121055
#4	Emphysem*:ti,ab,kw (Word variations have been searched)	1228
#3	COAD:ti,ab,kw	51
#2	COPD:ti,ab,kw	12534
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	5044

Cochrane Reviews	
• Review	14
• Protocol	1
Other Reviews	0
Trials	337
Methods Studies	4
Technology Assessment	1
Economic Evaluations	Nicht gesucht
Cochrane Groups	Nicht gesucht

**Anzahl der Treffer: 357**

### Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz	144	16	160
RCTs	239	341	1507
Beobachtungsstudien	927		
<b>Summe</b>			<b>1667</b>

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 168

A2 (nicht englisch/deutsch): 84

A3 (Conference Abstracts/Poster): 13

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 1402**

### Kriterien für Ein- und Ausschluss

Einschluss: Fragestellung passend; Systematic Review; Randomisierte kontrollierte Studien (RCT)

Ez: zurückgestellt. mit Experten diskutieren

Ausschluss

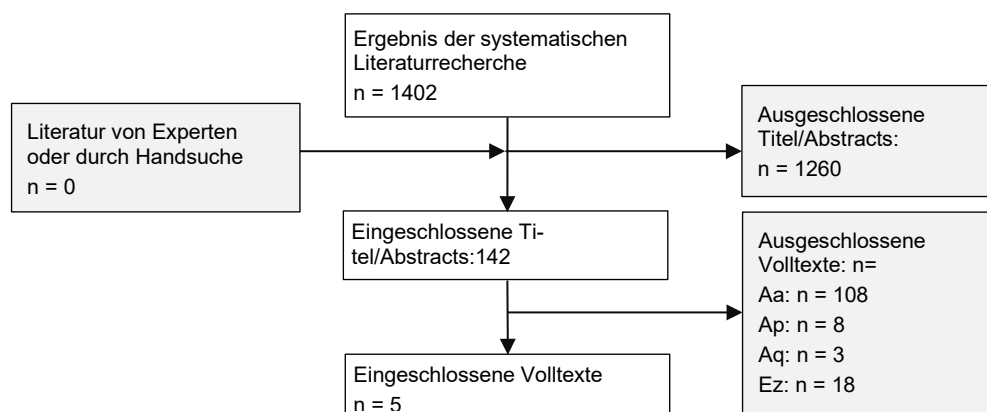
Aa: thematisch nicht passend: andere Erkrankung, andere Fragestellung, anderes Thema Verwendung anderer Equations als GLI-Referenzwerte (Bsp: NHANRS II reference equation)

Ap: Publikationstyp nicht passend: nicht-systematischer (narrativer) Review, Primärstudien (RCT, Kohorten etc.), Editorials, Kommentare, Letter etc., Guidelines

Aq: schwache methodische Qualität

Cross-over-Studien wurden in die Ergebnisse mit einbezogen. Vergleichsstudien, welche andere Referenzwerte als die GLI-Werte von 2012 für die spirometrische Beurteilung nutzen, wurden Aa ausgeschlossen. Ebenso wurden Studien, welche ausschließlich prebronchodilatatorische Werte betrachten Aa ausgeschlossen.

Flussdiagramm



Anhang 3.6 Phänotypisierung mittels Computertomographie

PICO-Fragestellung

Population: Patient\*innen mit COPD

Intervention: Computertomographie

Vergleich: jegliche

Endpunkte: Phänotypisierung der COPD

Studientyp: diagnostische Studien, aggregierte Evidenz, ggf. Beobachtungsstudien

Recherchestrategien

Die Spirometrie als Comparator wurde nicht mit einbezogen, da sich diese zu restriktiv in der Recherche auswirkte. Der McMaster (2) –Filter für diagnostische Studien wurde in dieser Recherche angewendet.

Medline via Pubmed (www.pubmed.gov) (18.06.2018)

Nr.	Suchfrage	Anzahl
#19	Search (#15 AND #17) NOT #18	145
#18	Search #15 AND #16	6
#17	Search sensitiv*[Title/Abstract] OR sensitivity and specificity[MeSH Terms] OR (predictive[Title/Abstract] AND value*[Title/Abstract]) OR predictive value of tests[MeSH Term] OR accuracy*[Title/Abstract]	1832919
#16	Search systematic[sb]	366468
#15	Search (#6 AND #14)	724
#14	Search (#9 AND #13)	28332
#13	Search ((#10 AND #11) OR #12)	1158158
#12	Search (morpholog*[tiab] OR phenotyp*[tiab] OR subtyp*[tiab])	1157574
#11	Search (focal[tiab] OR panacin*[tiab] OR panlobul*[tiab] OR centriacin*[tiab] OR centrilobul* OR parasept*[tiab])	142051
#10	Search (Emphysem*[tiab] OR "Pulmonary Emphysema"[Mesh])	30207
#9	Search (#7 OR #8)	635548
#8	Search ((Computed OR Computerized OR "Computer Assisted" OR x-ray OR xray) AND tomography[tiab] OR CT[tiab] OR CT-scan OR "CAT scan" OR CAT-scan OR "Electron Beam Tomography" OR MDCT OR MSCT OR multi-detector OR "multi detector" OR multidetector OR multi-slice OR "multi slice" OR multislice	635548
#7	Search "Tomography, X-Ray Computed"[Mesh]	381691
#6	Search #1 OR #2 OR #3 OR #4 OR #5	84586

Nr.	Suchfrage	Anzahl
#5	Search "Air trapping"[tiab] OR airtrapping[tiab]	1210
#4	Search COAD[tiab]	260
#3	Search COPD[tiab]	38797
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	48477
#1	Search (chronic*[tiab]) AND ((obstruct*[tiab]) AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab]))	53390

Anzahl der Treffer: Aggregierte Evidenz: 6; Diagnostische Studien: 145

#### Datenbanken der Cochrane Library (18.06.2018)

Nr.	Suchfrage	Anzahl
#34	<b>(#29 and #33) not "conference abstract":pt in Cochrane Reviews (Reviews and Protocols), Other Reviews, Trials and Technology Assessments</b>	<b>8</b>
#33	#30 or #31 or #32	85212
#32	((predictive and value* or accuracy* or sensitiv*):ti,ab,kw (Word variations have been searched)	84708
#31	MeSH descriptor: [Predictive Value of Tests] explode all trees	7863
#30	MeSH descriptor: [Sensitivity and Specificity] explode all trees	19485
#29	#8 and #28	70
#28	#21 and #27	1953
#27	(#24 and #25) or #26	16944
#26	(subtyp* or phenotyp* or morpholog*):ti,ab,kw (Word variations have been searched)	16940
#25	(parasep* or centrilobu* or centriacin* or panlobul* or panacin* or focal):ti,ab,kw (Word variations have been searched)	3581
#24	#22 or #23	1228
#23	MeSH descriptor: [Pulmonary Emphysema] explode all trees	292
#22	Emphysem*:ti,ab,kw	1228
#21	#9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20	93346
#20	(MDCT or MSCT):ti,ab,kw	464
#19	(multi-detector or "multi detector" or multidetector or multi-slice or "multi slice" or multislice):ti,ab,kw (Word variations have been searched)	1159
#18	"Electron Beam Tomography":ti,ab,kw (Word variations have been searched)	34
#17	"CAT scan":ti,ab,kw (Word variations have been searched)	18
#16	CT-scan:ti,ab,kw (Word variations have been searched)	3444
#15	CT:ti,ab,kw	86283
#14	"Xray tomography":ti,ab,kw (Word variations have been searched)	0
#13	"x-ray tomography":ti,ab,kw (Word variations have been searched)	12
#12	"Computer Assisted tomography":ti,ab,kw (Word variations have been searched)	4897
#11	"Computerized tomography":ti,ab,kw (Word variations have been searched)	657
#10	"Computed tomography":ti,ab,kw (Word variations have been searched)	9683
#9	MeSH descriptor: [Tomography, X-Ray Computed] explode all trees	5664
#8	#1 or #2 or #3 or #6 or #7	17253
#7	("air trapping" or airtrapping):ti,ab,kw (Word variations have been searched)	99
#6	(#5 and chronic*):ti,ab,kw	12332
#5	(#4 and obstruct*):ti,ab,kw	18193



Nr.	Suchfrage	Anzahl
#4	(pulmonary or lung* or airway* or airflow* or bronchi* or respirat*):ti,ab,kw (Word variations have been searched)	121058
#3	COAD:ti,ab,kw	51
#2	COPD:ti,ab,kw	12534
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	5044

Cochrane Reviews	
• Review	0
• Protocol	0
Other Reviews	0
Trials	8
Methods Studies	Nicht gesucht
Technology Assessment	0
Economic Evaluations	Nicht gesucht
Cochrane Groups	Nicht gesucht

Anzahl der Treffer: 8 Trials

### Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz	6	0	6
Diagnostische Studien/Trials	145	8	153
<b>Gesamt</b>			<b>159</b>

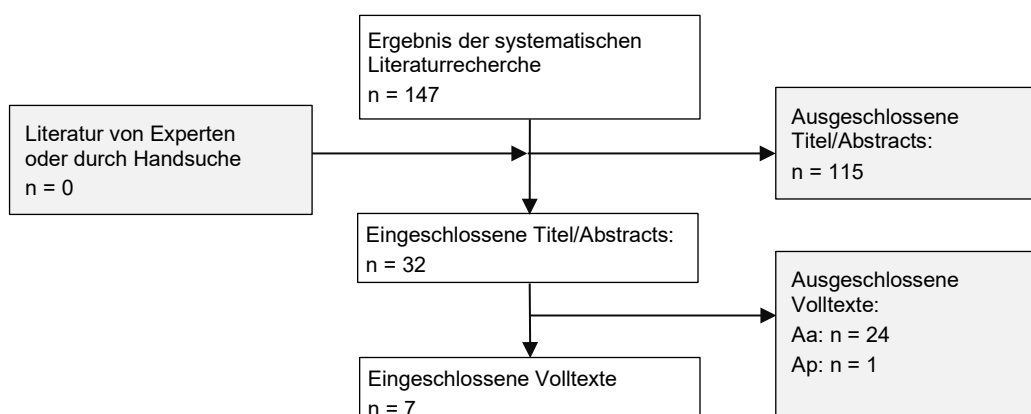
Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 7

A2 (nicht englisch/deutsch): 5

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 147**

### Flussdiagramm:



## Anhang 3.7 Cut-Off Symptomerfassung

### PICO-Fragestellung

Population: Patient\*innen mit COPD oder Verdacht auf COPD

Intervention: mMRC, CAT, CCQ, SGRQ

Vergleich: jegliche

Endpunkte: Cut Off für die Einschätzung: schwere vs. mittlere/geringe Symptomatik

Studientyp: Aggregierte Evidenz, RCTs, sonstige Primärpublikationen

### Recherchestrategien

#### Medline via Pubmed (www.pubmed.gov) (14.06.2018)

Nr.	Suchfrage	Anzahl
#15	Search (#10 NOT (#13 OR #14)) – Sonstige Primärpublikationen	168
#14	Search ((#10 AND #12) NOT #13) – RCT	33
#13	Search (#10 AND #11) – Aggregierte Evidenz	14
#12	Search (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic" [MeSH Terms:noexp] OR randomly [tiab] OR trial [ti])	1162149
#11	Search systematic[sb]	366144
#10	Search (#7 AND #8 AND #9)	215
#9	Search (Cutoff[tiab] OR "cut off" [tiab] OR cut-off[tiab] OR cut-score[tiab] OR cut-scores[tiab] OR "cut score" [tiab] OR "cut scores" [tiab] OR cut-point[tiab] OR cut-points[tiab] OR cutpoint[tiab] OR cutpoints[tiab] OR "cut point" [tiab] OR "cut points" [tiab] OR threshold[tiab] OR thresholds[tiab])	309594
#8	Search ((Symptom*[tiab] AND (test[tiab] OR Questionnaire*[tiab])) OR mMRC[tiab] OR "modified Medical Research Council" [tiab] OR (COPD[tiab] AND Clinical[tiab] AND Questionnaire[tiab]) OR CCQ[tiab] OR "Respiratory Questionnaire" [tiab] OR SGRQ[tiab] OR "COPD assessment test" [tiab] OR CAT[tiab])	255882
#7	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6	96456
#6	Search "Air trapping"[tiab] OR airtrapping[tiab]	1210
#5	Search COAD [tiab]	260
#4	Search COPD[tiab]	38765
#3	Search Emphysem*[tiab]	25595
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	48448
#1	Search ((chronic*[tiab] AND ((obstruct*[tiab] AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab])))	53348

Anzahl der Treffer: Sonstige Primärpublikationen: 168; RCT: 33; Aggregierte Evidenz: 14

#### Datenbanken der Cochrane Library (14.06.2018)

Nr.	Suchfrage	Anzahl
#15	(#9 and #13 and #14) not "conference abstract":pt in Cochrane Reviews (Reviews and Protocols), Other Reviews, Trials and Technology Assessments	65
#14	(Cutoff or "cut off" or cut-off or cut-score or cut-scores or "cut score" or "cut scores" or cut-point or cut-points or cutpoint or cutpoints or "cut point" or "cut points" or threshold or thresholds):ti,ab,kw (Word variations have been searched)	25680
#13	#10 or #11 or #12	50207
#12	(symptom* and (test or questionnaire)):ti,ab,kw (Word variations have been searched)	47674
#11	(COPD and Clinical and Questionnaire):ti,ab,kw (Word variations have been searched)	940

Nr.	Suchfrage	Anzahl
#10	(mMRC or "modified Medical Research Council" or CCQ or "Respiratory Questionnaire" or SGRQ or "COPD assessment test" or CAT):ti,ab,kw (Word variations have been searched)	3095
#9	#1 or #2 or #3 or #4 or #7 or #8	17799
#8	("air trapping" or airtrapping):ti,ab,kw (Word variations have been searched)	99
#7	(#6 and chronic*):ti,ab,kw	12332
#6	(#5 and obstruct*):ti,ab,kw	18193
#5	(pulmonary or lung* or airway* or airflow* or bronchi* or respirat*):ti,ab,kw (Word variations have been searched)	121057
#4	Emphysem*:ti,ab,kw (Word variations have been searched)	1228
#3	COAD:ti,ab,kw	51
#2	COPD:ti,ab,kw	12534
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	5044

Cochrane Reviews	
• Review	2
• Protocol	0
Other Reviews	0
Trials	63
Methods Studies	Nicht gesucht
Technology Assessment	0
Economic Evaluations	Nicht gesucht
Cochrane Groups	Nicht gesucht

### Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz	14	2	16
RCTs	33	63	96
Sonstige Primär	168		168
<b>Gesamt</b>			<b>280</b>

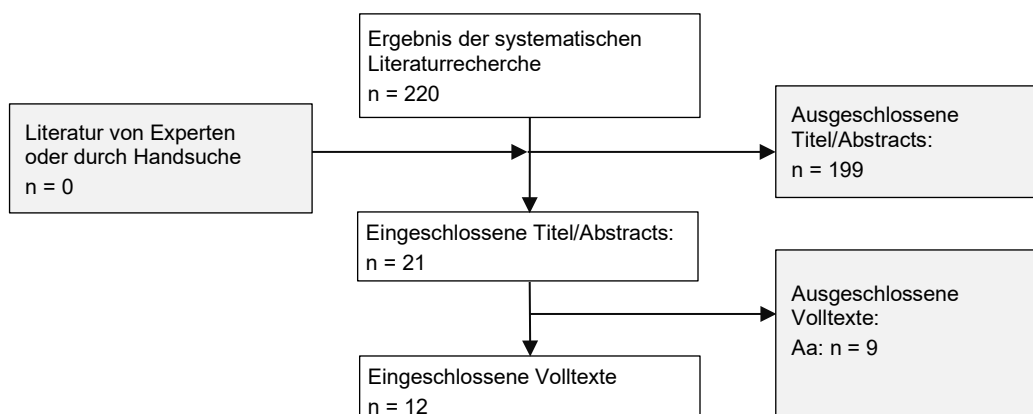
Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 41

A2 (nicht englisch/deutsch): 19

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 220**

Flussdiagramm:



Anhang 3.8 Angst/Depression

PICO-Fragestellung

Population: Patient\*innen mit COPD

Intervention: jegliche

Vergleich: jegliche

Endpunkte: Prävalenz/Koinzidenz von Angst und/oder Depression oder anderer psychischer Erkrankungen

Studientyp: systematische Übersichtsarbeiten, Beobachtungsstudien

Recherchestrategien

Der SIGN –Filter für Kohortenstudien wurde in dieser Recherche angewendet.

Medline via Pubmed ([www.pubmed.gov](http://www.pubmed.gov)) (29.08.2018)

Nr.	Suchfrage	Anzahl
#22	Search (#18 AND #20) NOT #21	353
#21	Search #18 AND #19	36
#20	Search (((((((("Case-Control Studies"[Mesh] OR "Cohort Studies"[Mesh])) OR "Cross-Sectional Studies"[Mesh]) OR ("Follow-Up Studies"[Mesh] OR ("follow-up" OR "follow up") AND (studies OR study)))))) OR ((longitudinal[tw] OR retrospective[tw] OR "cross-sectional"[tw] OR "cross sectional"[tw])) OR ("case control"[tw] OR (cohort[tw] AND analy*[tw])) OR "Observational Study"[pt]))	2815319
#19	Search systematic[sb]	374475
#18	Search #7 AND #14 AND #17	693
#17	Search #15 OR #16	618401
#16	Search "Prevalence"[Mesh]	256347
#15	Search Prevalence[tiab]	540197
#14	Search #8 OR #9 OR #10 OR #11 OR #12 OR #13	1392228
#13	Search Depressi*[tiab]	343143
#12	Search Anxiety[tiab]	163685
#11	Search "psychic disorder*[tiab]	60
#10	Search "Psychiatric disorder*[tiab]	8503
#9	Search "Mental Disorder*[tiab]	7535
#8	Search "Mental Disorders"[Mesh]	1132505
#7	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6	97641

Nr.	Suchfrage	Anzahl
#6	Search "Air trapping"[tiab] OR airtrapping[tiab]	1219
#5	Search COAD[tiab]	265
#4	Search COPD[tiab]	39462
#3	Search Emphysem*[tiab]	25766
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	49141
#1	Search ((chronic*[tiab]) AND ((obstruct*[tiab]) AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab])))	54152

Anzahl der Treffer: aggregierte Evidenz: 36; Beobachtungsstudien: 353

Datenbanken der Cochrane Library (29.08.2018)

Nr.	Suchfrage	Anzahl
#19	(#8 and #15 and #18) not "conference abstract":pt in Cochrane Reviews, Trials	56
#18	#16 or #17	34633
#17	MeSH descriptor: [Prevalence] explode all trees	4617
#16	(Prevalence):ti,ab,kw (Word variations have been searched)	34633
#15	#9 or #10 or #11 or #12 or #13 or #14	117770
#14	(Depressi*):ti,ab,kw (Word variations have been searched)	57699
#13	(Anxiety):ti,ab,kw (Word variations have been searched)	34392
#12	("Psychiatric disorder*"):ti,ab,kw (Word variations have been searched)	1770
#11	("Psychic disorder*"):ti,ab,kw (Word variations have been searched)	9
#10	("Mental Disorder*"):ti,ab,kw (Word variations have been searched)	6488
#9	MeSH descriptor: [Mental Disorders] explode all trees	61453
#8	#1 or #2 or #3 or #4 or #6 or #7	17528
#7	("air trapping" or airtrapping):ti,ab,kw (Word variations have been searched)	112
#6	((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*):ti,ab,kw (Word variations have been searched)	12022
#5	(pulmonary or lung* or airway* or airflow* or bronchi* or respirat*):ti,ab,kw (Word variations have been searched)	119726
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1214
#3	(COAD):ti,ab,kw	60
#2	(COPD):ti,ab,kw	12512
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4562

Cochrane Reviews	3
Trials	53

Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
<b>Aggregierte Evidenz</b>	36	3	39
<b>RCTs</b>		53	53
<b>Sonstige Primär</b>	353		353
<b>Gesamt</b>			<b>445</b>

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 12

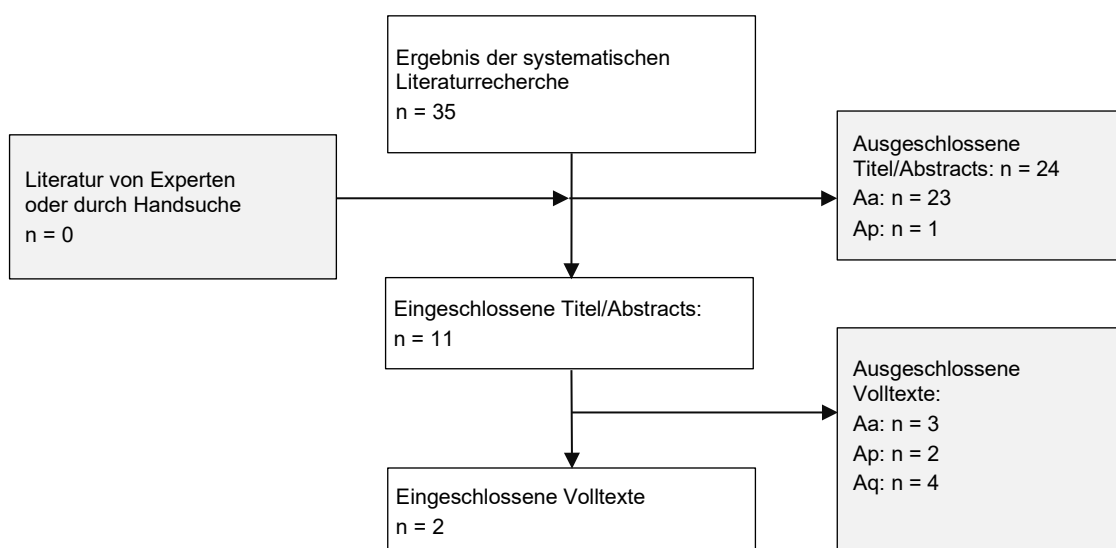
A2 (nicht englisch/deutsch): 12

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 421**

- aggregierte Evidenz: n=35
- Primärstudien: n=386

**Flussdiagramm aggregierte Evidenz**

Es wurden zunächst im Rahmen eines iterativen Vorgehens die Publikationen der aggregierten Evidenz gescreent. Der folgende Flowchart bezieht sich auf n=35 identifizierte aggregierte Evidenzen:



**Anhang 3.9 Rauchentwöhnung bei COPD: Update-Recherche**

**Fragestellung des Cochrane-Reviews [15]**

To evaluate the effectiveness of behavioural or pharmacological smoking cessation interventions, or both, in smokers with COPD.

**Recherchestrategien**

Professor Kotz (Mitglied der NVL COPD-Leitliniengruppe und Letztautor des 2016 aktualisierten Cochrane Reviews: van Eerd 2016; Smoking cessation for people with chronic obstructive pulmonary disease. {van Eerd 2016: 27017}) nahm Kontakt mit der Cochrane Airways Group auf, um die zuletzt im März 2016 durchgeführte Suche für diesen Review erneut durchführen zu lassen.

Für ein Suchupdate wurde die damals verwendete Suchstrategie seitens der Cochrane Airways Group erneut umgesetzt. Die Ergebnisse dieser Update-Suche (durchgeführt am 17.09.2019; n=143 Treffer) wurden dem ÄZQ im RIS-Format zur Verfügung gestellt. Das Titel/Abstract-Screening zur Update-Recherche wurde durch das ÄZQ durchgeführt werden.

**Medline search strategy used to identify trials for the CAGR (17.September 2019)**

Nr.	Suchfrage
1	Lung Diseases, Obstructive/
2	exp Pulmonary Disease, Chronic Obstructive/
3	emphysema\$.mp.
4	(chronic\$ adj3 bronchiti\$).mp.
5	(obstruct\$ adj3 (pulmonary or lung\$ or airway\$ or airflow\$ or bronch\$ or respirat\$)).mp.

Nr.	Suchfrage
6	COPD.mp.
7	COAD.mp.
8	COBD.mp.
9	AECB.mp.
10	or/1-9

Übernommen aus [15].

**Filter to identify RCTs**

Nr.	Suchfrage
1	exp “clinical trial [publication type]”/
2	(randomised or randomised).ab,ti.
3	placebo.ab,ti.
4	dt.fs.
5	randomly.ab,ti.
6	trial.ab,ti.
7	groups.ab,ti.
8	or/1-7
9	Animals/
10	Humans/
11	9 not (9 and 10)
12	8 not 11

Übernommen aus [15].

**Search strategy for the Cochrane Airways Group Register (17.September 2019)**

Nr.	Suchfrage
1	MeSH DESCRIPTOR Pulmonary Disease, Chronic Obstructive Explode All
2	MeSH DESCRIPTOR Bronchitis, Chronic
3	(obstruct*) near3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*)
4	COPD:MISC1
5	(COPD OR COAD OR COBD):TI,AB,KW
6	#1 OR #2 OR #3 OR #4 OR #5
7	MeSH DESCRIPTOR Smoking
8	MeSH DESCRIPTOR Smoking Cessation
9	MeSH DESCRIPTOR Tobacco
10	MeSH DESCRIPTOR Tobacco Use Disorder
11	MeSH DESCRIPTOR Tobacco Use Cessation
12	MeSH DESCRIPTOR Nicotine
13	((nicotin* or tobacco or smok* or cigarette*) NEAR5 (replac* or cessat* or ceas* or control* or quit* or stop* or abstin* or abstain* or self-help* or “self help*” or behaviour* or behavior* or educat* or counsel* or support* or advice or treatment* or intervention*)): ti,ab,kw
14	“nicotine replacement therapy” or NRT
15	(nicotin*) NEAR3 (gum or patch or inhal* or nasal* or spray or lozenge* or polacrilex or agonist* or vaccin*)

Nr.	Suchfrage
16	Varenicline
17	Champix
18	Chantix
19	Bupropion
20	Zyban
21	Nortriptyline
22	Nortrilen
23	(nicotin* or tobacco or smok* or cigarette*) NEAR5 (antidepressant*)
24	#7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23
25	#6 and #24

NOTE: The Airways Register is maintained in specialist software developed for The Cochrane Collaboration; the CRS (Cochrane Register of Studies). Line #4 in the strategy denotes the field in the CRS reference record in which the record has been coded for condition, in this case, COPD.

Übernommen aus [15].

### Übersicht der eingeschlossenen Treffer

	Cochrane Airways Group
Aggregierte Evidenz	-
RCTs	143
Sonstige Primär	-

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

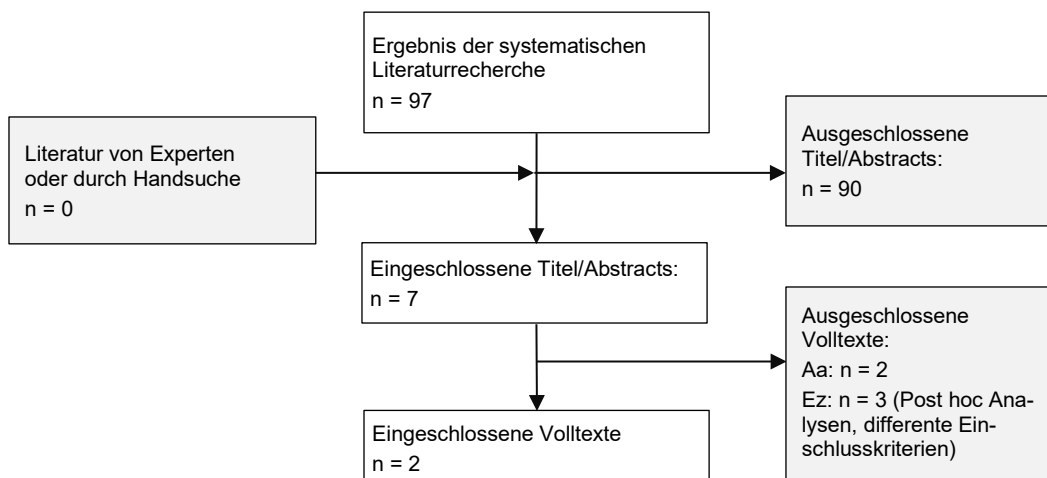
A1 (Dubletten): 3

A2 (nicht englisch/deutsch): 8

A3 (Conference Abstracts/Poster): 35

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 97**

### Flussdiagramm Update (03/2016 – 09/2019)





### Anhang 3.10 E-Zigaretten Schadenspotential

#### PICO-Fragestellung

Population: Alle

Intervention: E-Zigarette

Vergleich: Alle

Endpunkte: Alle

Studientyp: Systematische Übersichtsarbeiten, RCT

#### Recherchestrategien

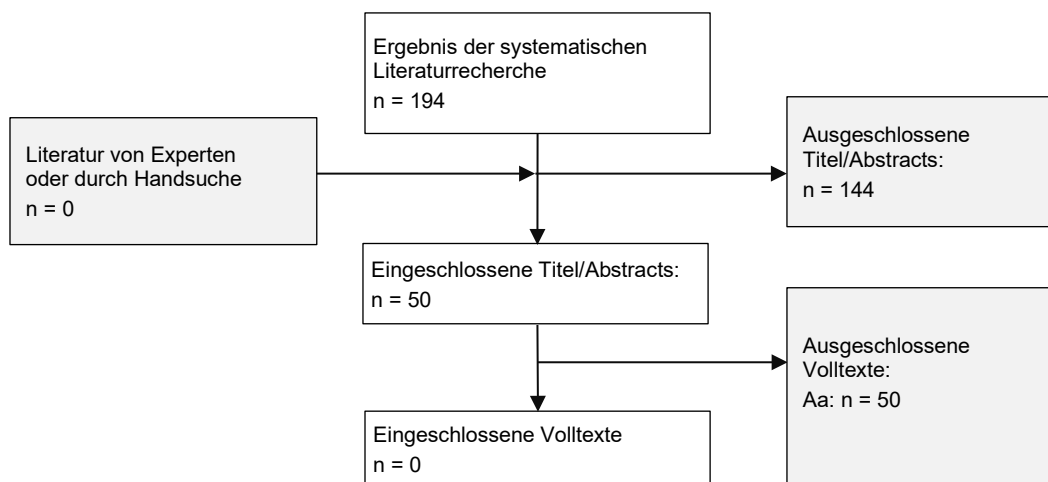
Im Rahmen der Aktualisierung der S3-Leitlinie „Screening, Diagnostik und Behandlung abhängiger Tabakkonsum (Rauchen)“ [113] wurde eine systematische Update- Recherche bezüglich der Nutzung von E-Zigaretten durchgeführt.

#### Medline via Pubmed (www.pubmed.gov) (10.10.2019)

Folgende Suchstrategie wurde verwendet: (((vaporizer[Title/Abstract]) OR e-cigarette[Title/Abstract]) OR electronic nicotine delivery system[Title/Abstract]) OR ENDS[Title/Abstract]) OR electronic cigarette[Title/Abstract] Filters: Systematic Reviews; Randomized Controlled Trial; Publication date from 2015/01/01 to 2019/10/10. Es konnten insgesamt 194 Publikationen identifiziert werden; 50 Artikel wurden in das Volltext-Screening eingeschlossen und der AG Tabakentwöhnung der NVL COPD zur Verfügung gestellt.

Diese 50 Publikationen wurden seitens des ÄZQ auf den Einschluss von Patient\*innen mit COPD untersucht; es konnten keine Studien für diese Population identifiziert werden.

#### Flussdiagramm:



Um ein mögliches Schadenspotential von E-Zigaretten darstellen zu können, wurden diese Publikationen erneut begutachtet und diesbezüglich extrahiert. Ziel war es, eine Aussage zu möglichen Schäden bei Nutzung von E-Zigaretten zu erfassen und diese auf Patient\*innen mit COPD zu extrapolieren. N=21 Studien berichteten über mögliche Schäden.

### Anhang 3.11 Ganzkörpervibration

#### PICO-Fragestellung

Population: Patient\*innen mit COPD

Intervention: Ganzkörpervibrationstraining

Vergleich: jegliche

Endpunkte:

- krankheitsspezifische Mortalität
- Morbidität
  - Symptomatik: Atemnot, Husten und Auswurf
  - Mobilität/Funktionalität
  - soziale Teilhabe
  - Exazerbationen
  - Reduktion des zukünftigen Krankheitsrisikos: COPD-bedingte Hospitalisierung
- Lebensqualität

Studientyp: Systematische Übersichtsarbeiten

### Recherchestrategien

#### Medline via Pubmed ([www.pubmed.gov](http://www.pubmed.gov)) (15. Januar 2019)

Nr.	Suchfrage	Anzahl
#16	Search (#12 and #14) NOT #15)	21
#15	Search (#12 and #13)	13
#14	Search (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic" [MeSH Terms:noexp] OR randomly [tiab] OR trial [ti])	1200343
#13	Search (systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta] OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw] OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt])	390425
#12	Search (#7 and #11)	61
#11	Search (#8 OR #9 OR #10)	5473
#10	Search (vibrat*[tiab] AND (train*[tiab] OR therap*[tiab]))	3430
#9	Search whole[tiab] AND body[tiab] AND vibrat*[tiab]	2076
#8	Search Galileo[tiab] OR WBV[tiab]	1649
#7	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6	99965
#6	Search "Air trapping"[tiab] OR airtrapping[tiab]	1244
#5	Search COAD[tiab]	277
#4	Search COPD[tiab]	40766
#3	Search Emphysem*[tiab]	26172

Nr.	Suchfrage	Anzahl
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	50399
#1	Search (chronic*[tiab]) AND ((obstruct*[tiab]) AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab]))	55742

Anzahl der Treffer: 13 aggregierte Evidenz, 21 RCTs

Datenbanken der Cochrane Library (15. Januar 2019)

Nr.	Suchfrage	Anzahl
#13	(#7 and #12) not "conference abstract":pt in Cochrane Reviews, Cochrane Protocols, Trials	55
#12	#8 or #9 or #10 or #11	1768
#11	(Galileo):ti,ab,kw	45
#10	((vibrat* and (train* or therap*)):ti,ab,kw (Word variations have been searched)	1552
#9	(wbv):ti,ab,kw	469
#8	((whole and body and vibrat*):ti,ab,kw (Word variations have been searched)	786
#7	#1 or #2 or #3 or #4 or #5 or #6	17318
#6	("air trapping" or airtrapping):ti,ab,kw (Word variations have been searched)	112
#5	(((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*)):ti,ab,kw (Word variations have been searched)	12103
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1185
#3	(COAD):ti,ab,kw	63
#2	(COPD):ti,ab,kw	12057
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4634

Cochrane Reviews	
• Review	1
• Protocol	0
Trials	54

### Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz	13	1	14
RCTs	21	54	75
<b>Gesamt</b>			<b>89</b>

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

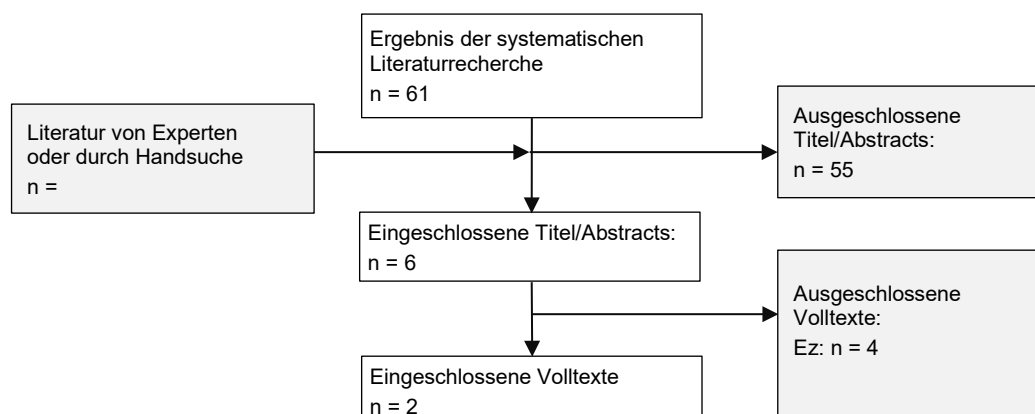
A1 (Dubletten): 21

A2 (nicht englisch/deutsch): 4

A2 (Conference Abstract): 3

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 61**

Flussdiagramm:



Es wurden der neueste Review mit den meisten Studien eingeschlossen (Zhou 2018 [63]); zusätzlich ein zweiter Review (Gloeckl 2015 [62]), welche noch zwei andere Primärstudien (Furness 2013 + Furness 2014; WBV vs. Sham-WBV) betrachtet hat. Vier Reviews wurden für eine Evidenzbegründung zurückgestellt, da sie entweder weniger (n=4) Primärstudien eingeschlossen haben bzw. in der methodischen Bewertung schlechter abschnitten.

### Anhang 3.12 Häusliche Trainingstherapie

#### PICO-Fragestellung

Population: Patient\*innen mit COPD

Intervention: häusliche Trainingstherapie

Vergleich: ambulantes Training

Endpunkte:

- krankheitsspezifische Mortalität
- Morbidität
  - Symptomatik: Atemnot, Husten und Auswurf
  - Mobilität/Funktionalität
  - soziale Teilhabe
  - Exazerbationen
  - Reduktion des zukünftigen Krankheitsrisikos: COPD-bedingte Hospitalisierung
- Lebensqualität

Studientyp: Systematische Übersichtsarbeiten

## Recherchestrategien

### Strukturiertes Vorgehen

Strukturierte Suche nach HTA-Berichten oder Übersichtsarbeiten bei ausgewählten Institutionen. Aufgrund ihrer evidenzbasierten Vorgehensweise, ihrer hohen Berichtsqualität, ihrer wissenschaftlichen Unabhängigkeit, eines weitergehenden Einblicks in Studiendossiers und ihres Bezugs zum deutschen bzw. europäischen Versorgungskontext sind diese (s.u.) besonders geeignet.

### IQWiG (06.12.2019)

Themencheck (<https://www.themencheck-medizin.iqwig.de/>):

- "häuslich": n=0
- "Training": n=0
- "COPD": n=0

IQWiG ([www.iqwig.de](http://www.iqwig.de)):

- "COPD"/alle Berichtsdocuments: n=110 Treffer; davon n=0 Publikationen zum Thema häusliche Trainingstherapie

### NICE (06.12.2019) (National Institute for Health and Care Excellence)

NICE guidance (<https://www.nice.org.uk/guidance>):

- "COPD"/Document Type: Guidance: n=44 Treffer; davon n=0 Übersichtsarbeiten zum Thema häusliche Trainingstherapie
- "chronic obstructive"/ Document Type: Guidance: n=63 Treffer; davon n=0 Übersichtsarbeiten zum Thema häusliche Trainingstherapie
- "home based"/ Document Type: Guidance: n=304 Treffer; davon n=0 Übersichtsarbeiten zum Thema häusliche Trainingstherapie

### Cochrane Collaboration (06.12.2019)

[www.cochranelibrary.com/search](http://www.cochranelibrary.com/search)

- „Home based“: n=244 Treffer, n=2 im VT-Screening
  - Home versus center based physical activity programs in older adults  
Cochrane Systematic Review - Intervention Version published: 24 January 2005  
<https://doi.org/10.1002/14651858.CD004017.pub2>  
>> auch Patient\*innen mit COPD eingeschlossen  
>> bereits in Cochrane-Recherche identifiziert--> E
  - Pulmonary rehabilitation for chronic obstructive pulmonary disease  
Cochrane Systematic Review - Intervention Version published: 24 February 2015 see what's new  
<https://doi.org/10.1002/14651858.CD003793.pub3>  
>> bereits in Cochrane-Recherche identifiziert --> E
- "COPD"/last year: n=9 Treffer; n=0 Publikationen zum Thema häusliche Trainingstherapie bei Patient\*innen mit COPD

### JBI Database of Systematic Reviews and Implementation Reports (06.12.2019)

[journals.lww.com/jbisrir/pages/advancedsearch.aspx](http://journals.lww.com/jbisrir/pages/advancedsearch.aspx)

- „COPD“/Content: Article/ Publication Date: all Dates: n=48 Treffer; davon n=1 Duplikat; n=0 Publikationen zum Thema häusliche Trainingstherapie bei Patient\*innen mit COPD
- "chronic obstructive": n=90 Treffer; davon n=2 Duplikate; n=0 Publikationen zum Thema häusliche Trainingstherapie bei Patient\*innen mit COPD

**AHRQ (06.12.2019)**

[www.ahrq.gov/research/findings/evidence-based-reports/search.html](http://www.ahrq.gov/research/findings/evidence-based-reports/search.html)

- "COPD": n=2 Treffer, n=1 im VT-Screening:
  - Comparative Effectiveness Review; Number 221: Pharmacologic and Nonpharmacologic Therapies in Adult Patients With Exacerbation of COPD: A Systematic Review 10/2019--> keine systematische Übersicht zur PICO-Frage: home-based vs. ambulantes Training--> Aa
- "home based" / Topic Lung conditions: n=18 Treffer; n=1 für VT-Screening: Aa (Comparative Effectiveness Review; Number 221 s.o.); n=0 Publikationen zum Thema häusliche Trainingstherapie bei Patient\*innen mit COPD
- "chronic obstructive" / Topic Lung conditions: n=2; n=0 Publikationen zum Thema häusliche Trainingstherapie bei Patient\*innen mit COPD

Übersicht der eingeschlossenen Treffer

	IQWiG	NICE	Cochrane	JBI	AHRQ	Summe
Aggregierte Evidenz	0	0	2	0	0	2

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 2**

Anhang 3.13 Atemtechniken

PICO-Fragestellung

Population: Patient\*innen mit COPD; evtl. mit Exazerbation

Intervention: Atemtechniken (längerfristige und Notfalltechniken)

Vergleich: Jegliche

Endpunkte:

- krankheitsspezifische Mortalität
- Morbidität
  - Symptomatik: Atemnot, Husten und Auswurf
  - Mobilität/Funktionalität (Körperliche Belastbarkeit, Fähigkeit Treppen zu steigen, Exercise Tolerance)
  - soziale Teilhabe
  - Exazerbationen
  - Reduktion des zukünftigen Krankheitsrisikos: COPD-bedingte Hospitalisierung
- Lebensqualität

Studientyp: Systematische Übersichtsarbeiten, RCTs

Recherchestrategien

Für diese Recherche wurde ein Suchupdate des Cochrane-Reviews von Holland 2012 [88] durchgeführt.

Ein weiterer Teil der Suchbegriffe wurde dem Cochrane-Review von Osadnik (2012) [80] entnommen. Diese Übersichtsarbeit beschäftigt sich mit Airway Clearance Techniken, welche ebenfalls in die Recherche aufgenommen wurden.

Da auch nach Notfalltechniken gesucht werden sollte, wurden die Suchbegriffe für COPD um die „Exazerbation“ bzw. „Verschlechterung des klinischen Zustands“ erweitert.

Medline via Pubmed ([www.pubmed.gov](http://www.pubmed.gov)) (28.02.2019)

Nr.	Suchfrage	Anzahl
#16	Search ((#12 AND #14) NOT #15) Filters: Publication date from 2011/10/01	455
#15	Search (#12 AND #13) Filters: Publication date from 2011/10/01	154

Nr.	Suchfrage	Anzahl
#14	Search (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic" [MeSH Terms:noexp] OR randomly [tiab] OR trial [ti])	1209550
#13	Search ((systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta]) OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw] OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt]))	396094
#12	Search (#10 AND #11)	8113
#11	Search (breath*[tiab] OR "ventilation-feedback training"[tiab] OR "yoga"[tiab] OR "chest physiotherapy"[tiab] OR "chest physical therapy"[tiab] OR "breath control"[tiab] OR "breathing control"[tiab] OR "breathing technique"[tiab] OR "forced expiratory technique"[tiab] OR "deep breath*"[tiab] OR "thoracic expansion"[tiab] OR "sustained maximal inspirat*"[tiab] OR "resistance breath*"[tiab] OR "breathing retraining"[tiab] OR "diaphragmatic breathing"[tiab] OR "pursed-lip breathing"[tiab] OR "pursed-lips breathing"[tiab] OR "positive expiratory pressure"[tiab] OR "controlled breathing"[tiab] OR "manual therapy"[tiab] OR "airway clearance"[tiab] OR "tracheobronchial clearance"[tiab] OR "airway* clearance"[tiab] OR "chest clearance"[tiab] OR "lung clearance"[tiab] OR "sputum clearance"[tiab] OR "mucus clearance"[tiab] OR "high frequency chest wall oscillat*"[tiab] OR "ELTGOL"[tiab] OR "active cycle of breathing technique"[tiab] OR ACBT[tiab] OR "active cycle of breathing techniques"[tiab] OR "positioning"[tiab] OR "lip brake assist"[tiab] OR oscillat*[tiab] OR OPEP[tiab] OR PEP[tiab])	270123
#10	Search (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9)	148526
#9	Search (Worse*[tiab] AND respiratory[tiab] AND symptom*[tiab])	1910
#8	Search (exacerbate*[tiab] OR AECOPD[tiab])	47681
#7	Search "Clinical Deterioration"[Mesh]	98
#6	Search ("Air trapping" [tiab] OR airtrapping[tiab])	1253
#5	Search COAD[tiab]	291
#4	Search COPD[tiab]	41285
#3	Search Emphysem*[tiab]	26313
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	50844
#1	Search (chronic*[tiab]) AND ((obstruct*[tiab]) AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab]))	56307

Anzahl der Treffer: 154 SR, 455 RCTs

**Datenbanken der Cochrane Library (01.03.2019)**

Nr.	Suchfrage	Anzahl
#13	(#10 and #11) not "conference abstract":pt with Publication Year from 2011 to present, in Trials	963
#12	(#10 and #11) not "conference abstract":pt with Publication Year from Oct 2011 to present in Cochrane Reviews, Cochrane Protocols	99
#11	(breath* or "ventilation-feedback training" or "yoga" or "chest physiotherapy" or "chest physical therapy" or "breath control" or "breathing control" or "breathing technique" or "forced expiratory technique" or "deep breath*" or "thoracic expansion" or "sustained maximal inspirat*" or "resistance breath*" or "breathing retraining" or "diaphragmatic breathing" or "pursed-lip breathing" or "pursed-lips breathing" or "positive expiratory pressure" or "controlled breathing" or "manual therapy" or "airway clearance" or "tracheobronchial clearance" or "airway* clearance" or "chest clearance" or "lung clearance" or "sputum clearance" or "mucus clearance" or "high frequency chest wall oscillat*" or "ELTGOL" or "active cycle of breathing technique" or ACBT or "active cycle of breathing techniques" or "positioning" or "lip brake assist" or oscillat* or OPEP or PEP):ti,ab,kw	29983
#10	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9	19488
#9	(Worse* and respiratory and symptom*):ti,ab,kw (Word variations have been searched)	470
#8	(exacerbate* or AECOPD):ti,ab,kw (Word variations have been searched)	2078
#7	MeSH descriptor: [Clinical Deterioration] explode all trees	5
#6	("air trapping" or airtrapping):ti,ab,kw (Word variations have been searched)	107
#5	((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*):ti,ab,kw (Word variations have been searched)	12283
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1191
#3	(COAD):ti,ab,kw	63
#2	(COPD):ti,ab,kw	11687
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4684

**Anzahl der Treffer: 99 SR, 963 RCTs**

**Übersicht der eingeschlossenen Treffer**

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz	154	99	253
RCTs	455	963	1418
<b>Gesamt</b>			<b>1671</b>

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 416

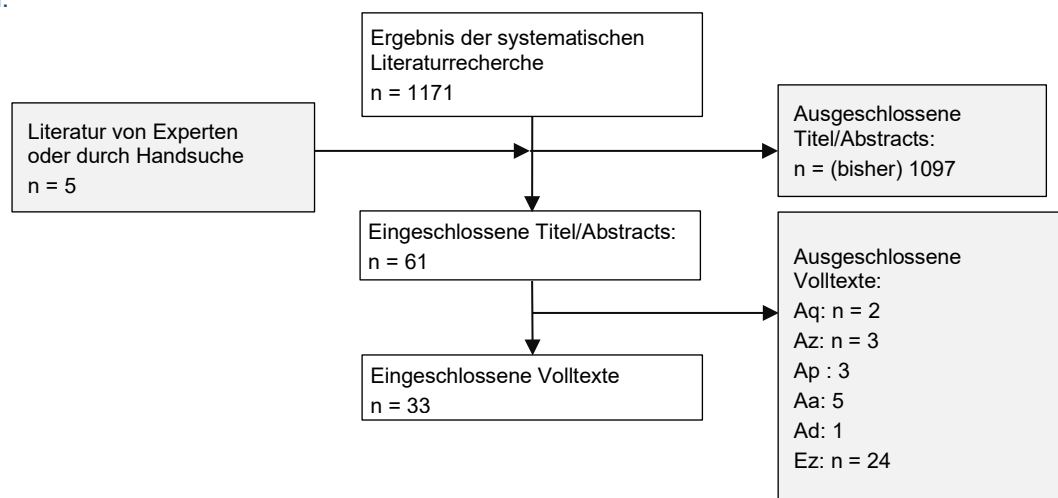
A2 (nicht englisch/deutsch): 32

A3 (Conference Abstracts): 52

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 1171**



Flussdiagramm:



Crossover-Studien mit sehr geringer Teilnehmerzahl (<20) wurden Ez gestellt; Ausnahme: Ubolsaka Jones(einzige Publikation zum Thema).

Legende: Az: bereits in strukturierter Recherche identifiziert, Aq: methodische Qualität, Ap: Publikationstyp; Ad: In Cochrane Review inkludiert, Aa: thematisch nicht passend

Anhang 3.14 Patientenschulung

PICO-Fragestellung

Population: Patient\*innen mit COPD

Intervention: Patientenschulung; Setting: Ambulant, stationär (Reha-, Fach- und Akutkliniken)

Vergleich: Jegliche

Endpunkte:

- krankheitsspezifische Mortalität
- Morbidität
  - Symptomatik: Atemnot, Husten und Auswurf
  - Mobilität/Funktionalität
  - soziale Teilhabe
  - Exazerbationen
  - Reduktion des zukünftigen Krankheitsrisikos: COPD-bedingte Hospitalisierung
- Lebensqualität

Studientyp: RCTs

Recherchestrategien

Die Suche wurde sowohl auf das ambulante als auch das stationäre Setting ausgerichtet. Gesucht wurde im deutschen Kontext. Device-Instruktionen werden gesondert im Kapitel Medikamentöse Therapie betrachtet.

Medline via Pubmed (www.pubmed.gov) (04.03.2019)

Nr.	Suchfrage	Anzahl
#17	Search (#15 AND #16)	29
#16	Search (German OR Germany)	1813743
#15	Search (#13 AND #14)	578
#14	Search (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic" [MeSH Terms:noexp] OR randomly [tiab] OR trial [ti])	1210271

Nr.	Suchfrage	Anzahl
#13	Search (#7 AND #12)	3922
#12	Search (#8 OR #9 OR #10 OR #11)	1087059
#11	Search Educat*[tiab]	554688
#10	Search "Health Education"[Mesh]	230604
#9	Search "Patient Education as Topic"[Mesh]	81576
#8	Search "Education"[Mesh]	761751
#7	Search (#1 OR #2 OR #3 OR #4 OR #5 OR #6)	100880
#6	Search ("Air trapping" [tiab] OR airtrapping[tiab])	1253
#5	Search COAD[tiab]	292
#4	Search COPD[tiab]	41313
#3	Search Emphysem*[tiab]	26325
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	50858
#1	Search ((chronic*[tiab]) AND ((obstruct*[tiab]) AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab])))	56364

**Anzahl der Treffer: 29 RCTs**

**Datenbanken der Cochrane Library (04.03.2019)**

Nr.	Suchfrage	Anzahl
#14	<b>(#7 and #12 and #13) not "conference abstract":pt in Trials</b>	<b>12</b>
#13	(German or Germany):ti,ab,kw (Word variations have been searched)	13100
#12	#8 or #9 or #10 or #11	64538
#11	(Educat*):ti,ab,kw (Word variations have been searched)	56730
#10	MeSH descriptor: [Health Education] explode all trees	17947
#9	MeSH descriptor: [Patient Education as Topic] explode all trees	8176
#8	MeSH descriptor: [Education] explode all trees	29567
#7	#1 or #2 or #3 or #4 or #5 or #6	17417
#6	("air trapping" or airtrapping):ti,ab,kw (Word variations have been searched)	107
#5	(((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*)):ti,ab,kw (Word variations have been searched)	12284
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1191
#3	(COAD):ti,ab,kw	63
#2	(COPD):ti,ab,kw	11688
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4684

**Anzahl der Treffer: 12 RCTs**

**Übersicht der eingeschlossenen Treffer**

	Medline	Cochrane Datenbanken	Gesamt
RCTs	29	12	<b>41</b>

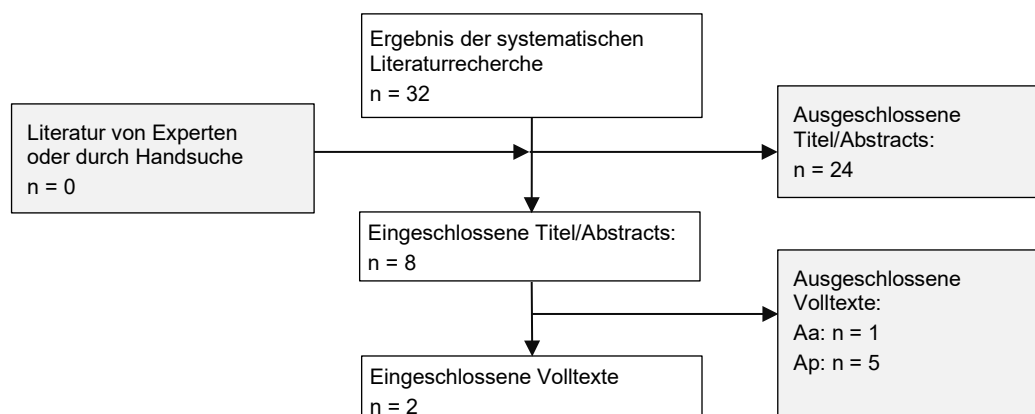
Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 8

A2 (Conference Abstract): 1

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 32**

Flussdiagramm:



Legende: Aa: andere Fragestellung, Ap: Publikationstyp (kein RCT).

### Anhang 3.15 Ernährung

#### PICO-Fragestellung

Population: Patient\*innen mit COPD

Intervention: Gewichtsmanagement-Strategien (bei Über- und Untergewicht, ggf. auch Normalgewicht)

Vergleich: Jegliche

Endpunkte:

- krankheitsspezifische Mortalität
- Morbidität
  - Symptomatik: Atemnot, Husten und Auswurf
  - Mobilität/Funktionalität
  - soziale Teilhabe
  - Exazerbationen
  - Reduktion des zukünftigen Krankheitsrisikos: COPD-bedingte Hospitalisierung
- Lebensqualität

Studientyp: Systematische Übersichtsarbeiten, RCTs

#### Recherchestrategien

##### Medline via Pubmed (www.pubmed.gov) (16. Januar 2019)

Nr.	Suchfrage	Anzahl
#23	Search (#19 AND #21) NOT #22	339
#22	Search #19 AND #20	154
#21	Search randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic" [MeSH Terms:noexp] OR randomly [tiab] OR trial [ti]	1200958
#20	Search (systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta]) OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR	390764

Nr.	Suchfrage	Anzahl
	therapeutics [mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw] OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt])	
#19	Search #7 AND #18	2865
#18	Search (#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17)	788335
#17	Search ("Exercise"[Mesh] OR exercise*[tiab] OR train*[tiab]) AND ("Body Weight"[Mesh] OR weight*[tiab] OR BMI[tiab])	73931
#16	Search Diet[tiab] OR dietary[tiab] OR nutrition*[tiab]	437028
#15	Search (Change[tiab] OR reduction[tiab] OR reducing[tiab] OR loss[tiab]) AND (weight[tiab] OR BMI[tiab])	222869
#14	Search Management[tiab] AND (obesity[tiab] OR overweight[tiab] OR underweight[tiab] OR thinness[tiab] OR leanness[tiab] OR weight[tiab] OR "Body Weight"[Mesh])	46166
#13	Search "Nutrition Therapy"[Mesh]	95021
#12	Search "Thinness/therapy"[Mesh]	274
#11	Search "Obesity Management"[Mesh]	22748
#10	Search "Diet, Reducing"[Mesh]	10787
#9	Search "Body Weight Changes"[Mesh]	65550
#8	Search "Weight Reduction Programs"[Mesh]	1681
#7	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6	100017
#6	Search "Air trapping"[tiab] OR airtrapping[tiab]	1246
#5	Search COAD[tiab]	278
#4	Search COPD[tiab]	40792
#3	Search Emphysem*[tiab]	26181
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	50450
#1	Search (chronic*[tiab]) AND ((obstruct*[tiab] AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab]))	55771

Anzahl der Treffer: 154 aggregierte; 339 RCTs

Datenbanken der Cochrane Library (16. Januar 2019)

Nr.	Suchfrage	Anzahl
#27	(#7 and #26) not "conference abstract":pt in Cochrane Reviews, Cochrane Protocols and Trials	631
#26	#8 or #9 or #10 or #11 or #12 or #13 or #14 or #17 or #18 or #19 or #25	116898
#25	#23 and #24	17087
#24	#22 or #16	100817
#23	#20 or #21	119869
#22	(Weight* or BMI):ti,ab,kw (Word variations have been searched)	96946
#21	(Exercise* or train*):ti,ab,kw (Word variations have been searched)	118258

Nr.	Suchfrage	Anzahl
#20	MeSH descriptor: [Exercise] explode all trees	21034
#19	(Diet or dietary or nutrition*):ti,ab,kw (Word variations have been searched)	65425
#18	((Change or reduction or reducing or loss) and (weight or BMI)):ti,ab,kw (Word variations have been searched)	58879
#17	#15 and #16	2201
#16	MeSH descriptor: [Body Weight] explode all trees	23944
#15	(Management):ti,ab,kw (Word variations have been searched)	96722
#14	(Management and (obesity or overweight or underweight or thinness or leanness or weight)):ti,ab,kw (Word variations have been searched)	9527
#13	MeSH descriptor: [Nutrition Therapy] explode all trees	8481
#12	MeSH descriptor: [Thinness] explode all trees	266
#11	MeSH descriptor: [Obesity Management] explode all trees	789
#10	MeSH descriptor: [Diet, Reducing] explode all trees	1936
#9	MeSH descriptor: [Body Weight Changes] explode all trees	7440
#8	MeSH descriptor: [Weight Reduction Programs] explode all trees	538
#7	#1 or #2 or #3 or #4 or #5 or #6	17318
#6	((("air trapping" or airtrapping)):ti,ab,kw (Word variations have been searched)	112
#5	(((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*)):ti,ab,kw (Word variations have been searched)	12103
#4	(Emphysem*):ti,ab,kw	1185
#3	(COAD):ti,ab,kw	63
#2	(COPD):ti,ab,kw	12056
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4634

Cochrane Reviews	
• Review	28
• Protocol	0
Trials	603

Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz	154	28	182
RCTs	339	603	942
<b>Gesamt</b>			<b>1124</b>

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 250

A2 (nicht englisch/deutsch): 49

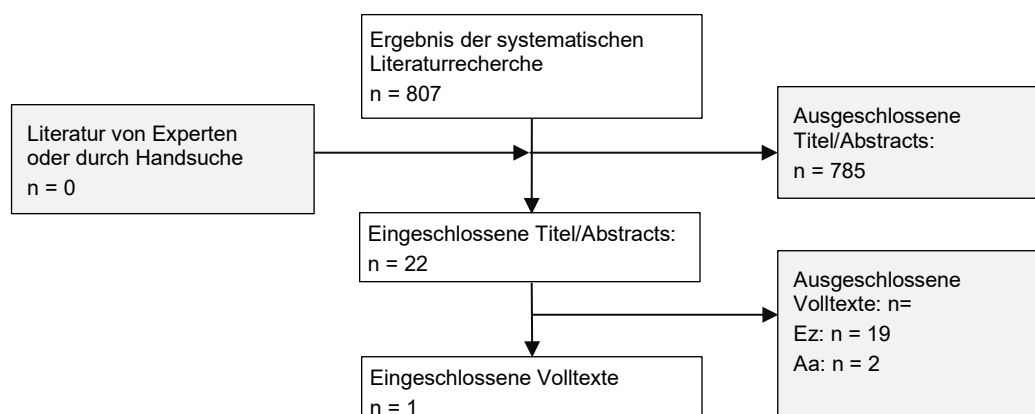
A2 (Conference Abstract): 18

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 807**

Alle Title/Abstracts, die sich mit dem Einfluss von Nahrungsergänzungsmitteln oder anderen Supplements auf bspw. Dyspnoe oder Exercise –Kapazität beschäftigen, im Abstract jedoch nicht den Einfluss auf das Gewicht bei Patient\*innen mit COPD beschreiben, wurden Aa ausgeschlossen, da sie die Fragestellung (Gewichtsmanagement) nicht beantworten. Studienprotokolle von thematisch passenden Primärstudien wurden nicht mit eingeschlossen.

Entsprechend einer sukzessiven Vorgehensweise wurden zunächst systematische Übersichtsarbeiten betrachtet.

Flussdiagramm:



Legende: Ez: keine klinische Relevanz (Bsp. Wachstumshormone; Progesteron; Kräuter); Aa: andere Fragestellung.

### Anhang 3.16 Gerätebasiertes Training

#### PICO-Fragestellung

Population: Patient\*innen mit COPD

Intervention: gerätebasiertes Training

Vergleich: Training ohne Geräte

Endpunkte:

- krankheitsspezifische Mortalität
- Morbidität
  - Symptomatik: Atemnot, Husten und Auswurf
  - Mobilität/Funktionalität
  - soziale Teilhabe
  - Exazerbationen
  - Reduktion des zukünftigen Krankheitsrisikos: COPD-bedingte Hospitalisierung
- Lebensqualität

Studientyp: Systematische Übersichtsarbeiten, RCTs

#### Recherchestrategien

In dieser Recherche wurden Interventionen im ambulanten und auch im stationären Bereich betrachtet.

#### Medline via Pubmed (www.pubmed.gov) (05.03.2019)

Nr.	Suchfrage	Anzahl
#16	Search ((#12 AND #14) NOT #15)	26
#15	Search (#12 AND #13)	7
#14	Search (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic" [MeSH Terms:noexp] OR randomly [tiab] OR trial [ti])	1210507
#13	Search ((systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw])	396735

Nr.	Suchfrage	Anzahl
	OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta] OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw]) OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt]))	
#12	Search (#7 AND #10 AND #11)	128
#11	Search (gym-based[tiab] OR gym[tiab] OR apparatus[tiab] OR equipment[tiab] OR equipment-based[tiab] OR calisthenics-based[tiab] OR callisthenics-based[tiab] OR callisthenic[tiab] OR calisthenic[tiab])	175111
#10	Search (#8 OR #9)	826022
#9	Search (Train*[tiab] OR "physical activity" [tiab] OR "physical activities" [tiab] OR exercise*[tiab] OR "exercise training"[tiab] OR "pulmonary rehabilitation"[tiab])	769062
#8	Search "Exercise"[Mesh]	175314
#7	Search (#1 OR #2 OR #3 OR #4 OR #5 OR #6)	100898
#6	Search ("Air trapping" [tiab] OR airtrapping[tiab])	1253
#5	Search COAD[tiab]	292
#4	Search COPD[tiab]	41325
#3	Search Emphysem*[tiab]	26329
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	50876
#1	Search ((chronic*[tiab] AND ((obstruct*[tiab] AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab])))	56375

Anzahl der Treffer: 7 SR, 26 RCT

**Datenbanken der Cochrane Library (05.03.2019)**

Nr.	Suchfrage	Anzahl
#14	<b>(#7 AND #11 AND #12) not "conference abstract":pt in Trials</b>	<b>99</b>
#13	<b>(#7 AND #11 AND #12) not "conference abstract":pt in Cochrane Reviews, Cochrane Protocols</b>	<b>3</b>
#12	(gym-based or gym or apparatus or equipment or equipment-based or calisthenics-based or callisthenics-based or callisthenic or calisthenic):ti,ab,kw (Word variations have been searched)	15333
#11	#8 or #9 or #10	134454
#10	(physical and (activity or activities)):ti,ab,kw (Word variations have been searched)	33606
#9	(Train* or exercise* or "exercise training" or "pulmonary rehabilitation"):ti,ab,kw (Word variations have been searched)	117199
#8	MeSH descriptor: [Exercise] explode all trees	21453

Nr.	Suchfrage	Anzahl
#7	#1 or #2 or #3 or #4 or #5 or #6	17417
#6	((("air trapping" or airtrapping)):ti,ab,kw (Word variations have been searched)	107
#5	(((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*)):ti,ab,kw (Word variations have been searched)	12284
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1191
#3	(COAD):ti,ab,kw	63
#2	(COPD):ti,ab,kw	11688
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4684

Anzahl der Treffer: 3 SR, 99 RCT

### Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz	7	3	10
RCTs	26	99	125
<b>Gesamt</b>			<b>135</b>

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

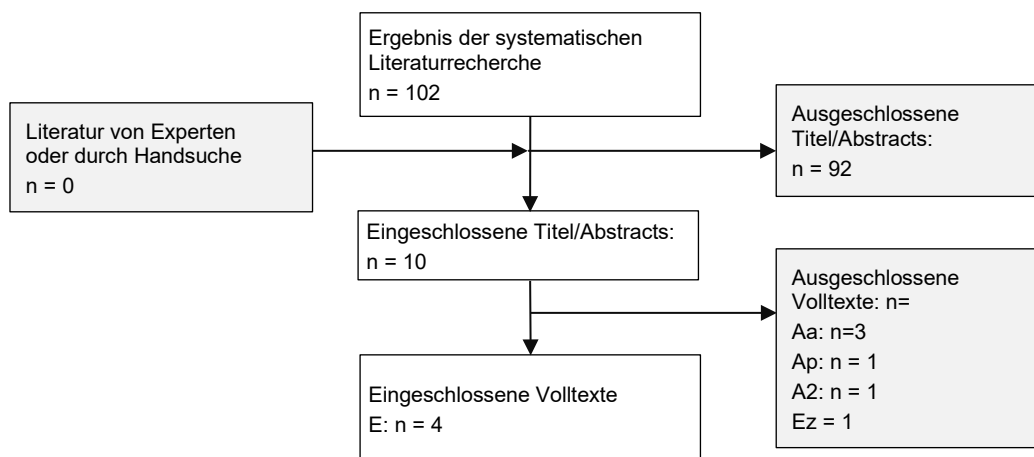
A1 (Dubletten): 27

A2 (nicht englisch/deutsch): 3

A3 (Conference Abstracts): 3

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 102**

### Flussdiagramm:



## Anhang 3.17 Telemedizin

### PICO-Fragestellung

Population: Patient\*innen mit COPD

Intervention: Telemonitoring/Telemedizin in der Rehabilitation

Vergleich: Jegliche

Endpunkte:

- krankheitsspezifische Mortalität



- Morbidität
  - Symptomatik: Atemnot, Husten und Auswurf
  - Mobilität/Funktionalität
  - soziale Teilhabe
  - Exazerbationen
  - Reduktion des zukünftigen Krankheitsrisikos: COPD-bedingte Hospitalisierung
- Lebensqualität

Studententyp: Systematische Übersichtsarbeiten, ggf. RCTs

### Recherchestrategien

Vor dieser Recherche wurde zunächst der vorhandene Cochrane-Review geprüft (McLean S. Telehealthcare for chronic obstructive pulmonary disease. [114]). Dieser ältere Review von 2011 beschäftigt sich im Allgemeinen mit Telehealthcare bei Patient\*innen mit COPD, beleuchtet jedoch nicht im Speziellen das Telemonitoring im Rahmen einer Rehabilitation.

Die Suchstrategie wurde in einem weiteren Schritt auf „Telemedizin“ ausgeweitet.

### Medline via Pubmed (www.pubmed.gov) (27.02.2019)

Nr.	Suchfrage	Anzahl
#21	Search ((#17 AND #19) NOT #20)	57
#20	Search (#17 AND #18)	21
#19	Search (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic" [MeSH Terms:noexp] OR randomly [tiab] OR trial [ti])	1209364
#18	Search ((systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta]) OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw] OR predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt]))	395947
#17	Search (#7 AND #16)	198
#16	Search (#14 OR #15)	6358
#15	Search (Telerehabilitations[tiab] OR telerehabilitation[tiab] OR tele-rehabilitations[tiab] OR tele-rehabilitation[tiab])	722
#14	Search (#10 AND #13)	6162
#13	Search (#11 OR #12)	148994
#12	Search "Telemedicine"[Mesh]	24365

Nr.	Suchfrage	Anzahl
#11	Search (Virtual[tiab] OR remote[tiab] OR tele[tiab] OR "Remote physiological Monitoring"[tiab] OR digihealth*[tiab] OR digi-health*[tiab] OR "digital health*"[tiab] OR "digital therap*"[tiab] OR "digital treat*"[tiab] OR ehealth[tiab] OR e-health[tiab] OR etherap*[tiab] OR e-therap*[tiab] OR etreat*[tiab] OR e-treat*[tiab] OR mhealth[tiab] OR m-health[tiab] OR "mobile health*"[tiab] OR telehealth*[tiab] OR tele-health*[tiab] OR telemedic*[tiab] OR tele-medic*[tiab] OR telecommunicat*[tiab] OR tele-communicat*[tiab] OR tele-homecare[tiab] OR telehomecare[tiab] OR tele-monitor*[tiab] OR telemonitor*[tiab] OR telemanage*[tiab] OR tele-manage*[tiab] OR teleconsult*[tiab] OR tele-consult*[tiab] OR telecare*[tiab] OR tele-care*[tiab] OR telepharmac*[tiab] OR tele-pharmac*[tiab] OR telenurs*[tiab] OR tele-nurs*[tiab] OR tele-support[tiab] OR telesupport[tiab])	140370
#10	Search (#8 OR #9)	386292
#9	Search (rehabilitation[tiab] OR rehabilitations[tiab])	151046
#8	Search "Rehabilitation"[Mesh]	283220
#7	Search (#1 OR #2 OR #3 OR #4 OR #5 OR #6)	100794
#6	Search ("Air trapping"[tiab] OR airtrapping[tiab])	1253
#5	Search COAD[tiab]	289
#4	Search COPD[tiab]	41274
#3	Search Emphysem*[tiab]	26309
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	50839
#1	Search (chronic*[tiab]) AND ((obstruct*[tiab]) AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab]))	56293

Anzahl der Treffer: 21 SR; 57 RCT

Nr.	Suchfrage	Anzahl
#17	<b>(#7 AND #16) not "conference abstract":pt in Cochrane Reviews, Cochrane Protocols, Trials</b>	<b>92</b>
#16	#14 OR #15	2547
#15	(Telerehabilitations or telerehabilitation or Tele-rehabilitations or tele-rehabilitation):ti,ab,kw (Word variations have been searched)	368
#14	#10 AND #13	2421
#13	#11 or #12	21299
#12	MeSH descriptor: [Telemedicine] explode all trees	1982
#11	(Virtual or remote or tele or digihealth* or digi-health* or digital health* or digital therap* or digital treat* or ehealth or e-health or etherap* or e-therap* or etreat* or e-treat* or mhealth or m-health or mobile health* or telehealth* or tele-health* or telemedic* or tele-medic* or telecommunicat* or tele-communicat* or tele-homecare or telehomecare or tele-monitor* or telemonitor* or telemanage* or tele-manage* or teleconsult* or tele-consult* or telecare* or tele-care* or telepharmac* or tele-pharmac* or telenurs* or tele-nurs* or tele-support or telesupport):ti,ab,kw (Word variations have been searched)	21260
#10	#8 OR #9	57303
#9	(Rehabilitation or rehabilitations):ti,ab,kw (Word variations have been searched)	36849
#8	MeSH descriptor: [Rehabilitation] explode all trees	30953
#7	#1 or #2 or #3 or #4 or #5 or #6	17309
#6	((("air trapping" or airtrapping)):ti,ab,kw (Word variations have been searched)	104
#5	(((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*)):ti,ab,kw (Word variations have been searched)	12195
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1183
#3	(COAD):ti,ab,kw	61

Nr.	Suchfrage	Anzahl
#2	(COPD):ti,ab,kw	11603
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4622

Anzahl der Treffer: 2 SR; 89 RCT

### Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz	21	3	24
RCTs	57	89	146
<b>Gesamt</b>			<b>170</b>

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 58

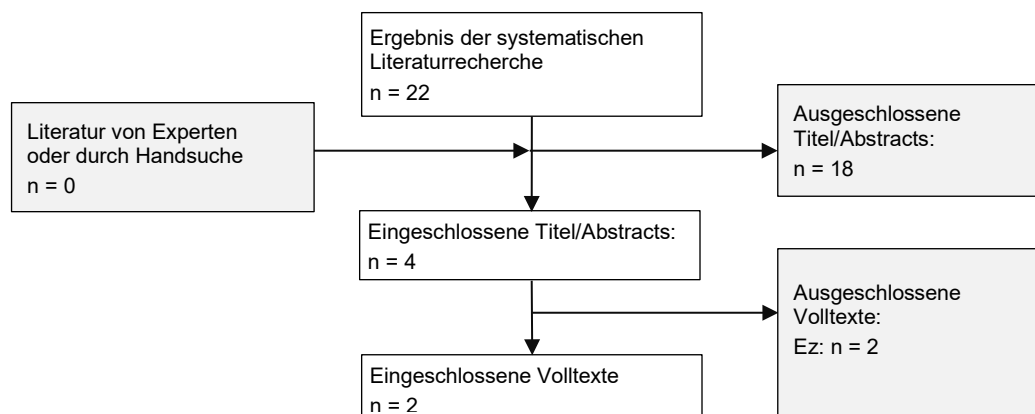
A2 (nicht englisch/deutsch): 1

A3 (Conference Abstracts): 6

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 105**

### Flussdiagramm für aggregierte Evidenz

(iteratives Vorgehen)



## Anhang 3.18 Triple-Therapie

### PICO-Fragestellung

Population: Patient\*innen mit COPD

Intervention: Triple Therapie

Vergleich: alle anderen bronchodilatatorischen Mono- oder Dualtherapien

Endpunkte:

- krankheitsspezifische Mortalität
- Morbidität
  - Symptomatik: Atemnot, Husten und Auswurf
  - Mobilität/Funktionalität
  - soziale Teilhabe
  - Exazerbationen
  - Reduktion des zukünftigen Krankheitsrisikos: COPD-bedingte Hospitalisierung
- Lebensqualität

Studientyp: RCTs

### Recherchestrategien

Grundlage für die Entwicklung dieser Recherche ist die Suchstrategie des Cochrane-Reviews „Inhaled corticosteroids with combination inhaled long-acting beta2-agonists and long-acting muscarinic antagonists for chronic obstructive pulmonary disease.“ (Tan 2016 [39]), welche um weitere Begriffe ergänzt wurde. Ziel ist es, alle Primärstudien (RCTs) zum Thema „Triple-Therapie“, welche nach dem Ende des Suchzeitraums des Cochrane-Reviews publiziert wurden, zu identifizieren.

#### Medline via Pubmed (www.pubmed.gov) (21.02.2019)

Nr.	Suchfrage	Anzahl
#18	<b>Search (#15 AND #16) Filters: Publication date from 2015/12/15</b>	<b>98</b>
#17	Search (#15 AND #16)	232
#16	Search (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic" [MeSH Terms:noexp] OR randomly [tiab] OR trial [ti])	1208195
#15	Search (#7 and #14)	584
#14	Search ((#12 AND #13) OR #8)	5915
#13	Search (Mometasone[tiab] OR Flunisolide[tiab] OR (Triamcinolone[tiab] OR "Triamcinolone"[Mesh]) OR (Beclomethasone[tiab] OR "Beclomethasone"[Mesh]) OR (Budesonide[tiab] OR "Budesonide"[Mesh]) OR (Fluticasone[tiab] OR "Fluticasone"[Mesh]) OR ("inhaled corticosteroid*" [tiab] OR "inhaled steroid*" [tiab] OR "inhaled glucocorticoid*" [tiab]) OR ICS[tiab])	32355
#12	Search ((#9 AND #10) OR #11)	1303
#11	Search QVA149[tiab]	44
#10	Search (PF-610355[tiab] OR (abediterol[tiab] OR LAS100977[tiab]) OR (Clenbuterol[tiab] OR "Clenbuterol"[Mesh]) OR carmoterol[tiab] OR olodaterol[tiab] OR indacaterol[tiab] OR vilanterol[tiab] OR bambuterol[tiab] OR Arfomoterol[tiab] OR (Formoterol[tiab] OR "Formoterol Fumarate"[Mesh]) OR (Salmeterol[tiab] OR "Salmeterol Xinafoate"[Mesh]) OR ("Adrenergic beta-2 Receptor Agonists"[Mesh]) OR ((long-acting[tiab] OR "longacting"[tiab]) AND adrenergic*[tiab] AND ("beta 2 Receptor Agonists"[tiab] OR "beta2-Agonists"[tiab] OR "beta-2 Agonists"[tiab])) OR LABA[tiab])	9323
#9	Search (darotropium[tiab] OR GSK233705[tiab]) OR (umeclidinium[tiab] OR GSK573719[tiab] OR Glycopyrronium[tiab] OR Acridinium[tiab] OR (tiotropium[tiab] OR "Tiotropium Bromide"[Mesh]) OR ("Muscarinic Antagonists"[Mesh]) OR ((Long-acting[tiab] OR longacting[tiab]) AND (anticholinergic*[tiab] OR anti-cholinergic*[tiab] OR antimuscarinic*[tiab] OR (Muscarinic*[tiab] AND Antagonist*[tiab]))) OR LAMA[tiab])	11340
#8	Search "triple therapy"[tiab]	5426
#7	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6	100701
#6	Search "Air trapping" [tiab] OR airtrapping[tiab]	1253
#5	Search COAD[tiab]	289
#4	Search COPD[tiab]	41218
#3	Search Emphysem*[tiab]	26294
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	50786
#1	Search (chronic*[tiab]) AND ((obstruct*[tiab]) AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab]))	56229

Anzahl der Treffer: 98 RCTs

#### Datenbanken der Cochrane Library (22.02.2019)

Nr.	Suchfrage	Anzahl
#32	<b>(#7 and #31) not "conference abstract":pt with Publication Year from 2015 to present, in Trials</b>	<b>164</b>

Nr.	Suchfrage	Anzahl
#31	(#23 and #30) or #8	2978
#30	#24 or #25 or #26 or #27 or #28 or #29	14485
#29	((Mometasone or Flunisolide:ti,ab,kw or Triamcinolone:ti,ab,kw or Beclomethasone or Budesonide or Fluticasone or ICS)):ti,ab,kw	12912
#28	MeSH descriptor: [Fluticasone] explode all trees	1532
#27	MeSH descriptor: [Budesonide] explode all trees	1655
#26	MeSH descriptor: [Beclomethasone] explode all trees	1070
#25	MeSH descriptor: [Triamcinolone Acetonide] explode all trees	937
#24	((("inhaled corticosteroid*" or "inhaled steroid*" or "inhaled glucocorticoid*")):ti,ab,kw (Word variations have been searched)	4425
#23	#21 or #22	1467
#22	#13 and #20	1387
#21	("QVA149"):ti,ab,kw	206
#20	#14 or #15 or #16 or #17 or #18 or #19	6335
#19	((PF-610355 or (abediterol or LAS100977) or clenbuterol or carmoterol or olodaterol or indacaterol or vilanterol or bambuterol or arfomoterol or Formoterol or Salmeterol or LABA)):ti,ab,kw	6182
#18	MeSH descriptor: [Adrenergic beta-2 Receptor Agonists] explode all trees	385
#17	MeSH descriptor: [Salmeterol Xinafoate] explode all trees	992
#16	MeSH descriptor: [Formoterol Fumarate] explode all trees	945
#15	MeSH descriptor: [Clenbuterol] explode all trees	43
#14	((("beta 2 Receptor Agonists" or "beta 2 Agonists" or "beta-2 Agonists") and (adrenergic* and (long-acting or "longacting"))):ti,ab,kw (Word variations have been searched)	400
#13	#9 or #10 or #11 or #12	3732
#12	((darotropium or GSK233705 or umeclidinium or GSK573719 or Glycopyrronium or Acridinium or Tiotropium or LAMA)):ti,ab,kw	2973
#11	((Long-acting or longacting) and ((anticholinergic* or anti-cholinergic* or antimuscarinic* or (Antagonist* AND Muscarinic*)))):ti,ab,kw (Word variations have been searched)	696
#10	MeSH descriptor: [Muscarinic Antagonists] explode all trees	824
#9	MeSH descriptor: [Tiotropium Bromide] explode all trees	527
#8	("triple therapy"):ti,ab,kw (Word variations have been searched)	2425
#7	#1 or #2 or #3 or #4 or #5 or #6	17309
#6	((("air trapping" or airtrapping)):ti,ab,kw (Word variations have been searched)	104
#5	((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*)):ti,ab,kw (Word variations have been searched)	12195
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1183
#3	(COAD):ti,ab,kw	61
#2	(COPD):ti,ab,kw	11603
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4622

#### Anzahl der Treffer: 164 RCTs

Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
RCTs	98	164	262

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

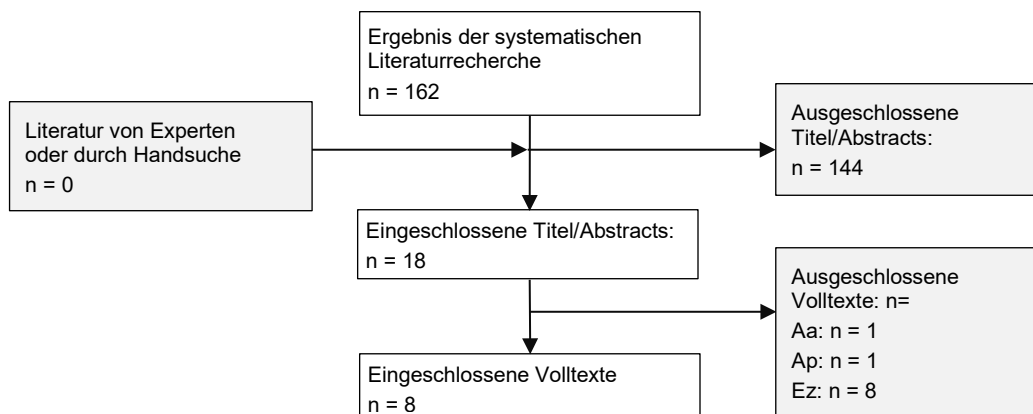
A1 (Dubletten): 77

A2 (nicht englisch/deutsch): 4

A3 (Conference Abstracts): 19

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 162**

Flussdiagramm:



Anhang 3.19 Kardiale Nebenwirkungen bei inhalativer Dauertherapie mit einem LAMA oder LABA

PICO-Fragestellung

Population: therapienaive Patient\*innen mit COPD

Intervention: inhalative Dauertherapie mit einem LAMA als Ersttherapie

Vergleich: inhalative Dauertherapie mit einem LABA als Ersttherapie

Endpunkte: kardiale Nebenwirkungen

Studientyp: SR, RCTs, ggf. Kohortenstudien

Recherchestrategien

Der SIGN –Filter für Kohortenstudien wurde in dieser Recherche angewendet. Zusätzlich wurde dieser um den Begriff „(cohort AND( study OR studies))“ erweitert.

Medline via Pubmed (www.pubmed.gov) (29. April 2019)

Nr.	Suchfrage	Anzahl
#27	Search (#21 AND #24) NOT (#25 OR #26) - Beobachtungsstudien	21
#26	Search (#21 AND #23) NOT #25 - RCTs	78
#25	Search (#21 AND #22) – Aggregierte Evidenz	26
#24	Search (((((((("Case-Control Studies"[Mesh] OR "Cohort Studies"[Mesh])) OR "Cross-Sectional Studies"[Mesh] OR ("Follow-Up Studies"[Mesh] OR ("follow-up" OR "follow up") AND (studies OR study)))))) OR ((longitudinal[tw] OR retrospective[tw] OR "cross-sectional"[tw] OR "cross sectional"[tw])) OR ("case control"[tw] OR (cohort[tw] AND analy*[tw])) OR "Observational Study"[pt]) OR (cohort AND( study OR studies)))	3001991

Nr.	Suchfrage	Anzahl
#23	Search ((randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic" [MeSH Terms:noexp] OR randomly [tiab] OR trial [ti]))	1221076
#22	Search (systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta] OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline [pt] OR pmc-book)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw] OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw] OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt]))	403566
#21	Search #7 AND #8 AND #9 AND #20	156
#20	Search #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19	874936
#19	Search "Adverse event*" [tiab] OR "Adverse effect*" [tiab]	51725
#18	Search "Heart Failure" [Mesh]	112878
#17	Search "Cardiac failure" [tiab] OR "myocardial failure" [tiab] OR "heart decompensation" [tiab]	12444
#16	Search "Acute Coronary Syndrome" [Mesh]	13709
#15	Search "Acute Coronary Syndrome" [tiab]	20286
#14	Search "Myocardial Infarction" [Mesh]	168159
#13	Search "Myocardial infarct*" [tiab] OR "heart attack*" [tiab] OR "cardiovascular stroke" [tiab]	23769
#12	Search "Arrhythmias, Cardiac" [Mesh]	198655
#11	Search Cardiac [tiab] AND (arrhythmia* [tiab] OR dysrhythmia* [tiab])	44342
#10	Search (cardiovascular [tiab] OR cardiac [tiab]) AND (events [tiab] OR safety [tiab] OR risk [tiab] OR outcome [tiab] OR effect [tiab])	417460
#9	Search (PF-610355 [tiab] OR (abediterol [tiab] OR LAS100977 [tiab]) OR (Clenbuterol [tiab] OR "Clenbuterol" [Mesh]) OR carmoterol [tiab] OR olodaterol [tiab] OR indacaterol [tiab] OR vilanterol [tiab] OR bambuterol [tiab] OR Arfomoterol [tiab] OR (Formoterol [tiab] OR "Formoterol Fumarate" [Mesh]) OR (Salmeterol [tiab] OR "Salmeterol Xinafoate" [Mesh]) OR ("Adrenergic beta-2 Receptor Agonists" [Mesh]) OR ((long-acting [tiab] OR "longacting" [tiab]) AND ("beta 2 Receptor Agonists" [tiab] OR "beta2-Agonists" [tiab] OR "beta-2 Agonists" [tiab] OR $\beta$ -agonists [tiab])) OR LABA [tiab])	10178
#8	Search (darotropium [tiab] OR GSK233705 [tiab]) OR (umeclidinium [tiab] OR GSK573719 [tiab]) OR Glycopyrronium [tiab] OR Acridinium [tiab] OR (tiotropium [tiab] OR "Tiotropium Bromide" [Mesh]) OR ("Muscarinic Antagonists" [Mesh]) OR ((Long-acting [tiab] OR longacting [tiab]) AND (anticholinergic* [tiab] OR anti-cholinergic* [tiab] OR antimuscarinic* [tiab] OR (Muscarinic* [tiab] AND Antagonist* [tiab]))) OR LAMA [tiab]	11447

Nr.	Suchfrage	Anzahl
#7	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6	101733
#6	Search "Air trapping" [tiab] OR airtrapping[tiab]	1265
#5	Search COAD[tiab]	295
#4	Search COPD[tiab]	41800
#3	Search Emphysem*[tiab]	26477
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	51410
#1	Search (chronic*[tiab]) AND ((obstruct*[tiab]) AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab]))	56958

Anzahl der Treffer: 26 SR / 78 RCTs / 21 Beobachtungsstudien

Datenbanken der Cochrane Library (29. April 2019)

Nr.	Suchfrage	Anzahl
#32	<b>(#7 and #12 and #19 and #30) not "conference abstract":pt in Trials</b>	<b>281</b>
#31	<b>(#7 and #12 and #19 and #30) not "conference abstract":pt in Cochrane Reviews, Cochrane Protocols</b>	<b>16</b>
#30	#20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29	315384
#29	("Adverse event*" or "Adverse effect*"):ti,ab,kw (Word variations have been searched)	216745
#28	MeSH descriptor: [Heart Failure] explode all trees	8158
#27	("Cardiac failure" or "myocardial failure" or "heart decompensation"):ti,ab,kw (Word variations have been searched)	869
#26	MeSH descriptor: [Acute Coronary Syndrome] explode all trees	1588
#25	("Acute Coronary Syndrome"):ti,ab,kw (Word variations have been searched)	6152
#24	MeSH descriptor: [Myocardial Infarction] explode all trees	10241
#23	("Myocardial infarct*" or "heart attack*" or "cardiovascular stroke"):ti,ab,kw (Word variations have been searched)	28459
#22	MeSH descriptor: [Arrhythmias, Cardiac] explode all trees	8644
#21	(cardiac and (arrhythmia* or dysrhythmia*)):ti,ab,kw (Word variations have been searched)	5990
#20	((cardiovascular or cardiac) and (events or safety or risk or outcome or effect)):ti,ab,kw (Word variations have been searched)	98781
#19	#13 or #14 or #15 or #16 or #17 or #18	7625
#18	((((PF-610355 or (abediterol or LAS100977) or clenbuterol or carmoterol or olodaterol or indacaterol or vilanterol or bambuterol or arfomoterol or Formoterol or Salmeterol or LABA))):ti,ab,kw	7390
#17	MeSH descriptor: [Adrenergic beta-2 Receptor Agonists] explode all trees	401
#16	MeSH descriptor: [Salmeterol Xinafoate] explode all trees	1003
#15	MeSH descriptor: [Formoterol Fumarate] explode all trees	962
#14	MeSH descriptor: [Clenbuterol] explode all trees	44
#13	((("beta 2 Receptor Agonists" or "beta 2 Agonists" or "beta-2 Agonists" or $\beta$ -agonists) and (long-acting or "longacting"))):ti,ab,kw (Word variations have been searched)	716
#12	#8 or #9 or #10 or #11	4365
#11	((darotropium or GSK233705 or umeclidinium or GSK573719 or Glycopyrronium or Acridinium or Tiotropium or LAMA)):ti,ab,kw	3548
#10	((Long-acting or longacting) and ((anticholinergic* or anti-cholinergic* or antimuscarinic*) or ((Antagonist* AND Muscarinic*)))):ti,ab,kw (Word variations have been searched)	858
#9	MeSH descriptor: [Muscarinic Antagonists] explode all trees	840
#8	MeSH descriptor: [Tiotropium Bromide] explode all trees	542



Nr.	Suchfrage	Anzahl
#7	#1 or #2 or #3 or #4 or #5 or #6	20406
#6	((("air trapping" or airtrapping)):ti,ab,kw (Word variations have been searched)	134
#5	14636	
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1411
#3	(COAD):ti,ab,kw	80
#2	(COPD):ti,ab,kw	14342
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4722

Cochrane Reviews	16
Cochrane Protocols	-
Trials	281

### Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz	26	16	42
RCTs	78	281	359
Kohortenstudien	21		21
<b>Gesamt</b>			<b>422</b>

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

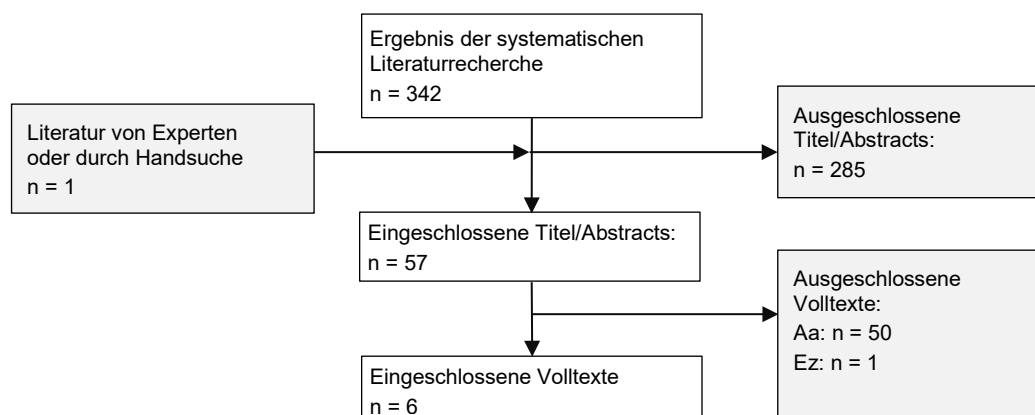
A1 (Dubletten): 74

A2 (nicht englisch/deutsch): 3

A3 (Conference Abstracts): 3

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 342**

Flussdiagramm:



## Anhang 3.20 Eosinophile

### PICO-Fragestellung

Population: Patient\*innen mit COPD

Intervention: Eosinophile im Blut oder Sputum

Vergleich: Jegliche

Endpunkte:

- Cut-Off für Eosinophilie bezüglich dem Einsatz von Steroiden (Initiierung oder Absetzen von ICS bzw. der Langzeittherapie) sowie Morbidität
- dem Einsatz von Antibiotika im Rahmen einer Pneumonie.

Studientyp: aggregierte Evidenz, RCT, ggf. Beobachtungsstudien, diagnostische Studien

### Recherchestrategien

Der SIGN-Filter für Kohortenstudien und der McMaster (2) Filter für diagnostische Studien wurden in dieser Recherche angewendet. Es konnten keine diagnostischen Studien identifiziert werden.

#### Medline via Pubmed ([www.pubmed.gov](http://www.pubmed.gov)) (14.08.2018)

Nr.	Suchfrage	Anzahl
#17	Search (#9 AND #13) NOT (#14 OR #15 OR #16) - diagnostische Studien	89
#16	Search (#9 AND #12) NOT (#14 OR #15) - Beobachtungsstudien	271
#15	Search (#9 AND #11) NOT #14 - RCTs	132
#14	Search (#9 AND #10) – aggregierte Evidenz	23
#13	Search ((sensitivity*[Title/Abstract] OR sensitivity and specificity[MeSH Terms] OR (predictive[Title/Abstract] AND value*[Title/Abstract]) OR predictive value of tests[MeSH Term] OR accuracy*[Title/Abstract]))	1849988
#12	Search (((((((("Case-Control Studies"[Mesh] OR "Cohort Studies"[Mesh]))) OR "Cross-Sectional Studies"[Mesh]) OR ("Follow-Up Studies"[Mesh] OR ("follow-up" OR "follow up") AND (studies OR study)))))) OR ((longitudinal[tw] OR retrospective[tw] OR "cross-sectional"[tw] OR "cross sectional"[tw])) OR ("case control"[tw] OR (cohort[tw] AND analy*[tw])) OR "Observational Study"[pt]))	2807057
#11	Search randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic" [MeSH Terms:noexp] OR randomly [tiab] OR trial [ti]	1173322
#10	Search systematic[sb]	372798
#9	Search #7 AND #8	1512
#8	Search "Eosinophils"[Mesh] OR Eosinophil*[tiab]	74531
#7	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6	97414
#6	Search "Air trapping"[tiab] OR airtrapping[tiab]	1218
#5	Search COAD[tiab]	264
#4	Search COPD[tiab]	39326
#3	Search Emphysem*[tiab]	25740
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	49021
#1	Search (chronic*[tiab]) AND ((obstruct*[tiab]) AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab]))	53999

**Datenbanken der Cochrane Library (14.08.2018)**

Nr.	Suchfrage	Anzahl
#13	<b>(#9 AND #12) not "conference abstract":pt</b>	<b>172</b>
#12	#10 or #11	3763
#11	MeSH descriptor: [Eosinophils] explode all trees	742
#10	(Eosinophil*):ti,ab,kw (Word variations have been searched)	3763
#9	#1 or #2 or #3 or #4 or #7 or #8	17528
#8	("air trapping" or airtrapping):ti,ab,kw (Word variations have been searched)	112
#7	((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*):ti,ab,kw	12022
#6	((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*):ti,ab,kw	17831
#5	(pulmonary or lung* or airway* or airflow* or bronchi* or respirat*):ti,ab,kw (Word variations have been searched)	119721
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1213
#3	(COAD):ti,ab,kw	60
#2	(COPD):ti,ab,kw	12511
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4562

Cochrane	
• Reviews	0
• Protocols	0
Trials	172

**Übersicht der eingeschlossenen Treffer**

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz	23		23
RCTs	132	172	304
Sonstige Primär	360		360
<b>Gesamt</b>			<b>687</b>

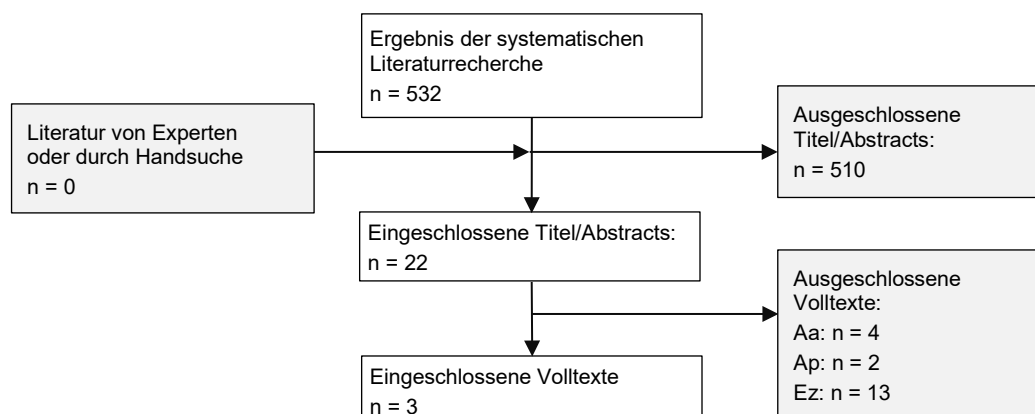
Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 112

A2 (nicht englisch/deutsch): 43

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 532**

Flussdiagramm:



Anhang 3.21 Roflumilast

PICO-Fragestellung

Population: Patient\*innen mit COPD

Intervention: LAMA/LABA + Roflumilast als Add on

Vergleich: Jegliche

Endpunkte:

- krankheitsspezifische Mortalität
- Morbidität
  - Symptomatik: Atemnot, Husten und Auswurf
  - Mobilität/Funktionalität
  - soziale Teilhabe
  - Exazerbationen
  - Reduktion des zukünftigen Krankheitsrisikos: COPD-bedingte Hospitalisierung
- Lebensqualität
- Sicherheit

Studientyp: Systematische Übersichtsarbeiten, RCTs

Recherchestrategie

Sukzessives Vorgehen. Zunächst wurden alle systematischen Übersichtsarbeiten geprüft. Anschließend wurden alle Primärstudien hinsichtlich der Fragestellung betrachtet, insbesondere jene, welche nach dem Suchzeitraum des Cochrane-Reviews zum Thema (Chong 2017 [51]) veröffentlicht wurden.

Medline via Pubmed (www.pubmed.gov) (06.12.2019)

Nr.	Suchfrage	Anzahl
#16	Search (#12 AND #14) NOT #15	131
#15	Search (#12 AND #13)	37
#14	Search randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic" [MeSH Terms:noexp] OR randomly [tiab] OR trial [ti]	1262909
#13	Search (systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta])	431687

Nr.	Suchfrage	Anzahl
	OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta] OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline [pt] OR pmcbook)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw]) OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND (survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt])	
#12	Search #7 AND #11	842
#11	Search #8 OR #9 OR #10	31459
#10	Search "Phosphodiesterase 4 Inhibitors"[Mesh]	1056
#9	Search PDE4*[tiab] OR Phosphodiesterase*[tiab]	31205
#8	Search "Roflumilast"[tiab]	546
#7	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6	105447
#6	Search "Air trapping" [tiab] OR airtrapping[tiab]	1294
#5	Search COAD[tiab]	333
#4	Search COPD[tiab]	43945
#3	Search Emphysem*[tiab]	27028
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	53480
#1	Search ((chronic*[tiab]) AND ((obstruct*[tiab]) AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab])))	59493

Anzahl der Treffer: 37 Aggregierte Evidenz; 131 RCTs

**Datenbanken der Cochrane Library (06.12.2019)**

Nr.	Suchfrage	Anzahl
#12	<b>(#7 and #11) not "conference abstract":pt in Cochrane Reviews, Cochrane Protocols, Trials</b>	<b>257</b>
#11	#8 or #9 or #10	2989
#10	MeSH descriptor: [Phosphodiesterase 4 Inhibitors] explode all trees	91
#9	((PDE4* or Phosphodiesterase*)):ti,ab,kw (Word variations have been searched)	2823
#8	(Roflumilast):ti,ab,kw	354
#7	#1 or #2 or #3 or #4 or #5 or #6	21323
#6	((("air trapping" or airtrapping)):ti,ab,kw (Word variations have been searched)	141
#5	15454	
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1457
#3	(COAD):ti,ab,kw	82
#2	(COPD):ti,ab,kw	15008
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4944

**Treffer**

Cochrane Reviews	2
Trials	255

**Datenbank: Epistemonikos (06.12.2019)**

Nr.	Suchfrage	Anzahl
#3	#1 Filters: Publication type: Primary study	30
#2	#1 Filters: Publication type: Systematic review	26
#1	(title:(title:(COPD OR COAD OR Emphysem OR "chronic obstructive pulmonary disease") OR abstract:(COPD OR COAD OR Emphysem OR "chronic obstructive pulmonary disease"))) OR abstract:(title:(COPD OR COAD OR Emphysem OR "chronic obstructive pulmonary disease") OR abstract:(COPD OR COAD OR Emphysem OR "chronic obstructive pulmonary disease")))) AND (title:(Roflumilast OR PDE4 OR Phosphodiesterase) OR abstract:(Roflumilast OR PDE4 OR Phosphodiesterase))	65

**Übersicht der eingeschlossenen Treffer**

	Medline	Cochrane Datenbanken	Epistemonikos	Summe
Aggregierte Evidenz	37	2	26	65
RCTs/Sonstige	131	255	30	416
<b>Gesamt</b>				<b>481</b>

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

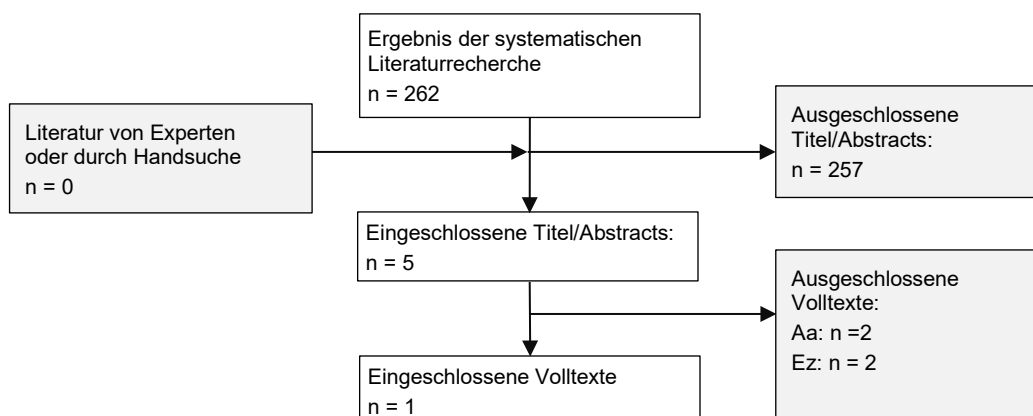
A1 (Dubletten): 132

A2 (nicht englisch/deutsch): 2

A3 (Conference Abstracts): 85

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 262**

**Flussdiagramm:**



**Anhang 3.22 Wirksamkeit von Instruktionen in Inhalationssysteme**

**Recherchestrategie**

Die systematischen Recherchen der NVL Asthma wurden herangezogen und für Patient\*innen mit COPD extrapoliert.

In einer systematischen Recherche der NVL Asthma, 3. Auflage (Leitlinienreport S. 56/ Evidenztabelle S. 221) [115] wurde unter anderem eine systematische Übersichtsarbeit identifiziert, die die Wirksamkeit von Instruktionen in Inhalationssysteme untersuchte [52]

Die Evidenztabelle aus der NVL Asthma, 3. Auflage ([www.leitlinien.de/nvl/asthma](http://www.leitlinien.de/nvl/asthma)) wurde adaptiert. Alle dargestellten Ergebnisse wurden geprüft und nur diejenigen dargestellt, die ausschließlich für Erwachsene berechnet wurden.

### Anhang 3.23 Mukolytika

#### PICO-Fragestellung

Population: Patient\*innen mit COPD

Intervention: Mukopharmaka

Vergleich: jegliche

Endpunkte:

- krankheitsspezifische Mortalität
- Morbidität
  - Symptomatik: Atemnot, Husten und Auswurf
  - Mobilität/Funktionalität
  - soziale Teilhabe
  - Exazerbationen
  - Reduktion des zukünftigen Krankheitsrisikos: COPD-bedingte Hospitalisierung
- Lebensqualität

Studientyp: SR, (ggf. RCTs)

#### Recherchestrategien

Die Suchbegriffe des Cochrane Reviews: Poole P. Mucolytic agents versus placebo for chronic bronchitis or chronic obstructive pulmonary disease (Update 05/2019) wurden für diese Recherche herangezogen und um weitere Begriffe ergänzt. Da dieser Cochrane-Review Studien scheinbar ausschloss, welche Mukolytika mit Bronchodilatoren kombinieren, diese Patientengruppe aber im deutschen Versorgungsalltag nicht ausgeschlossen werden kann, wurde die Recherche nochmals durchgeführt. Es wurde iterativ vorgegangen; zunächst wurden systematische Übersichtsarbeiten gesichtet.

#### Medline via Pubmed ([www.pubmed.gov](http://www.pubmed.gov)) (30.07.2019)

Nr.	Suchfrage	Anzahl
#16	Search (#12 AND #14) NOT #15	189
#15	Search #12 AND #13	62
#14	Search ((randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR "clinical trials as topic" [MeSH Terms:noexp] OR randomly [tiab] OR trial [ti]))	1238751
#13	Search (systematic review [ti] OR meta-analysis [pt] OR meta-analysis [ti] OR systematic literature review [ti] OR this systematic review [tw] OR pooling project [tw] OR (systematic review [tiab] AND review [pt]) OR meta synthesis [ti] OR meta-analy*[ti] OR integrative review [tw] OR integrative research review [tw] OR rapid review [tw] OR umbrella review [tw] OR consensus development conference [pt] OR practice guideline [pt] OR drug class reviews [ti] OR cochrane database syst rev [ta] OR acp journal club [ta] OR health technol assess [ta] OR evid rep technol assess summ [ta] OR jbi database system rev implement rep [ta] OR (clinical guideline [tw] AND management [tw]) OR ((evidence based[ti] OR evidence-based medicine [mh] OR best practice* [ti] OR evidence synthesis [tiab]) AND (review [pt] OR diseases category[mh] OR behavior and behavior mechanisms [mh] OR therapeutics [mh] OR evaluation studies[pt] OR validation studies[pt] OR guideline [pt] OR pmc-book)) OR ((systematic [tw] OR systematically [tw] OR critical [tiab] OR (study selection [tw] OR (predetermined [tw] OR inclusion [tw] AND criteri* [tw]) OR exclusion criteri* [tw] OR main outcome measures [tw] OR standard of care [tw] OR standards of care [tw]) AND	415190

Nr.	Suchfrage	Anzahl
	(survey [tiab] OR surveys [tiab] OR overview* [tw] OR review [tiab] OR reviews [tiab] OR search* [tw] OR handsearch [tw] OR analysis [ti] OR critique [tiab] OR appraisal [tw] OR (reduction [tw]AND (risk [mh] OR risk [tw]) AND (death OR recurrence))) AND (literature [tiab] OR articles [tiab] OR publications [tiab] OR publication [tiab] OR bibliography [tiab] OR bibliographies [tiab] OR published [tiab] OR pooled data [tw] OR unpublished [tw] OR citation [tw] OR citations [tw] OR database [tiab] OR internet [tiab] OR textbooks [tiab] OR references [tw] OR scales [tw] OR papers [tw] OR datasets [tw] OR trials [tiab] OR meta-analy* [tw] OR (clinical [tiab] AND studies [tiab]) OR treatment outcome [mh] OR treatment outcome [tw] OR pmcbook)) NOT (letter [pt] OR newspaper article [pt])	
#12	Search #7 AND #11	831
#11	Search #8 OR #9 OR #10	43723
#10	Search mucolytic*[tiab] OR mucoactiv*[tiab]	1692
#9	Search Acetylcysteine[tiab] OR bromhexine[tiab] OR carboxymethylcysteine[tiab] OR ambroxol[tiab] OR sobrerol[tiab] OR "iodinated glycerol"[tiab] OR isobutyrylcysteine[tiab] OR myrtol[tiab] OR NAC[tiab] OR methylcysteine[tiab] OR carbocysteine[tiab] OR erdosteine[tiab] OR stepronin[tiab] OR gelsolin[tiab] OR mesna*[tiab] OR cineole[tiab] OR neltenexine[tiab] OR eucalyptus[tiab] OR eprazinone[tiab] OR guacetisal[tiab] OR Guaifenesin[tiab] OR letosteine[tiab] OR mecysteine[tiab] OR "Potassium Citrate"[tiab] OR rosaprostol[tiab] OR terpin[tiab]	35801
#8	Search "Expectorants" [Pharmacological Action]	17056
#7	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6	103250
#6	Search "Air trapping" [tiab] OR airtrapping[tiab]	1284
#5	Search COAD[tiab]	306
#4	Search COPD[tiab]	42668
#3	Search Emphysem*[tiab]	26713
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	52203
#1	Search (chronic*[tiab]) AND (obstruct*[tiab]) AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab])	58023

Anzahl der Treffer: 62 SR / 189 RCTs

**Datenbanken der Cochrane Library (30.07.2019)**

Nr.	Suchfrage	Anzahl
#13	(#7 and #11) not "conference abstract":pt in Trials	342
#12	(#7 and #11) not "conference abstract":pt in Cochrane Reviews, Cochrane Protocols	2
#11	#8 or #9 or #10	4476
#10	((mucolytic* or mucoactiv*):ti,ab,kw (Word variations have been searched)	463
#9	((Acetylcysteine OR bromhexine OR carboxymethylcysteine OR ambroxol OR sobrerol OR "iodinated glycerol" OR isobutyrylcysteine OR myrtol OR NAC OR methylcysteine OR carbocysteine OR erdosteine OR stepronin OR gelsolin OR mesna* OR cineole OR neltenexine OR eucalyptus OR eprazinone OR guacetisal OR Guaifenesin OR letosteine OR mecysteine OR "Potassium Citrate" OR rosaprostol OR terpin):ti,ab,kw (Word variations have been searched)	4194
#8	MeSH descriptor: [Expectorants] explode all trees	285
#7	#1 or #2 or #3 or #4 or #5 or #6	20835
#6	((("air trapping" or airtrapping)):ti,ab,kw (Word variations have been searched)	136
#5	15013	
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1435
#3	(COAD):ti,ab,kw	81



Nr.	Suchfrage	Anzahl
#2	(COPD):ti,ab,kw	14661
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4813

Cochrane Reviews	2
Cochrane Protocols	0
Trials	342

### Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz	62	2	64
RCTs	189	342	531
<b>Gesamt</b>			<b>595</b>

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

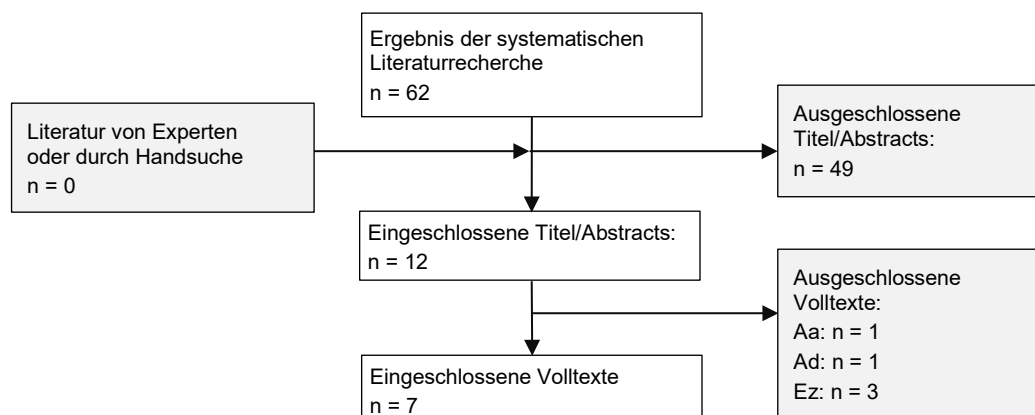
A1 (Dubletten): 139

A2 (nicht englisch/deutsch): 62

A3 (Conference Abstracts): 55

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 339 (62 SR; 277 RCTs)**

### Flussdiagramm aggregierte Evidenz



## Anhang 3.24 Wechsel des Inhalationssystems

### PICO-Fragestellung

Population: Patient\*innen mit COPD

Intervention: Wechsel des Inhalationssystems ohne erneute Instruktion

Vergleich: Wechsel des Inhalationssystems mit erneuter Instruktion

Endpunkte: Schaden

Studientyp: Primärstudien

## Recherchestrategie

## Medline via Pubmed (www.pubmed.gov) (23.10.2019)

Nr.	Suchfrage	Anzahl
#11	<b>Search (#7 AND #8 AND #9) Filters: Publication date from 2009/01/01</b>	<b>471</b>
#10	Search (#7 AND #8 AND #9)	813
#9	Search change*[tiab] OR changing*[tiab] OR switch*[tiab] OR replac*[tiab]	3432247
#8	Search "Nebulizers and Vaporizers"[Mesh] OR Vaporizer*[tiab] OR Vaporiser*[tiab] OR Nebuliser*[tiab] OR Nebulizer*[tiab] OR Atomizer*[tiab] OR Atomiser*[tiab] OR Inhaler*[tiab] OR Inhalator*[tiab] OR Device*[tiab]	409013
#7	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6	104604
#6	Search "Air trapping" [tiab] OR airtrapping[tiab]	1290
#5	Search COAD[tiab]	326
#4	Search COPD[tiab]	43454
#3	Search Emphysem*[tiab]	26912
#2	Search "Pulmonary Disease, Chronic Obstructive"[Mesh]	53079
#1	Search ((chronic*[tiab]) AND ((obstruct*[tiab]) AND (pulmonary[tiab] or lung*[tiab] or airway*[tiab] or airflow*[tiab] or bronchi*[tiab] or respirat*[tiab])))	58918

## Datenbanken der Cochrane Library (24.10.2019)

Nr.	Suchfrage	Anzahl
#20	<b>#18 - Trials ab 2009</b>	<b>434</b>
#19	<b>#18 - Cochrane Reviews ab 2009-01-01</b>	<b>16</b>
#18	(#17) NOT (conference abstract):pt	693
#17	#7 and #15 and #16	893
#16	(change* or changing* or switch* or replace*):ti,ab,kw (Word variations have been searched)	316516
#15	#8 or #9 or #10 or #11 or #12 or #13 or #14	57079
#14	(device*):ti,ab,kw (Word variations have been searched)	49747
#13	(inhalator*):ti,ab,kw (Word variations have been searched)	167
#12	(inhaler*):ti,ab,kw (Word variations have been searched)	6170
#11	(atomizer* or atomiser*):ti,ab,kw (Word variations have been searched)	90
#10	(nebulizer* or nebuliser*):ti,ab,kw (Word variations have been searched)	3410
#9	(vaporizer* or vaporiser*):ti,ab,kw	1982
#8	MeSH descriptor: [Nebulizers and Vaporizers] explode all trees	2259
#7	#1 or #2 or #3 or #4 or #5 or #6	21117
#6	((("air trapping" or airtrapping)):ti,ab,kw (Word variations have been searched)	139
#5	(((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*)):ti,ab,kw (Word variations have been searched)	15271
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1437
#3	(COAD):ti,ab,kw	82
#2	(COPD):ti,ab,kw	14860
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	4893

Übersicht eingeschlossene Treffer

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz		16	16
RCTs		434	434
Alle	471		471
<b>Gesamt</b>			<b>921</b>

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

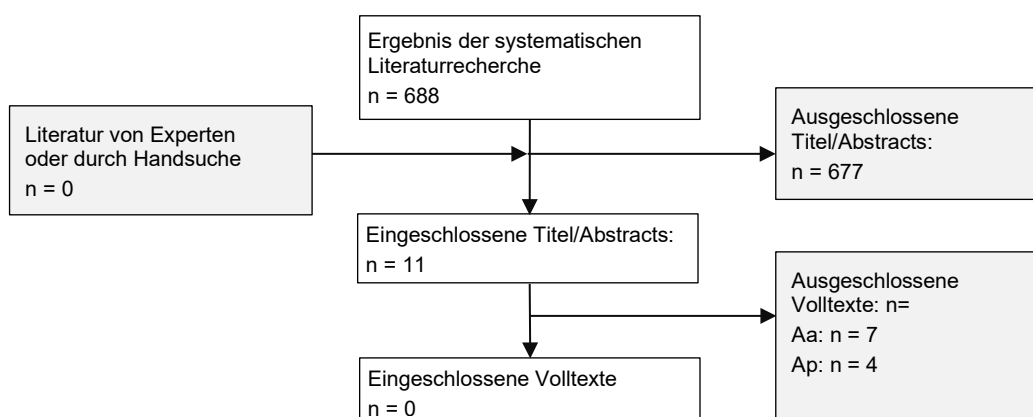
A1 (Dubletten): 207

A2 (nicht englisch/deutsch): 20

A3 (Conference Abstracts): 6

**Eingeschlossene Treffer insgesamt nach Ausschlüssen: 688**

Flussdiagramm



Es konnten keine Primärstudien zur Fragestellung identifiziert werden.

In einer analogen systematischen Recherche der NVL Asthma, 3. Auflage (Leitlinienreport S. 70/ Evidenztabelle S.223) [115] konnten eine qualitative Studie [53] und zwei Auswertungen von Registerdaten [54,55] identifiziert werden. Eine Übertragung und Extrapolation dieser Ergebnisse auf Patient\*innen mit COPD ist nach Einschätzung der Leitliniengruppe möglich.

## Anhang 4 Evidenztabelle Definition und Epidemiologie

### Gezielte Suche: Epidemiologische Daten

**Zitat**

Armatov MK; Steffen A; Holstiege J; Bätzing J (2019): Die chronisch obstruktive Lungenerkrankung (COPD) in der ambulanten Versorgung in Deutschland – Zeitliche Trends und kleinräumige Unterschiede (Versorgungsatlas-Bericht, Nr. 19/06). Online verfügbar unter [https://www.versorgungsatlas.de/fileadmin/ziva\\_docs/99/VA\\_19-06\\_Bericht\\_COPD\\_2019-08-20\\_V2.pdf](https://www.versorgungsatlas.de/fileadmin/ziva_docs/99/VA_19-06_Bericht_COPD_2019-08-20_V2.pdf), zuletzt geprüft am 02.09.2019.)

Steppuhn H, Kuhnert R, Scheidt-Nave C (2017): 12-Monats-Prävalenz der bekannten chronisch obstruktiven Lungenerkrankung (COPD) in Deutschland. In: Journal of health monitoring 2 (3), S. 46–54. DOI: 10.17886/RKI-GBE-2017-053.

## Anhang 5 Evidenztabelle Diagnostik und Monitoring

### Anhang 5.1 NVL Asthma // ACO

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
Alshabanat A. Asthma and COPD Overlap Syndrome (ACOS): A Systematic Review and Meta Analysis. PLoS One 2015;10(9):e0136065	Suchzeitraum: 2015/02	<ul style="list-style-type: none"> <li>- gepoolte Prävalenz des ACOS bei COPD-Patienten: 27% in Populationsbasierten Studien (95% CI: 0.16–0.38, p&lt;0.0001) und 28% in Krankenhausbasierten Studien (95% CI: 0.09–0.47, p = 0.0032)</li> <li>- Alter: 7 studies; ACOS subjects were younger than patients with only COPD, significant in five studies. 2 studies reported that ACOS patients were significantly older than patients with asthma alone with a mean (SD) age (in years) of 60.4 (11.3) and 61 (7) Vs. 54.9 (10.9) and 53 (13) (p&lt;0.001).</li> <li>- Geschlecht von ACOS-Patienten: Difference in prevalence of ACOS among COPD patients for males versus females was -0.085 (95% CI: -0.178–0.008, p = 0.073)</li> <li>- Inanspruchnahme: 5 studies reported that patients with ACOS had more frequent exacerbations, hospitalizations, and emergency department visits in comparison to patients with COPD alone</li> <li>-LQ: quality of life of ACOS subjects was lower than COPD</li> <li>-weitere EP: Medikationsbedarf, Raucherstatus, LuFu</li> </ul>	<ul style="list-style-type: none"> <li>- nur 5/11 Punkten im AMSTAR</li> <li>- wegen Relevanz und Alleinstellung Einschluss</li> <li>- 12 Querschnitts-, 5 Kohortenstudien</li> </ul>

Selektive eingebrachte Literatur: Epidemiologische Daten ACO

**Zitat**  
 Akmatov MK, Ermakova T, Holstiege J, Kohring C, Ng F, Völker S, Bätzing J. Überlappung von Asthma und COPD in der ambulanten Versorgung – Analyse anhand vertragsärztlicher Abrechnungsdaten. 2020 (Versorgungsatlas-Bericht; Nr. 20/06) [cited: 2021-02-08]. DOI: 10.20364/VA-20.06. [https://www.versorgungsatlas.de/fileadmin/ziva\\_docs/113/VA\\_20-06\\_Bericht\\_ACO\\_2020-11-10.pdf](https://www.versorgungsatlas.de/fileadmin/ziva_docs/113/VA_20-06_Bericht_ACO_2020-11-10.pdf), zuletzt geprüft am 08.04.2021.)

Anhang 5.2 Diagnostische Verfahren

Indextest CT

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Li J-s. Diagnostic value of computed tomography in chronic obstructive pulmonary disease: A systematic review and meta-analysis. COPD 2012; 9(5):563–70.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pub-med/22708710">https://www.ncbi.nlm.nih.gov/pub-med/22708710</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>• China</li> <li>• Ziel: to evaluate the accuracy of CT in diagnosing COPD</li> <li>• n=8 diagnostische Genauigkeitsstudien (3926 subjects)</li> <li>• Suchzeitraum: Inception - 10/2010 (Cochrane:2011)</li> <li>• Interventionen:                             <ul style="list-style-type: none"> <li>- CT (HRCT (n=1), LDCT (n=3), MSCT (n=3))</li> <li>- PFT (Spirometry)</li> </ul> </li> <li>• Einschlusskriterien:                             <ol style="list-style-type: none"> <li>1) The type of research was a diagnostic test that assessed the diagnostic accuracy of CT, HRCT, LDCT or MSCT for COPD</li> <li>2) sens and spec were reported or 2x2 table could be constructed</li> <li>3) diagnostic method for evaluation of test was CT imaging diagnosis, and reference standard was PFT</li> <li>4) publication was full reported</li> </ol> </li> </ul>	<p><b>All included studies (95% CI):</b>                      Sens 0.83 (0.73-0.89)                      Spec 0.87 (0.70-0.90)                      PLR 6.2 (2.5-15.5)                      NLR 0.20 (0.12-0.34)                      DOR 31 (8-116)</p> <p><u>Subgroup "using lung density index"</u> (n=4)                      Sens 0.80 (0.74-0.84)                      Spec 0.77 (0.58-0.89)                      PLR 3.5 (1.8-6.9)                      NLR 0.26 (0.20-0.34)                      DOR 13 (6-32)</p> <p><u>Subgroup "other index"</u> (emphysema index in inspiration, pixel index in max expiratory, blood flow, diagnostic model) (n=4)                      Sens 0.87 (0.64-0.96)                      Spec 0.95 (0.66-0.99)                      PLR 17.5 (1.8-171.5)                      NLR 0.14 (0.04-0.45)                      DOR 127 (5-2982)</p> <p><u>LDCT (95%CI)</u>                      Sens 0.66 (0.61-0.70)                      Spec 0.88 (0.86-0.89)                      PLR 5.89 (4.57-7.59)                      NLR 0.25 (0.12-0.53)                      DOR 21.27 (8.47-53.41)</p> <p>No metaanalysis for MSCT studies because of heterogeneity</p>	<p>AMSTAR: 7/11</p> <p>n-y-y-n-n-y-y-y-y-n</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
		<p><u>authors conclusion:</u> Our results suggest that quantitative measures in CT scans can be useful to identify suspected subjects with COPD, although there was heterogeneity among the studies. Because the early stages of COPD are substantially under diagnosed, early detection of airflow limitation with chest CT and early intervention can improve outcomes for patients with COPD.</p>	

### Indextest Ganzkörperbodyplethysmographie

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Tang Y. The measurement of lung volumes using body plethysmography and helium dilution methods in COPD patients: A correlation and diagnosis analysis. Sci Rep 2016; 6:37550.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pub-med/27876834">https://www.ncbi.nlm.nih.gov/pub-med/27876834</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>• China</li> <li>• January 2014 to March 2015</li> <li>• prospective correlation and diagnosis analysis</li> <li>• n= 170 patients with stable COPD</li> <li>• Ziel: to assess lung volumes stratified by airflow limitation severity</li> <li>• Interventionen/Measurements:                             <ul style="list-style-type: none"> <li>- <b>Multi-breath Helium dilution method (MBHD)</b> and</li> <li>- <b>whole-body plethysmography (WBP)</b>, Master-Screen PFT System (Jaeger Corp, Germany) vs.</li> <li>- <b>COPD defined by GOLD</b> classification of airflow limitation (we combined mild and moderate COPD patients, defined by GOLD classification of airflow limitation, as 'non-severe' group; while the severe and very severe COPD patients were combined as 'severe' group.)</li> </ul> </li> <li>• Einschlusskriterien: FEV1 /FVC ratio &lt; 0.7 after bronchodilation; (b) no acute exacerbation during previous 4 weeks; (c) stop the medications, which may influence pulmonary function testing for at least 3 days</li> <li>• Ausschlusskriterien: coexisting medical conditions that would interfere with pulmonary function testing</li> </ul>	<ul style="list-style-type: none"> <li>• The discrepancies between these two methods (WBP + MBHD) were recorded as <math>\Delta RV\%pred</math>, <math>\Delta TLC\%pred</math>, and <math>\Delta RV/ TLC</math>.</li> <li>The <math>\Delta TLC\%pred</math> value of 34.2 would have a sensitivity of 93.1% and specificity of 79.6%, with the positive and negative likelihood ratio of 4.56 and 0.09, respectively. <math>\Delta RV\%pred</math>, and <math>\Delta RV/TLC</math> also had a relatively high sensitivity and specificity to differentiate COPD severity.</li> <li>• <b>value of <math>\Delta RV\%pred</math>, <math>\Delta TLC\%pred</math>, and <math>\Delta RV/TLC</math> in discriminating between mild/moderate and severe/very severe COPD patients:</b> <ul style="list-style-type: none"> <li>- <math>\Delta RV\%pred</math> cutoff Point 63.4: Sens 0.875, Spec 0.724, LR+ 3.17 , LR- 0.17</li> <li>- <math>\Delta TLC\%pred</math> cutoff Point 34.2: Sens 0.931, Spec 0.796, LR+ 4.56 , LR- 0.09</li> <li>- <math>\Delta RV/TLC</math> cutoff Point 10.3: Sens 0.861, Spec 0.663, LR+ 2.55 , LR- 0.21</li> </ul> </li> <li>• authors conclusion: The differences of lung volume parameters measured by body plethysmography and helium dilution methods were associated with airflow limitation and can effectively differentiate COPD severity, which may be a supportive method to assess the lung function of stable COPD</li> </ul>	<p>QUADAS II (schwierig anzuwenden, da keine direkte diagnostische Genauigkeitsstudie)</p> <p>Domain 1: Patient Selection</p> <p>Could the selection of patients have introduced bias? <b>LOW</b></p> <p>Domain 2: Index Test</p> <p>Could the conduct or interpretation of the index test have introduced bias? <b>NOT APPLICABLE</b></p> <p>Domain 3: Reference Standard</p> <p>Could the reference standard, its conduct, or its interpretation have introduced bias? <b>UNCLEAR</b></p> <p>Domain 4: Flow and Timing</p> <p>Could the patient flow have introduced bias? <b>LOW</b></p> <p><b>Concerns regarding applicability: UNCLEAR</b> (Fragestellung passend?)</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
		patients.  >> Unterscheidung zwischen milder/moderater und schwerer/sehr schwerer COPD	

**Indextest Spirometrie**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Lutchmedial SM. How Common Is Airflow Limitation in Patients With Emphysema on CT Scan of the Chest? Chest 2015; 148(1):176–84.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pub-med/25539080">https://www.ncbi.nlm.nih.gov/pub-med/25539080</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>• USA</li> <li>• 01/2011 - 12/2011</li> <li>• n=274</li> <li>• retrospektive Analyse: assessed the prevalence of obstruction by GOLD and LLN criteria in patients with emphysema on CT scan and determine which radiographic criteria were associated with a clinical diagnosis of COPD</li> <li>• Interventionen/Measurements:                         <ul style="list-style-type: none"> <li>- <b>Spirometrie</b></li> <li>- <b>CT</b> (16-, 40-, 64-, 128-, and 256-slice scanners; Brilliance and iCT)</li> <li>- klinische Daten</li> </ul> </li> <li>• Einschlusskriterien: to define COPD clinically, all of which had to be fulfilled: symptoms including cough, sputum production, wheezing, and dyspnea; a smoking history; a physician diagnosis of COPD; medication use including the need for a long-acting b<sub>2</sub> agonist, a long-acting muscarinic antagonist, and/or inhaled corticosteroids; and no other diagnosis or reason to suspect another disease besides COPD</li> <li>• Ausschlusskriterien: lack of visible emphysema on CT imaging (when reviewed by the radiologist), concomitant fibrosis of any cause, significant bronchiectasis (requiring airway clearance therapy), extensive infiltrate or lung mass, moderate or large pleural effusions, or previous surgical resection</li> </ul>	<ul style="list-style-type: none"> <li>• mean age was 66.9 ± 10.4 years, and 55% were men</li> <li>• GOLD criteria detected obstruction in 228 patients (83%), and LLN detected obstruction in 206 patients (75%). However, GOLD failed to correctly identify 19 patients (6.9%) and LLN failed to identify 38 patients (13.9%) (average 10.4%) who had radiographic emphysema and a clinical diagnosis of COPD.</li> </ul> <p>Identification of patients with clinical COPD by:</p> <ul style="list-style-type: none"> <li>- GOLD: Sens 92%, Spec 77%</li> <li>- LLN: Sens 84%, Spec 91%</li> </ul> <p>• authors conclusion: Spirometry missed 10.4% of patients with clinical COPD who have significant emphysema on chest CT scan.</p>	<p>QUADAS II</p> <p>Domain 1: Patient Selection</p> <p>Could the selection of patients have introduced bias? <b>LOW</b></p> <p>Domain 2: Index Test</p> <p>Could the conduct or interpretation of the index test have introduced bias? <b>UNCLEAR</b></p> <p>Domain 3: Reference Standard</p> <p>Could the reference standard, its conduct, or its interpretation have introduced bias? <b>LOW</b></p> <p>Domain 4: Flow and Timing</p> <p>Could the patient flow have introduced bias? <b>HIGH</b></p> <p>Concerns regarding applicability <b>LOW</b></p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Bhatt SP. Comparison of spirometric thresholds in diagnosing smoking-related airflow obstruction. <i>Thorax</i> 2014; 69(5):409–14. <a href="https://www.ncbi.nlm.nih.gov/pub-med/23525095">https://www.ncbi.nlm.nih.gov/pub-med/23525095</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>• USA</li> <li>• Zeitraum nicht angegeben</li> <li>• retrospektive Datenanalyse; large multicenter study (COPDGene)</li> <li>• n= 7743 Smokers and former smokers with and without airflow obstruction</li> <li>• Ziel: compared the accuracy and discrimination of GOLD recommended Fixed ratio of FEV1/FVC&lt;0.70 with LLN in diagnosing smoking related airflow obstruction using computed tomography defined emphysema and gas trapping as the disease gold standard</li> <li>• Interventionen: <ul style="list-style-type: none"> <li>- <b>spirometry (fixed ratio of FEV1/FVC&lt;0.70) &amp; LLN (NHANES III)</b>; post-bronchodilator values were used</li> <li>vs.</li> <li>- <b>quantitative CT</b></li> </ul> </li> <li>• Einschlusskriterien: ages of 45 and 80 years with at least 10 packyears of cigarette smokin</li> <li>• Ausschlusskriterien: Subjects with lung diseases other than asthma and COPD; further patients with physician diagnosed asthma</li> <li>• Follow up: every 6 months by telephone; using a questionnaire</li> </ul>	<ul style="list-style-type: none"> <li>• age range 45 to 80 years</li> <li>• There was very good agreement between the two spirometric cutoffs (kappa=0.85; 95% CI 0.83 to 0.86, p&lt;0.001). 7.3% were discordant.</li> <li>• <b>accuracy of FEV1/FVC cut offs in detecting emphysema and gas trapping:</b> <ul style="list-style-type: none"> <li>Emphysema at least 10% (Prevalence = 18%): <ul style="list-style-type: none"> <li>- Fixed: Sens 94 ( 95% CI 92.6–95.2), Spec 69.6 (95% CI 68.4–70.8)</li> <li>- LLN: Sens 89.9 (95% CI88.2–91.4), Spec 77.1 (95% CI76.0–78.1)</li> </ul> </li> <li>Gas Trapping at least 15% (Prevalence = 48%): <ul style="list-style-type: none"> <li>- Fixed: Sens 70.2 (95% CI68.7–71.8), Spec 84.2 (95% CI83.0–85.4)</li> <li>- LLN: Sens 61.2 (95% CI59.6–62.9), Spec 89.0 (95% CI87.9–90.0)</li> </ul> </li> </ul> </li> <li>• authors conclusions: We have shown a high degree of discordance between CT and both spirometric thresholds. Overall, LLN appears to be marginally more specific for disease in older age groups, but will not identify a large number of older patients who have significant respiratory symptoms and CT emphysema</li> </ul>	<p>QUADAS II</p> <p>Domain 1: Patient Selection</p> <p>Could the selection of patients have introduced bias? <b>UNCLEAR</b></p> <p>Domain 2: Index Test</p> <p>Could the conduct or interpretation of the index test have introduced bias? <b>UNCLEAR</b></p> <p>Domain 3: Reference Standard</p> <p>Could the reference standard, its conduct, or its interpretation have introduced bias? <b>UNCLEAR</b></p> <p>Domain 4: Flow and Timing</p> <p>Could the patient flow have introduced bias? <b>LOW</b></p> <p>Concerns regarding applicability <b>LOW</b></p>
<p>Schneider A. Diagnostic accuracy of spirometry in primary care. <i>BMC Pulm Med</i> 2009; 9:31. <a href="https://www.ncbi.nlm.nih.gov/pub-med/19591673">https://www.ncbi.nlm.nih.gov/pub-med/19591673</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>• Deutschland/Niederlande</li> <li>• 01/2006 - 12/2007</li> <li>• Cross sectional diagnostic study; primary care</li> <li>• n=219 patients suspected of having obstructive airway disease (OAD)</li> <li>• Endpunkte: evaluate the sensitivity, specificity and predictive values of spirometry for the diagnosis of chronic obstructive pulmonary disease (COPD) and asthma</li> <li>• Interventionen: <ul style="list-style-type: none"> <li>- <b>Spirometrie</b> (Medikro SpiroStar USB®)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• n=50 with COPD, mean age 56.9 (SD 11.5); female 26 (54.1%)</li> <li>• Obstructive airway disease was diagnosed if FEV1/VC ≤ 70% and/or FEV1 &lt; 80%</li> <li>• <b>diagnosing airway obstruction in COPD</b> <ul style="list-style-type: none"> <li>- sensitivity 92% (95%CI 80-97)</li> <li>- specificity 84% (95%CI 77-89)</li> <li>- PPV 63% (95%CI 51-73)</li> <li>- NPV 97% (95%CI 93-99)</li> </ul> </li> </ul>	<p>QUADAS II</p> <p>Domain 1: Patient Selection</p> <p>Could the selection of patients have introduced bias? <b>LOW</b></p> <p>Domain 2: Index Test</p> <p>Could the conduct or interpretation of the index test have introduced bias? <b>LOW</b></p> <p>Domain 3: Reference Standard</p>



Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<p>- <b>Ganzkörperbodyplethysmographie</b> + bronchiale Provokation (If there was no bronchial obstruction, bronchial provocation was performed to determine bronchial hyper-responsiveness (BHR))</p> <ul style="list-style-type: none"> <li>• Einschlusskriterien: symptoms such as dyspnea, coughing or expectoration; no previous diagnosis for obstructive airway disease</li> <li>• Ausschlusskriterien: contra-indications for bronchodilator reversibility testing or bronchial provocation (untreated hyperthyreosis, unstable coronary artery disease, and cardiac arrhythmia); Pregnancy also led to exclusion.</li> </ul>	<ul style="list-style-type: none"> <li>• authors conclusion: OPD can be estimated with high diagnostic accuracy using spirometry.[...]</li> </ul>	<p>Could the reference standard, its conduct, or its interpretation have introduced bias? <b>LOW</b></p> <p>Domain 4: Flow and Timing</p> <p>Could the patient flow have introduced bias? <b>LOW</b></p> <p>Concerns regarding applicability <b>LOW</b></p>

**Indextest Spirometrie inklusive DLCO (n=3)**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Hesselbacher SE. Cross-sectional analysis of the utility of pulmonary function tests in predicting emphysema in ever-smokers. Int J Environ Res Public Health 2011; 8(5):1324–40.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/21655122">https://www.ncbi.nlm.nih.gov/pubmed/21655122</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>• USA</li> <li>• Cross-Sectional Analysis, Sens und Spez gegeben</li> <li>• n=224 ever-smokers (current or former), &gt; 40 years of age; part of the Longitudinal Exacerbation Study of COPD (LES-COPD)</li> <li>• Ziel: to determine the sensitivity and specificity of pulmonary function tests (PFTs) in assessing emphysema using quantitative CT scans as the reference standard</li> <li>• Einschlusskriterien: age over 40, no history of concurrent lung cancer, chest surgery, or chronic lung diseases other than COPD (e.g., sarcoidosis, fibrosis, etc.)</li> <li>• Interventionen:             <ul style="list-style-type: none"> <li>- PFT (<b>Spirometrie inklusive DLCO</b>) vs.</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Significant emphysema (&gt;7%) was detected in 122 (54%) subjects. Twenty six (21%) emphysema subjects had no evidence of airflow obstruction (FEV1/FVC ratio &lt;70%), while all subjects with &gt;23% emphysema showed airflow obstruction.</li> <li>• <b>Spirometry for detecting radiographic emphysema:</b> <ul style="list-style-type: none"> <li>• <b>FEV1/FVC &lt; 70%:</b> Sens 79 (95%CI 71–85), Spec 75 (95%CI 65–82), PPV 79%, NPV 75%</li> <li>• <b>FEV1/FVC &lt; LLN (NHANES):</b> Sens 73 (95%CI 65–80), Spec 74 (95%CI 64–81), PPV 77%, NPV 68%</li> <li>• <b>FEV1 &lt; LLN:</b> Sens 67 (95%CI 59–75), Spec 74 (95%CI 64–81), PPV 75%, NPV 65%</li> </ul> </li> <li>• <b>DLCO</b> for detecting emphysema:             <ul style="list-style-type: none"> <li>- Sens 91 % (95%CI 84-95), Spec 23 (95%CI 16–33), PPV 59%, NPV 68%</li> </ul> </li> </ul>	<p>QUADAS II</p> <p>Domain 1: Patient Selection</p> <p>Could the selection of patients have introduced bias? <b>LOW</b></p> <p>Domain 2: Index Test</p> <p>Could the conduct or interpretation of the index test have introduced bias? <b>LOW</b></p> <p>Domain 3: Reference Standard</p> <p>Could the reference standard, its conduct, or its interpretation have introduced bias? <b>UNCLEAR</b></p> <p>Domain 4: Flow and Timing</p> <p>Could the patient flow have introduced bias? <b>HIGH</b></p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	- <b>CT</b> (Siemens Cardiac Sensation Cardiac scanner (Siemens Medical Solutions))	<ul style="list-style-type: none"> <li>• authors conclusion: [...] A proposed strategy in the evaluation of ever smokers may be to measure full pulmonary function tests, including spirometry and lung volumes, and diffusion capacity; if spirometry is normal but hyperinflation, air trapping, or reduced gas exchange are noted, a CT should be considered to evaluate for isolated emphysema. Detection of emphysema without airflow obstruction may also provide an explanation of symptoms such as dyspnea or exercise intolerance in ever smokers with normal spirometry, who might otherwise be identified as normal.[...]</li> </ul>	Concerns regarding applicability <b>UNCLEAR</b> (Fragestellung?)
<p>Lee JS. Validation of the lower limit of normal dif-fusing capacity for detect-ing emphysema. Respiration 2011; 81(4):287–93.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/20110663">https://www.ncbi.nlm.nih.gov/pubmed/20110663</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>• Korea</li> <li>• 08/2005 - 04/2008</li> <li>• Diagnostische Genauigkeitsstudie</li> <li>- n=197 COPD-Patient*innen aus der Korean Obstructive Lung Disease (KOLD) cohort +</li> <li>- n=103 gesunde Erwachsene</li> <li>• Ziel: to validate the LLN (<b>Pellegrino 2005</b>) for DLco and to determine the optimum LLN cutoff value for detecting emphysema in patients with COPD</li> <li>• Interventionen: <ul style="list-style-type: none"> <li>- <b>Spirometrie</b> (Vmax22 instrument (SensorMedics, Yorba Linda, Calif., USA) <b>inklusive DLCO</b> (measured by the single-breath method using a Vmax229D instrument (SensorMedics) or a Masterlab Body (Jaeger, Würzburg, Germany)</li> <li>vs.</li> <li>- <b>CT</b> (16- slice multidetector CT scanners including the Somatom Sensation 16 (Siemens Medical Systems, Erlangen, Germany), the GE Lightspeed Ultra (General Electric Healthcare, Milwaukee, Wisc., USA), and the Philips Brilliance 16 (Philips Medical Systems, Best, The Netherlands)</li> </ul> </li> <li>• COPD was diagnosed based on smoking history (more than 10 pack-years) and the</li> </ul>	<ul style="list-style-type: none"> <li>• COPD-Patienten: Age: 66.1 ± 7.2 years; FEV 1 48.0 ± 15.9% predicted</li> <li>• male/female: 190/7</li> <li>• <b>ROC curve analysis: lower 5th percentile used as the LLN for DLco</b> <ul style="list-style-type: none"> <li>- sensitivity of 68.3% ; specificity of 84.5%, PPV 88.7%, NPV 60.0% to differentiate COPD patients with emphysema from COPD patients without emphysema</li> <li>- sensitivity of 68.3% and a specificity of 98.1%, PPV 97.7%, NPV 71.6% to differentiate COPD patients with emphysema from healthy subjects</li> </ul> </li> <li>• <b>ROC curve analysis: lower 9th percentile</b> <ul style="list-style-type: none"> <li>- sens 79.4%, spec 77.5%, PPV 86.2%, NPV 67.5% for differentiating COPD patients with emphysema from COPD patients without emphysema</li> <li>- sens 79.4%, spec 94.2%, PPV 94.2%, NPV 77.0% for differentiating COPD patients with emphysema from healthy subjects was 87.2%.</li> </ul> </li> <li>• conclusions: <ul style="list-style-type: none"> <li>- lower 9th percentile was the best LLN cutoff value for DLco to differentiate COPD patients with emphysema from COPD patients without emphysema and from healthy subjects</li> <li>- our findings indicate that the lower 5th percentile of the reference population may not be the best LLN cutoff value for D Lco because this value had a low sensitivity for detecting COPD patients with emphysema.</li> </ul> </li> </ul>	<p>QUADAS II</p> <p>Domain 1: Patient Selection</p> <p>Could the selection of patients have introduced bias? <b>UNCLEAR</b></p> <p>Domain 2: Index Test</p> <p>Could the conduct or interpretation of the index test have introduced bias? <b>UNCLEAR</b></p> <p>Domain 3: Reference Standard</p> <p>Could the reference standard, its conduct, or its interpretation have introduced bias? <b>UNCLEAR</b></p> <p>Domain 4: Flow and Timing</p> <p>Could the patient flow have introduced bias? <b>UNCLEAR</b></p> <p>Concerns regarding applicability <b>HIGH</b> (Fragestellung passend?)</p>

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	<p>presence of airflow limitation that was not fully reversible [post-bronchodilator forced expiratory volume in 1 s (FEV<sub>1</sub>)/forced vital capacity (FVC) &lt; 70%]</p> <ul style="list-style-type: none"> <li>• COPD patients with emphysema were defined as COPD patients in whom volumetric CT showed that the volume fraction of the lung at less than –950 Hounsfield units (HU) at full inspiration was more than 15%</li> </ul>		
<p>van der Lee I. Nitric oxide diffusing capacity versus spirometry in the early diagnosis of emphysema in smokers. <i>Respir Med</i> 2009; 103(12):1892–7.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/19586765">https://www.ncbi.nlm.nih.gov/pubmed/19586765</a></p> <ul style="list-style-type: none"> <li>• Nicht zitiert.</li> </ul>	<ul style="list-style-type: none"> <li>• Niederlande</li> <li>• n=263 randomly selected heavy smokers (participating in the NELSON-project, a Dutch-Belgian multi-centre lung cancer screening trial)</li> <li>• Diagnostische Genauigkeitsstudie</li> <li>• Ziele: <ul style="list-style-type: none"> <li>- whether the DLNO is more sensitive in diagnosing emphysema in a large group of heavy smokers than the DLCO</li> <li>- whether the DLNO/DLCO ratio differs in subjects with emphysema compared to healthy individuals</li> </ul> </li> <li>• Interventionen <ul style="list-style-type: none"> <li>- <b>Spirometrie</b> via pneumotachography (flow-volumes curves, DLNO, DLCO, the transfer coefficients KNO (DLNO/VA) and KCO (DLCO/VA)) vs.</li> <li>- <b>CT</b> 16 detector-row scanner (Mx8000 IDT or Brilliance 16P, Philips Medical Systems, Cleveland, OH)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• all male, 50-75 years of age with a smoking history of at least 20 pack years</li> <li>• Detection of emphysema: <ul style="list-style-type: none"> <li>- DLCO: Sens 58.3%, Spec 81.5%, PPV 33.3%, NPV 92.5%</li> <li>- DLNO: Sens 50.0%, Spec 81.9%, PPV 30.5%, NPV 91.2%</li> <li>- KCO: Sens 88.9%, Spec 57.3%, PPV 24.8%, NPV 97.0%</li> <li>- KNO: Sens 91.7%, Spec 72.7%, PPV 34.7%, NPV 98.2%</li> <li>- FEV<sub>1</sub>/FVC: Sens 77.8%, Spec 70.1%, PPV 29.5%, NPV 95.2%</li> </ul> </li> <li>• authors conclusion: spirometry is very important for the diagnosis of emphysema, but it only measures airway obstruction. The KNO is a very sensitive measure for the detection of CT-based emphysema. The DLNO/DLCO ratio is increased in (ex)smokers, which could be explained by the hypothesis that pulmonary endothelial dysfunction precedes extensive parenchymal loss ultimately leading to airway obstruction. Further studies are needed to explore this concept, in which the DLNO/DLCO ratio could be used as a sensitive tool to detect microvascular malfunctioning.</li> </ul>	<p>QUADAS II</p> <p>Domain 1: Patient Selection</p> <p>Could the selection of patients have introduced bias? <b>LOW</b></p> <p>Domain 2: Index Test</p> <p>Could the conduct or interpretation of the index test have introduced bias? <b>UNCLEAR</b></p> <p>Domain 3: Reference Standard</p> <p>Could the reference standard, its conduct, or its interpretation have introduced bias? <b>UNCLEAR</b></p> <p>Domain 4: Flow and Timing</p> <p>Could the patient flow have introduced bias? <b>LOW</b></p> <p>Concerns regarding applicability <b>LOW</b></p>

**Indextests Spirometrie und Bodyplethysmographie**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
Tashkin DP. The UCLA population studies of	<ul style="list-style-type: none"> <li>• USA</li> <li>• 1972 - 1974</li> </ul>	<ul style="list-style-type: none"> <li>• Reference "Test": physician defined diagnosis: taking into consideration the results of all lung function tests, responses</li> </ul>	<p>QUADAS II schwer anzuwenden, da Studie &gt; 40 Jahre alt ist</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>chronic obstructive respiratory disease. II. Determination of reliability and estimation of sensitivity and specificity. Environ Res 1979; 20(2):403–24.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/546647">https://www.ncbi.nlm.nih.gov/pubmed/546647</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>• n=218 adults (2 Kohorten: one exposed to high levels of photochemical/oxidant-type pollutants; other: low levels of chemical pollutants); tested in mobile lung function (field) laboratory vs. retesting in UCLA reference laboratory</li> <li>• Interventionen:                             <ul style="list-style-type: none"> <li>- <b>Spirometry, Bodyplethysmography</b>, single-breath nitrogen test and modified NHLBI questionnaire</li> <li>- <b>physician defined diagnosis</b> (to judge the presence or absence of chronic obstructive respiratory disease/CORD)</li> </ul> </li> </ul>	<p>to the respiratory questionnaire, and reported findings on physical examination.</p> <ul style="list-style-type: none"> <li>- physicians were not coached with regard to the relative weights to assign to the different kinds of subject data (symptoms, physical findings, pulmonary function test results) presented to them.</li> <li>• Sens Spirometrie 58%</li> <li>• Sens Plethysmography: 58%</li> <li>• Spezifitäten nicht angegeben: FEV1, FVC and plethysmography were estimated to be specific but relatively insensitive.</li> </ul>	<p>Domain 1: Patient Selection</p> <p>Could the selection of patients have introduced bias? <b>UNCLEAR</b></p> <p>Domain 2: Index Tests</p> <p>Could the conduct or interpretation of the index test have introduced bias? <b>UNCLEAR</b></p> <p>Domain 3: Reference Standard</p> <p>Could the reference standard, its conduct, or its interpretation have introduced bias? <b>UNCLEAR</b></p> <p>Domain 4: Flow and Timing</p> <p>Could the patient flow have introduced bias? <b>LOW</b></p> <p>Concerns regarding applicability <b>UNCLEAR</b> (Aktualität?)</p>

### Anhang 5.3 Über-/ Unterdiagnose

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Quanjer PH. Implications of adopting the Global Lungs Initiative 2012 all-age reference equations for spirometry. Eur Respir J 2013; 42(4):1046–54.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/23520323">https://www.ncbi.nlm.nih.gov/pubmed/23520323</a></p>	<ul style="list-style-type: none"> <li>• Vergleich der predictive equations von GLI 2012, NHANES III und ESCS/ERS; GOLD</li> <li>• Australien, Polen, multicenter</li> <li>• <b>Studientyp:</b> retrospective analysis of routinely obtained spirometric data</li> <li>• <b>Studienstart/Studienende:</b> Data were collected between August 2008 and June 2012 (John Hunter Hospital), January 2011 and May 2012 (Austin Hospital) and April 2009 and June 2012 (National</li> </ul>	<ul style="list-style-type: none"> <li>• All spirometry data used were baseline or pre-bronchodilator status</li> <li>• Mean predicted values and Z-scores were derived using prediction equations from the European Community for Steel and Coal (ECSC)/ERS, National Health and Nutrition Examination Survey (NHANES) III and GLI 2012</li> <li>• spirometric records from 17 572 subjects (49.5% females), aged 18–85 years</li> <li>• <b>GLI 2012 vs. GOLD:</b> ( Figure 4 (S. 5); geschlechtsabhängig) weiblich: GOLD--&gt; Unterdiagnose bei jüngeren Patientinnen männlich: GOLD--&gt; Unterdiagnose bei jüngeren Patienten und Überdiagnose in älteren Patienten</li> <li>In conclusion, the transition from NHANES III to GLI 2012 spirometry reference data will lead to limited changes in the predicted values of FEV1 and</li> </ul>	<p>Bias-Bewertung für nicht-vergleichende Studien (AWMF 2016) --&gt; Vertrauen in Studienergebnisse:</p> <p><b>(i) prospektive Planung mit Protokoll</b>, in dem Einschlusskriterien und Interventionen sowie interessierende Endpunkte hinterlegt sind: nicht eindeutig beschrieben</p> <p><b>(ii) konsekutiver Patienteneinschluss:</b> ja</p> <p><b>(iii) transparentes, nicht-selektives Berichten</b> in Bezug auf Patientencharakteristika, Intervention und Ergebnis: ja</p>

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	<p>Tuberculosis and Lung Diseases Research Institute)</p> <ul style="list-style-type: none"> <li>• <b>Einschlusskriterien:</b> limited to Caucasians, patients aged between 18 - 85 years</li> </ul>	<p>FVC for adults. In contrast, users of ECSC/ERS prediction equations should be aware that predicted values for FEV1 and FVC will increase by a few hundred millilitres on transition to GLI 2012 data. This will lead to a substantial increase in the prevalence rate of low FVC when changing from ECSC/ERS, or a moderate decrease if changing from NHANES III. There are substantial differences in the predicted levels of FEV1/FVC ratio but not in their LLN, so that adopting the GLI 2012 prediction equations will have small effects on the rates of detection of obstructive ventilator defects. Our analysis confirms previous findings in clinical populations that GOLD definitions for stage 2 and higher lead to .20% underdiagnosis of airway obstruction in those aged f55 years, and to 16–23% overdiagnosis in older subjects.</p>	
<p>Llordes M. Prevalence, Risk Factors and Diagnostic Accuracy of COPD Among Smokers in Primary Care. COPD 2015; 12(4):404–12.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/25474184">https://www.ncbi.nlm.nih.gov/pubmed/25474184</a></p>	<ul style="list-style-type: none"> <li>• Prävalenz der COPD in Katalonien/Spanien, single-center</li> <li>• <b>Einschlusskriterien:</b> subjects older than 45 years with a history of smoking</li> <li>• <b>Interventionen:</b> clinical questionnaire and spirometry with bronchodilator test (400 mcg of salbutamol)</li> <li>• participants with newly diagnosed COPD, defined as postbronchodilator FEV1/FVC&lt;0.7, underwent 4-week treatment with formoterol (12 mcg/12 hours) and budesonide (200 mcg/12 hours) to rule out reversible airflow obstruction</li> <li>• <b>Studientyp:</b> population-based, epidemiological study ( cross-sectional)</li> <li>• <b>primärer Endpunkt:</b> prevalence of COPD among smokers</li> <li>• <b>sekundärer Endpunkt:</b> accuracy of diagnosis of COPD in primary care</li> </ul>	<p>To investigate the possible overdiagnosis of COPD by fixed ratio, we also calculated the frequency of airflow obstruction by the lower limit of normal (LLN) of the FEV1/FVC ratio using the GLI 2012 equations to calculate the LLN</p> <ul style="list-style-type: none"> <li>• n=1738 (valid spirometry)</li> <li>• <b>post-bronchodilator (salbutamol):</b> <u>fixed ratio FEV1/FVC &lt; 0.7:</u> n=422 (24.3%;95% CI: 22.3%-26.4%) (27.8 % for men, 5.1 % for women) <u>FEV1/FVC below LLN:</u> n=287 (15.5%, 95%CI: 13.8%–17.1%) --&gt; n= 135 (7.7%) discordant subjects (obstructive by fixed ratio but normal by LLN) --&gt; n=0 individuals obstructed by LLN with FEV1/FVC &gt; 0.7</li> <li>• <b>new diagnosis of COPD:</b> undergo treatment for 4 weeks with inhaled formoterol and budesonide <u>fixed ratio FEV1/FVC &lt; 0.7:</u> n=239; n=199 (83.3%) undergo treatment --&gt; n=32 (16%) showed a non-obstructive spirometry and were considered false positive cases of COPD. <u>FEV1/FVC below LLN:</u> n=124 undergo treatment --&gt; n=31 (25%) were no longer obstructive by LLN after 4 weeks of treatment.</li> </ul> <p>On the other hand, 217 (12.5%) individuals from the target population of 1,738 had a diagnosis of COPD in their medical records, and 90.2% were receiving regular inhaled treatment for COPD, despite 34 (15.6%) not fulfilling the spirometric criteria for COPD.</p>	<p>Bias-Bewertung für nicht-vergleichende Studien (AWMF 2016) --&gt; Vertrauen in Studienergebnisse:</p> <p><b>(i) prospektive Planung mit Protokoll:</b> ja</p> <p><b>(ii) konsekutiver Patienteneinschluss:</b> nicht eindeutig beschrieben</p> <p><b>(iii) transparentes, nicht-selektives Berichten</b> in Bezug auf Patientencharakteristika, Intervention und Ergebnis: teilweise Daten nicht abgebildet</p>

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<p>Guerriero M. COPD prevalence in a north-eastern Italian general population. <i>Respir Med</i> 2015; 109(8):1040–7.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/26052037">https://www.ncbi.nlm.nih.gov/pubmed/26052037</a></p>	<ul style="list-style-type: none"> <li>• Prävalenz der COPD in Nord-Ost-Italien</li> <li>• gemessen nach GOLD-Kriterien vs. LLN nach GLI 2012 (ERS/ATS)</li> <li>• <b>Patienten:</b> subjects aged between 18 and 79 years, municipal registry was used as the data source.</li> <li>• <b>Studienstart:</b> November 2011</li> <li>• <b>Studienende:</b> Februar 2012</li> <li>• <b>Interventionen:</b> Questionnaire, spirometry</li> <li>• <b>Studientyp:</b> observational cross-sectional study</li> <li>• <b>Ein- und Ausschlusskriterien:</b> nicht beschrieben</li> <li>• <b>primäre Endpunkte:</b> prevalence and clinical features of COPD, as defined by GOLD and ERS/ATS recommendations</li> </ul>	<p>n=1275 completed questionnaire n=1236 were able to correctly perform the spirometric tests</p> <p><b>pre-bronchodilator:</b> <u>FEV1/FVC ratio &lt;0.70:</u> airway obstruction in n=288 subjects (23.3%; 95%CI: 20.9% - 25.7%). <u>LLN 5% (z-score-1.64):</u> airway obstruction in n=204 subjects (16.5%; 95%CI: 14.4% - 18.6%).</p> <p><b>post-bronchodilator (salbutamol):</b> <u>FEV1/FVC ratio &lt;0.70:</u> airway obstruction in n= 145 subjects (11.7% - 95%CI: 9.9%-13.5%) <u>LLN 5% (z-score-1.64):</u> airway obstruction in n=109 subjects (9.1%; 95%CI: 7.5%10.7%)</p> <ul style="list-style-type: none"> <li>• <b>multivariate logistic regression:</b> association between categorical variables and LLN and GOLD defined COPD respectively. According to both LLN and GOLD criterion, a statistically significant association can be detected between COPD and             <ul style="list-style-type: none"> <li>• male gender: LLN OR 1.69 (95% Ci 1.08 - 2.66; p 0.022); GOLD OR 1.84 (95% CI1.21 - 2.79; p 0.004)</li> <li>• decade of pack-years (borderline): LLN OR 1.12 (95%CI 0.99 - 1.27 p 0.083); GOLD OR 1.11 (95% CI 0.99 - 1.25; p 0.080)</li> <li>• current smoking: LLN OR 1.98 (95% CI 1.06 - 3.68; p 0.032); GOLD OR 2.10 (95%CI 1.15 - 3.84; p 0.016)</li> <li>• history of respiratory disease during childhood: LLN OR 1.74 (95% CI 1.07 - 2.83; p 0.025); GOLD OR 2.08 (95%CI 1.33 - 3.26; p 0.001)</li> </ul> </li> </ul> <p>Moreover in the case of GOLD-based COPD diagnosis only, Odds ratio estimation suggests a statistically significant association with</p> <ul style="list-style-type: none"> <li>• age: GOLD OR 1.76 (95%CI 1.4-2.11; p &lt;0.001)</li> <li>• age: LLN OR 1.12 (95% CI 0.95 - 1.32; p 0.192)</li> </ul>	<p>Bias-Bewertung für nicht-vergleichende Studien (AWMF 2016) --&gt; Vertrauen in Studienergebnisse:</p> <p><b>(i) prospektive Planung mit Protokoll,</b> in dem Einschlusskriterien und Interventionen sowie interessierende Endpunkte hinterlegt sind: nicht eindeutig beschrieben</p> <p><b>(ii) konsekutiver Patienteneinschluss:</b> nicht eindeutig beschrieben</p> <p><b>(iii) transparentes, nicht-selektives Berichten</b> in Bezug auf Patientencharakteristika, Intervention und Ergebnis: ja</p>
<p>Borlee F. Spirometry, questionnaire and electronic medical record based COPD in a population survey: Comparing prevalence, level of agreement and associations with potential risk factors. <i>PLoS One</i> 2017;</p>	<ul style="list-style-type: none"> <li>• Prävalenz der COPD in Holland</li> <li>• general population (aged 18-70 years) in the south of the Netherlands</li> <li>• <b>Studienstart:</b> 2012: Screening questionnaire; 03/2014-Februar 2015: Extended questionnaire, lung function, serum</li> </ul>	<p>Prävalenz der COPD je nach genutzter Definition:</p> <ul style="list-style-type: none"> <li>• Self-reported data</li> <li>• Electronic Medical Records</li> <li>• Spirometry</li> </ul> <p>1) post-BD measurement of FEV1/FVC below the LLN (GLI 2012) 2) a post-BD measurement of FEV1/FVC &lt;0.70 (GOLD)</p> <ul style="list-style-type: none"> <li>• n=1793</li> </ul>	<p>Bias-Bewertung für nicht-vergleichende Studien (AWMF 2016) --&gt; Vertrauen in Studienergebnisse:</p> <p><b>(i) prospektive Planung mit Protokoll,</b> in dem Einschlusskriterien und Interventionen sowie interessierende Endpunkte hinterlegt sind: ja</p> <p><b>(ii) konsekutiver Patienteneinschluss:</b> nicht eindeutig</p>

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<p>12(3):e0171494.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/28273094">https://www.ncbi.nlm.nih.gov/pubmed/28273094</a></p>	<ul style="list-style-type: none"> <li>• <b>Interventionen:</b> Self-reported data, Electronic Medical Records, Spirometry (GOLD and LLN GLI 2012)</li> <li>• <b>Studientyp:</b> cross-sectional study; Follow-Up Studie</li> <li>• <b>inclusion criteria:</b> 1) living in the eastern part of Noord-Brabant or the northern part of Limburg; 2) inhabitant of a municipality with &lt;30000 residents; and 3) aged 18–70 years</li> <li>• <b>exclusion: farmers</b> (those who reported to be living or working on a farm) (entnommen aus Ref. 16 des Artikels)</li> <li>• <b>Endpunkt:</b> COPD-prevalence based on four different operational definitions</li> </ul>	<ul style="list-style-type: none"> <li>• The highest COPD-prevalence was found based on spirometry using the GOLD-definition (10.9%; n=196), followed by LLN-definition (5.9%, n=105), self-report (4.6%, n=82) and EMR (2.9%, n=52)</li> <li>• Associations of patients' characteristics (Tabelle 4; Auswahl; ohne Werte für EMR und SRD) <ul style="list-style-type: none"> <li><u>Age (per 10 years), mean (SD)</u></li> <li>Spirometry GOLD: OR 1.81 (1.47-2.22)</li> <li>Spirometry LLN: OR 1.10 (0.87-1.39)</li> <li><u>Female gender</u></li> <li>Spirometry GOLD: OR 0.49 (0.35-0.68)</li> <li>Spirometry LLN: OR 0.74 (0.48-1.13)</li> <li><u>Ever smoker</u></li> <li>Spirometry GOLD: OR 3.50 (2.35-5.22)</li> <li>Spirometry LLN: OR 4.10 (2.35-7.17)</li> <li><u>Pack years (per 10 years), Mean* (SD)</u></li> <li>Spirometry GOLD: OR 1.23 (1.13-1.35)</li> <li>Spirometry LLN: OR 1.31 (1.19-1.44)</li> <li><u>BMI &lt; 20 (ref = BMI 20-25)</u></li> <li>Spirometry GOLD: OR 2.91 (1.04-8.11)</li> <li>Spirometry LLN: OR 6.44 (2.43-17.11)</li> <li><u>BMI &gt; 25 (ref = BMI 20-25)</u></li> <li>Spirometry GOLD: OR 0.57 (0.40-0.82)</li> <li>Spirometry LLN: OR 0.57 (0.36-0.90)</li> </ul> </li> </ul>	<p>beschrieben</p> <p><b>(iii) transparentes, nicht-selektives Berichten</b> in Bezug auf Patientencharakteristika, Intervention und Ergebnis: ja</p>
<p>Fisher AJ. Respiratory health and disease in a U.K. population-based cohort of 85 year olds: The Newcastle 85+ Study. Thorax 2016; 71(3):255–66.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/26732736">https://www.ncbi.nlm.nih.gov/pubmed/26732736</a></p>	<ul style="list-style-type: none"> <li>• UK; North-East England</li> <li>• population-based single year birth-cohort of 85 year olds</li> <li>• <b>Studienstart/Studienende:</b> 17 - month-period spanning 2006 and 2007</li> <li>• <b>Interventionen:</b> self-reporting of symptoms and measurement of spirometry</li> <li>• <b>Studientyp:</b> Prävalenzstudie (Fall-Kontroll-Studie)</li> </ul>	<ul style="list-style-type: none"> <li>• <u>healthy reference group aged 85 (HRG):</u> with no respiratory symptoms, no respiratory diagnoses, no current use of respiratory medications and no non-respiratory diagnosis which might influence lung function (eg, Parkinson's disease, kyphoscoliosis, heart failure, ankylosing spondylitis) in their GPRR. Those with a BMI &gt;30 were also excluded from HRG.</li> <li>• Spirometry: n=737 (HRG comprised 20.5% (151/737) of the spirometry cohort) <ul style="list-style-type: none"> <li><u>normal FEV1/FVC ratio:</u> 31.2% (230/737)</li> <li><u>restrictive pattern:</u> 15.2% (112/737)</li> <li><u>obstructive spirometry:</u> men: 58.4%, 171/293; women: 50.5%, 224/444 --&gt; but with no gender difference in the spread of severity</li> </ul> </li> <li>• COPD group (physician diagnosed) (n=123 mit auswertbarer Spirometrie) <ul style="list-style-type: none"> <li><u>obstructive spirometry by GOLD criteria:</u> 75.6% (93/123) ; 76.9% (40/52)</li> </ul> </li> </ul>	<p>Bewertung des Biasrisikos nach der Newcastle Ottawa Skala (NOS)</p> <p><b>I. Selektion der Studienteilnehmer</b></p> <ol style="list-style-type: none"> <li>1) Wurden die ‚Fälle‘ adäquat definiert?: ja</li> <li>2) Sind die ‚Fälle‘ repräsentativ?: ja</li> <li>3) Sind die ‚Kontrollen‘ repräsentativ, erfolgte eine adäquate Auswahl der ‚Kontrollen‘?: ja (‚Kontrollen‘ stammen aus einer vergleichbaren Population wie die ‚Fälle‘)</li> <li>4) Wurden die Kontrollen adäquat definiert?: ja</li> </ol> <p><b>II. Vergleichbarkeit</b></p> <ol style="list-style-type: none"> <li>1) Ist die Vergleichbarkeit der ‚Fälle‘ und ‚Kontrollen‘ gegeben?: ja</li> </ol>

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	<ul style="list-style-type: none"> <li>• <b>Einschlusskriterien:</b> people living at home or in institutional care and regardless of their current health status</li> <li>• <b>Ausschlusskriterien:</b> have end-stage terminal illness or whose behaviour might prove a threat to a research nurse visiting alone</li> <li>• <b>primäre Endpunkte:</b> respiratory health, prevalence of respiratory disease and use of spirometry in respiratory diagnosis</li> </ul>	<p>men and 74.7% (53/71) woman  <u>obstructive spirometry by GLI prediction models:</u> 49.6% (61); 48.1% (25/52) men and 50.7% (36/71) women</p> <p>Approximately half of the HRG (men: 47.4%, 27/57; women: 42.6%, 40/94) had a spirometry definition of airflow obstruction by GOLD criteria yet did not fulfil the requirements for a diagnosis of COPD through lack of symptoms. (All: 44.4% (67/151))                      When applying the GLI criteria to HRG only 17.5% (10/57) men and 16% (15/94) women fulfilled criteria for airflow obstruction suggesting that GLI offered superiority to GOLD in spirometry interpretation in this age group. (All: 16.6% (25/151))</p> <p><u>Conclusion:</u> Current definitions of COPD based on spirometry may lead to overdiagnosis in a group with transient symptoms and 'normal' lung ageing, whereas at the same time failure to use spirometry to assess symptoms in this age group may lead to mislabelling those with breathlessness or cough as having COPD when there are other explanations.</p>	<p><b>III. Expositionserfassung</b></p> <p>1) Erfolgte eine valide Erfassung der Exposition?: ja                      2) Erfolgte die Erfassung der ‚Fälle‘ und ‚Kontrollen‘ identisch?: ja                      3) Kann die ‚Non-Response-Rate‘ als valide betrachtet werden?: ja</p>

### Anhang 5.4 Phänotypisierung mittels Computertomographie

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Occipinti M. Emphysematous and Nonemphysematous Gas Trapping in Chronic Obstructive Pulmonary Disease: Quantitative CT Findings and Pulmonary Function. Radiology 2018; 287(2):683–92.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/29361243">https://www.ncbi.nlm.nih.gov/pubmed/29361243</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>• Two-Center study; Italien</li> <li>• Retrospektive Interpretation einer prospektiven, konsekutiven Korrelationsstudie</li> <li>• <b>Ziel:</b> To identify a prevalent computed tomography (CT) subtype in patients with chronic obstructive pulmonary disease (COPD) by separating emphysematous from nonemphysematous contributions to total gas trapping and to attempt to predict and grade the emphysematous gas trapping by using clinical and functional data.</li> <li>• Patienten mit COPD (GOLD stages I - IV)</li> <li>• <b>Interventionen:</b> - Pulmonary function testing: pre- and postbronchodila-</li> </ul>	<p>n=224; n=202 included in analysis (159 men; 43 women; mean age 71 years range 41 - 85 / 67 years range 46 - 84)</p> <p>Patients with similar values of %LAA-950insp had different values in %LAA-856exp</p> <ul style="list-style-type: none"> <li>• prevalent emphysema group: n=29 (14,4%) (%LAA-950insp higher than the mean value and percentage of functional gas trapping lower than the mean value)</li> <li>• prevalent functional gas trapping group: n= 46 (22,8%) (%LAA-950insp lower than the mean value and percentage of functional gas trapping higher than the mean value)</li> <li>• greater degree of both components: n=57 (28,2%)</li> <li>• lower degree of both components: n=70 (34,6%)</li> </ul> <p>• authors conclusion (Auszug): In conclusion, our study</p>	<p><b>Beurteilung mit QUADAS II</b> (jedoch eingeschränkte Beurteilbarkeit, da dies keine explizite diagnostische Genauigkeitsstudie ist)</p> <p><u>Domain 1: patient Selection</u></p> <p>Could the selection of patients have introduced bias? LOW</p> <p><u>Domain 2: Index Test(s)</u></p> <p>Could the conduct or interpretation of the index test have introduced bias? UNCLEAR</p> <p><u>Domain 3: Reference Standard</u></p>



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	<p>for Spirometry, static lung volumes, single breath diffusing capacity for carbon monoxide</p> <p>- Chest-CT at full inspiration and expiration: Somatom Sensation 64/ Somatom Definition Flash 128; 120 kPv; 200 mAs; rotation time 0.5 sec; pitch 1:1; section thickness 0.75mm</p> <p>Thresholds at -950 HU (inspiration) and -856 HU (expiration) were chosen as densitometric cut-off values consistent with emphysema and total gas trapping --&gt; post-processing image analysis of lung parenchyma and airways</p> <p>+ analysis with deformable coregistration of paired inspiratory and expiratory CT scans, to obtain voxel-by-voxel attenuation maps (pulmonary parametric response maps)</p> <p>●<b>Einschlusskriterien:</b> age 40-85 years, smoking history of &gt;10 pack-years, with nonreversible postbronchodilator airway obstruction, underwent Chest CT within 48 h of pulmonary function evaluation</p> <p>●<b>Ausschlusskriterien:</b> exacerbation within 1 month, asthma, diffuse bronchiectasis, interstitial lung disease, acute heart failure, chemotherapy and/or radiation therapy, lung cancer, lung surgery, metal objects in chest</p>	<p>demonstrated that standard imaging metrics obtained at inspiratory and expiratory thoracic CT scans can be used to identify and quantify the relative contribution of emphysematous and nonemphysematous gas trapping, permitting a better definition of COPD subtypes.</p>	<p>Could the reference standard, its conduct, or its interpretation have introduced bias? UNCLEAR</p> <p><u>Domain 4: Flow and Timing</u></p> <p>Could the patient flow have introduced bias?: LOW</p> <p>●possible concerns regarding applicability: Matching our review question?</p>
<p>Hong Y. Sex differences of COPD phenotypes in nonsmoking patients. Int J Chron Obstruct Pulmon Dis 2016; 11:1657–62.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/27524891">https://www.ncbi.nlm.nih.gov/pubmed/27524891</a></p> <p>• Nicht zitiert.</p>	<p>●Korea</p> <p>● nonsmoking patients with COPD from a Korean COPD cohort</p> <p>● Subgruppenanalyse einer Kohortenstudie (n=445; n=335 with COPD --&gt;97 patients were selected for this study if they had a cigarette smoking history of &lt;1 pack-year)</p> <p>●<b>Ein- und Ausschlusskriterien Primärstudie:</b> aged &gt;45 years and had a postbronchodilator forced expiratory volume in 1 second (FEV<sub>1</sub>)/forced vital capacity &lt;0.7.</p>	<p>&gt;&gt;Geschlechtsunterschiede untersucht (Emphysemindex per CT)</p> <p>n=97 (62 female, 35 male)</p> <p>● <u>sex-related phenotypes of COPD</u></p> <p>Emphysema index was significantly lower (3.5±4.2 vs 6.2±5.7, P&lt;0.01) and mean WA% on computed tomography was significantly higher (71.8%±5% vs 69.4%±5%, P&lt;0.01) in females than in males</p> <p>●MMRC, CAT, history of exacerbation, and FEV<sub>1</sub> (% of predicted) did not differ significantly between males and females</p> <p>● "authors conclusion": WA% was higher and emphysema</p>	<p>AWMF-Manual Bias-Bewertung nichtvergleichende Studien:</p> <p><u>1. prospektive Planung mit Protokoll:</u> keine definitive Beurteilung möglich</p> <p><u>2. konsekutiver Patienteneinschluss:</u> unklar</p> <p><u>3. transparentes, nicht-selektives Berichten:</u> ja</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<ul style="list-style-type: none"> <li>●<b>Interventionen:</b> All patients were evaluated at the enrollment visit by a medical interview, a physical examination, spirometry, laboratory tests, and a CT scan (first-generation dual source).</li> <li>●<b>primärer Endpunkt:</b> sex-related phenotypes of COPD</li> </ul>	<p>extent was lower in nonsmoking females with COPD than in nonsmoking males with COPD. These findings suggest that males may be predisposed to an emphysema phenotype and females may be predisposed to an airway phenotype of COPD.</p>	
<p>Mohamed Hoesein FA. Discriminating dominant computed tomography phenotypes in smokers without or with mild COPD. <i>Respir Med</i> 2014; 108(1):136–43.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/24035313">https://www.ncbi.nlm.nih.gov/pubmed/24035313</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>●1140 male smokers without or with mild COPD</li> <li>●<b>Ziel:</b> to discriminate emphysematous, large airway wall thickening and small airways disease dominant phenotypes</li> <li>●sub-study of the Dutch and Belgium Lung Cancer Screening Trial (NELSON trial; RCT)</li> <li>●Ergebnisse des Screening-Armes wurden in dieser Subgruppenanalyse ausgewertet</li> <li>●<b>Interventionen:</b> 1. Screen arm:                         <ol style="list-style-type: none"> <li>a. 16-detector multi-slice computed tomography of the chest in year 1, 2 and 4 of the study;</li> <li>b. Pulmonary function test;</li> <li>c. Blood sampling;</li> <li>d. Questionnaires;</li> <li>e. Smoking cessation advice for current smokers.</li> </ol> </li> <li>●<b>Einschlusskriterien Primärstudie:</b> <ol style="list-style-type: none"> <li>1. Born between 1928 and 1956;</li> <li>2a. Smoked &gt; 15 cigarettes/day during &gt; 25 years or;</li> <li>2b. Smoked &gt; 10 cigarettes/day during &gt; 30 years;</li> <li>3. Current or former smokers who quit smoking =&lt; 10 years ago.</li> </ol> </li> <li>●<b>Ausschlusskriterien Primärstudie:</b> <p>Subjects</p> <ol style="list-style-type: none"> <li>1. With a moderate or bad self-reported health who were unable to climb two flights of stairs;</li> <li>2. With a body weight &gt;= 140 kilogram;</li> <li>3. With current or past renal cancer, melanoma or breast cancer;</li> <li>4. With lung cancer diagnosed less than 5 years ago or 5 years or more ago but still under treatment;</li> <li>5. Who had a chest CT examination less than one year before they filled in the first NELSON questionnaire.</li> </ol> </li> </ul>	<p>&gt;&gt;3 verschiedene COPD-Phänotypen: Detektion durch CT</p> <ul style="list-style-type: none"> <li>●COPD subjects (86%) were in GOLD stage 1, 14% had GOLD stage 2 or 3</li> <li>●573 subjects had any of the three CT measures in the upper quartile. Of these                         <ul style="list-style-type: none"> <li>●n=367 (64%) were in a single dominant group and n=206 (36%) were in a mixed group.</li> <li>●Of all included subjects 143 (13%) subjects were emphysema dominant, 91 (8%) air trapping dominant and 133 (12%) AWT dominant.</li> <li>●Airway wall thickening dominance was associated with younger age (<math>p &lt; 0.001</math>), higher body mass index (<math>p &lt; 0.001</math>), more wheezing (<math>p &lt; 0.05</math>) and lower FEV %predicted (<math>p &lt; 0.001</math>).</li> <li>●Emphysema dominant subjects had lower FEV1/FVC (<math>p &lt; 0.05</math>) and Kco %predicted (<math>p &lt; 0.05</math>).</li> <li>●There was no significant difference in respiratory related hospitalizations (<math>p = 0.09</math>).</li> </ul> </li> </ul> <p>"authors conclusion": CT measures can discriminate three different CT dominant groups of disease in male smokers without or with mild COPD.</p>	<p>AWMF-Manual Bias-Bewertung nichtvergleichende Studien:</p> <p><u>1. prospektive Planung mit Protokoll:</u> ja (online verfügbar)</p> <p><u>2. konsekutiver Patienteneinschluss:</u> unklar</p> <p><u>3. transparentes, nicht-selektives Berichten:</u> ja</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Bafadhel M. The role of CT scanning in multidimensional phenotyping of COPD. Chest 2011; 140(3):634–42.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/21454400">https://www.ncbi.nlm.nih.gov/pubmed/21454400</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>●England</li> <li>●consecutive study (longitudinal Biomarkers in COPD Exacerbation study)</li> <li>●n=75</li> </ul> <p>●<b>Einschlusskriterien:</b> Patients with a physician diagnosis of COPD (GOLD); obstructive spirometry with a postbronchodilator FEV1/FVC ratio of &lt;0.7</p> <p>- patients with COPD who demonstrated bronchodilator reversibility were not excluded</p> <p>●<b>Ausschlusskriterien:</b> Patients with a diagnosis of asthma, current active pulmonary TB, or any other clinically relevant lung disease</p> <p>●<b>Measurements:</b></p> <ul style="list-style-type: none"> <li>- Full lung function, including reversibility testing with 400 mg inhaled albuterol</li> <li>- SGRQ, Chronic Respiratory Disease Interviewer-Administered Questionnaire BMI, Spontaneous or induced sputum analysis (PCR), Venous blood was collected for assessment of peripheral blood differential cell counts and serum C-reactive protein</li> <li>- CT Imaging: Sensation 16-slice scanner</li> </ul>	<p>n=58 men; n=17 women</p> <ul style="list-style-type: none"> <li>●radiologic COPD disease groups seen in clinical practice: emphysema (EM; included the presence of centrilobular, panlobular, and paraseptal EM), bronchial wall thickening (BWT), and bronchiectasis (BE)</li> <li>●The presence of emphysema (EM), bronchiectasis (BE), and bronchial wall thickening (BWT) was found in 67%, 27%, and 27% of subjects, respectively. The presence of EM was associated with lower lung function (mean difference % FEV1 -20%; 95% CI, -28 to -11; P&lt; .001).</li> </ul> <p>"authors conclusion"</p> <p>CT imaging provides additional value to clinical and physiologic parameters in the multidimensional phenotyping of COPD</p>	<p>AWMF-Manual Bias-Bewertung nichtvergleichende Studien:</p> <p><u>1. prospektive Planung mit Protokoll:</u> unklar</p> <p><u>2. konsekutiver Patienteneinschluss:</u> ja</p> <p><u>3. transparentes, nicht-selektives Berichten:</u> ja</p>
<p>Han MK. Clinical significance of radiologic characterizations in COPD. COPD 2009; 6(6):459–67.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/19938970">https://www.ncbi.nlm.nih.gov/pubmed/19938970</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>●USA</li> <li>●Korrelationsstudie, subset of the multicenter Lung Tissue Research Consortium LTRC</li> <li>●n=156 (von n=1400 der Hauptstudie)</li> </ul> <p>●<b>Einschlusskriterien</b></p> <ul style="list-style-type: none"> <li>- &gt;10 pack-years smoking history</li> <li>- airflow obstruction FEV1/FVC &lt;0.70</li> <li>- clinical diagnosis of COPD</li> </ul> <p>●<b>Ausschlusskriterien:</b></p> <ul style="list-style-type: none"> <li>-additional pathological or imaging chronic lung disease other than malignancy</li> </ul> <p>●<b>Measurements:</b></p> <ul style="list-style-type: none"> <li>- HRCT (8 detector or greater)</li> </ul>	<p>We hypothesized HRCT phenotype would strongly influence clinical outcomes including health status, exacerbation frequency, and BODE</p> <ul style="list-style-type: none"> <li>●emphysema percent is significantly correlated with both FEV1 and systemic components of BODE, with the strongest correlation between emphysema percent and total BODE score</li> <li>●FEV1 and HRCT features (emphysema percent and VBT) are both significantly related to health status, even when accounting for FEV1</li> <li>●the airway thickness VBT, but not emphysema, predicts self-reported exacerbation frequency among patients who experienced an exacerbation in the prior year, but with an attenuated effect for older ages, due to an age-bronchial</li> </ul>	<p>AWMF-Manual Bias-Bewertung nichtvergleichende Studien:</p> <p><u>1. prospektive Planung mit Protokoll:</u> unklar</p> <p><u>2. konsekutiver Patienteneinschluss:</u> unklar</p> <p><u>3. transparentes, nicht-selektives Berichten:</u> ja</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	-SGRQ, BODE Index, self-reported exacerbation frequency, mMRC - Spirometry (before and after albuterol) + DLCO	thickness interaction	
<p>Kim WJ. CT metrics of airway disease and emphysema in severe COPD. Chest 2009; 136(2):396–404.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/19411295">https://www.ncbi.nlm.nih.gov/pubmed/19411295</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>●International</li> <li>●Subgruppenanalyse von n=338 in the National Emphysema Treatment Trial (NETT) Genetics Ancillary Study</li> <li>●patients with severe COPD</li> <li>●Einschlusskriterien: FEV1 &lt; 45% predicted; CT scan evidence of severe emphysematous destruction</li> <li>●Measurements:                             <ul style="list-style-type: none"> <li>- CT</li> <li>- Spirometry, questionnaires, BODE Index</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>●Male subjects exhibited significantly thicker airway wall phenotypes (p = 0.007 for WT and p = 0.0006 for SRWA).</li> <li><u>wall thickness (WT):</u> male: 1,56 ± 0,23 mm female: 1,48 ± 0,27 mm</li> <li><u>square root of wall area (SRWA)</u> male: 4,66 ± 4,47 mm<sup>2</sup> female: 4,47 ± 0,54 mm<sup>2</sup></li> <li><u>%LAA-950</u> male: 0,17 ± 0,10 female: 01,6 ± 0,12 p=0,81</li> <li>"authors conclusion" : Airway disease and emphysema detected by CT scanning are inversely related in patients with severe COPD. Airway wall phenotypes were influenced by gender and associated with lung function in subjects with severe emphysema.</li> </ul>	<p>AWMF-Manual Bias-Bewertung nichtvergleichende Studien:</p> <p><u>1. prospektive Planung mit Protokoll:</u> unklar</p> <p><u>2. konsekutiver Patienteneinschluss:</u> unklar</p> <p><u>3. transparentes, nicht-selektives Berichten:</u> ja</p>
<p>Copley SJ. Thin-section CT in obstructive pulmonary disease: Discriminatory value. Radiology 2002; 223(3):812–9.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/12034954">https://www.ncbi.nlm.nih.gov/pubmed/12034954</a></p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>●UK/Canada</li> <li>●Thin-section CT of n=105 patients with obstructive pulmonary disease (asthma n=35; centrilobular emphysema n=30; panlobular emphysema n=21; obliterative bronchiolitis n=19) and healthy subjects</li> <li>●Diagnostic accuracy for first-choice diagnosis by two observers were calculated</li> <li>Interventionen                             <ul style="list-style-type: none"> <li>●electron-beam CT scanner or HiSpeed Advantage CT Scanner</li> <li>●pulmonary function test within 3 month of CT scanning</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>●A correct first-choice diagnosis was made [...] in 53 of 60 (88%) observations in patients with centrilobular emphysema, [...] and in 20 of 42 (48%) observations in patients with panlobular emphysema.</li> <li>●One major sources of diagnostic inaccuracy were differentiation between panlobular and centrilobular emphysema [...]</li> <li>Centrilobular emphysema (n=60) Sensitivity(%) 88 (53/60) Specificity (%) 90 (194/216) Accuracy (%) 89 (247/276)</li> <li>Panlobular emphysema (n=42) Sensitivity(%) 48 (20/42) Specificity (%) 97 (227/234) Accuracy (%) 89 (247/276)</li> </ul>	<p><b>Beurteilung mit QUADAS II</b></p> <p><u>Domain 1: patient Selection</u></p> <p>Could the selection of patients have introduced bias? LOW</p> <p><u>Domain 2: Index Test(s)</u></p> <p>Could the conduct or interpretation of the index test have introduced bias? UNCLEAR</p> <p><u>Domain 3: Reference Standard</u></p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
		The prevalence of CT features in patients with centrilobular vs. panlobular emphysema was also assessed. The only significant difference in favor of panlobular emphysema was the presence of long lines (adjoining visible interlobular septa, not linear atelectasis) (p=0.02.) Likewise, there was no significant difference between the extent of CT features, apart from long lines (median extent for centrilobular emphysema: 0.5; range 0-4.5; median extent for panlobular emphysema: 2.5; range 0-5-5; p<0.05)	<p>Could the reference standard, its conduct, or its interpretation have introduced bias? UNCLEAR</p> <p><u>Domain 4: Flow and Timing</u></p> <p>&gt;&gt;Could the patient flow have introduced bias?: LOW</p> <ul style="list-style-type: none"> <li>possible concerns regarding applicability: Matching our review question?</li> </ul>

### Anhang 5.5 Cut-Off Symptomerfassung

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Karloh M. The COPD Assessment Test: What Do We Know So Far?: A Systematic Review and Meta-Analysis About Clinical Outcomes Prediction and Classification of Patients Into GOLD Stages. Chest 2016; 149(2):413–25.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/26513112">https://www.ncbi.nlm.nih.gov/pubmed/26513112</a></p>	<ul style="list-style-type: none"> <li><b>Ziel des Reviews:</b> <ul style="list-style-type: none"> <li>-review the determinants of the CAT score</li> <li>-its ability to predict clinical outcome</li> <li>-agreement between CAT (≥ 10) and mMRC (≥2)</li> </ul> </li> <li><b>Suchzeitraum:</b> 01/2009 - 06/2015</li> <li><b>untersuchte Tests:</b> CAT, mMRC Metaanalyse CAT und mMRC agreement: n=8 Studien</li> <li><b>Population:</b> patients with COPD or suspected of COPD</li> <li><b>Einchlusskriterien:</b> English, Spanish and Portuguese language, published in peer-reviewed journals</li> <li><b>Ausschluss:</b> meeting abstracts, case reports, editorials, comments, reviews</li> <li><b>eingeschlossenen Studientypen:</b> Cross-sectional, prospective observational cohort, retrospective cohort, cross-sectional surveys</li> </ul>	<p>Ten studies have evaluated the distribution of patients in each stage of the new GOLD grading classification according to the tool used to assess symptoms. All studies found a different proportion of patients in each category using CAT ≥ 10 or mMRC ≥2. There was a misclassification of 13% in all GOLD categories. Eight of them reported agreement analysis comparing the frequencies of patients classified according to CAT or mMRC. The agreement between CAT and mMRC ranged from poor to substantial. The pooled k is not presented due to heterogeneity across studies (I<sup>2</sup>=99,3). Based on the discrepancy with respect to the of CAT or mMRC, Jones et al. [Ref ID 28142] suggested the cut point of ≥1 for the mMRC showing greater k coefficients</p> <p>The results also showed that CAT and mMRC are not equivalent for the purpose of assessing a patients' symptoms,</p> <p><b>&gt;&gt; systematischer Review</b></p> <p><b>&gt;&gt; vergleicht Cut off von mMRC vs. CAT ein mMRC ≥ 1 (anstatt ≥ 2) entspricht eher dem CAT ≥ 10</b></p> <p><b>&gt;&gt; Verteilung der Patient*innen mit COPD auf das GOLD-System --&gt; Unterschiede, je nachdem welcher Test genutzt wird</b></p>	<p>AMSTAR: 6/11</p> <p>n-y-y-n-n-y-y-y-n-ca</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Hering T. COPD Classification GOLD I-IV vs. GOLD A-D in Real Life: Comparing Impact on Application, Advantages and Disadvantages. Pneumologie 2015; 69(11):645–53.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/26458126">https://www.ncbi.nlm.nih.gov/pubmed/26458126</a></p>	<ul style="list-style-type: none"> <li>• 18 pneumologischen Facharztpraxen: schriftliche Befragung von erwachsene Patient*innen mit COPD</li> <li>• <b>Patienten:</b> mit COPD</li> <li>• <b>Studienstart/ Studienende:</b> 4. Quartal 2014</li> <li>• <b>Einchlusskriterien:</b> erwachsene Patient*innen (mindestens 18 Jahre alt) mit COPD, die Diagnose muss vom Pneumologen bestätigt sein, der Patient muss nicht „neu“ sein, und der Patient/die Patientin wurde vom Hausarzt überwiesen bzw. wird gemeinsam mit dem Hausarzt betreut.</li> <li>• <b>Endpunkte:</b> Erhebung von CAT, Exazerbationen+ Ermittlung der GOLD-Gruppenzugehörigkeit</li> </ul>	<p>n=1274</p> <p>Mit den Angaben zu CAT, Exazerbationen und Schweregrad wurde die Gruppenzugehörigkeit nach GOLD A–D ermittelt.</p> <ul style="list-style-type: none"> <li>• Es zeigte sich, dass der Schweregrad nach GOLD nicht unbedingt einen Rückschluss auf die Beeinträchtigung durch die COPD zulässt.</li> <li>• Wesentlich beeinflusst werden die Anteile der Patient*innen an den jeweiligen Gruppen auch durch das Ergebnis des CAT mit 10 Punkten als Schwellenwert der Beeinträchtigung. Verschiebt man diesen Wert auf 15 oder 20 Punkte, hat das einen erheblichen Einfluss auf die Patientenverteilung nach Gruppen. Bei einem Schwellenwert von 15 Punkten erhöhen sich die Anteile der Gruppen A und C mit geringer Beeinträchtigung bereits um mehr als das Doppelte von 12% auf 25% und von 6 % auf 14 %. Die Gruppe D mit hohem Risiko und hoher Beeinträchtigung sinkt von 46% auf 39 %. Bei einem Schwellenwert von 20 Punkten sinkt die Gruppe D auf 28 %.</li> </ul> <p>&gt;&gt; untersuchen Verteilung der Patient*innen mit COPD auf das 2015er GOLD-System I-IV und A-D in deutscher Versorgung                  &gt;&gt; hypothetische Verteilung, wenn der Cut-Off beim CAT für die Einschätzung geringe/starke Symptome bei &gt;15 oder &gt; 20 Punkten liegt                  &gt;&gt; mögliche über- und Untertherapie                  &gt;&gt; bei 15 Punkten anscheinend homogenere Verteilung der Patient*innen in die Gruppen</p>	<p>"Bias-Bewertung für nicht-vergleichende Studien; AWMF 2016:</p> <p><b>(I) prospektive Planung mit Protokoll:</b> keine Angaben</p> <p><b>(II) konsekutiver Patientenein-schluss:</b> nicht eindeutig beschrieben</p> <p><b>(II) transparentes, nicht-selektives Berichten in Bezug auf Patientencharakteristika, Intervention und Ergebnis:</b> detaillierte Angaben zu den eingeschlossenen Patienten fehlen</p>
<p>Zhou Z. A comparison of the assessment of health status between CCQ and CAT in a Chinese COPD clinical population: A cross-sectional analysis. Int J Chron Obstruct Pulmon Dis 2018; 13:1675–82.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/29872285">https://www.ncbi.nlm.nih.gov/pubmed/29872285</a></p>	<ul style="list-style-type: none"> <li>• <b>Chinesische Population</b></li> <li>• <b>Patient*innen:</b> outpatients with stable COPD</li> <li>• <b>Studienstart:</b> 11/2015 to 12/2016 (Enrollment)</li> <li>• <b>untersuchte Tests:</b> CAT, CCQ</li> <li>• <b>Studientyp:</b> observational, cross-sectional, cohort study</li> <li>• <b>Einchlusskriterien:</b> Patients &gt; 40 years of age</li> <li>• <b>Ausschlusskriterien:</b> Patients who refused to complete questionnaires,</li> </ul>	<p>n=372</p> <p>The CCQ cutoff point of 1.0 classified 97.3% of patients into the high symptom group (groups B and D), which was statistically higher than that of the CAT (82.3%) and CCQ with a cutoff point of 1.5 (78.0%). No significant difference was observed in the proportion of subjects who had more symptoms between the CAT and CCQ with the cutoff point of 1.5. The kappa of agreement for the symptom groups by CAT and CCQ (cutoff point 1.5) was 0.495, suggesting moderate agreement (Table 2), but slight agreement (0.144) was found between the CAT and CCQ with the cutoff point of 1.0.</p> <p>main findings: 1) compared with the CAT, the CCQ was more likely to classify the patients into more severe categories, and it seemed that 1.5 rather than 1.0 might be a better cutoff point for the CCQ and 2) both the CAT and the overall CCQ with its 3 domains could discriminate between groups of patients who differ in COPD severity.</p> <p>The CAT and CCQ results can be categorized into 4 levels: scores of 0–10, 11–20, 21–30, and 31–40 represent low, medium, high, and very high impact level by CAT. Correspondingly,</p>	<p>"Bias-Bewertung für nicht-vergleichende Studien; AWMF 2016:</p> <p><b>(I) prospektive Planung mit Protokoll:</b> ja</p> <p><b>(II) konsekutiver Patientenein-schluss:</b> nicht eindeutig beschrieben</p> <p><b>(II) transparentes, nicht-selektives Berichten in Bezug auf Patientencharakteristika, Intervention und Ergebnis:</b> ja</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<p>asthma, lung cancer or other lung disease under active treatment (eg tuberculosis or pneumonia)</p> <ul style="list-style-type: none"> <li>• <b>primärer Endpunkt:</b> compare the evaluation of symptom severity between the CAT and the CCQ and to find a cutoff value of the CCQ for the Chinese clinical population</li> <li>• <b>sekundäre Endpunkte:</b> correlation between the CAT, the CCQ, the modified Medical Research Council (mMRC) questionnaire, lung function, and exacerbation history.</li> </ul>	<p>scores of the CCQ can be considered as acceptable (<math>CCQ &lt; 1</math>), acceptable for moderate disease (<math>1 \leq CCQ &lt; 2</math>), instable-severe limited (<math>2 \leq CCQ &lt; 3</math>), and very instable-very severe limited (<math>CCQ \geq 3</math>).</p> <p><b>&gt;&gt; CCQ cut-off von 1,5 Punkten (anstatt 1,0) entspricht eher dem CAT cut-off von 10 Punkten</b></p>	
<p>Jo YS. The cutoff point of clinical chronic obstructive pulmonary disease questionnaire for more symptomatic patients. BMC Pulm Med 2018; 18(1):38.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/29482616">https://www.ncbi.nlm.nih.gov/pubmed/29482616</a></p>	<ul style="list-style-type: none"> <li>• <b>South Korea</b></li> <li>• <b>Patient*innen:</b> COPD patients</li> <li>• <b>Diagnosis of COPD:</b> 4/2013 - 12/2015 + 3/2014 - 12/2015; multicenter</li> <li>• <b>untersuchte Tests:</b> SGRQ, CCQ, (CAT, mMRC)</li> <li>• <b>Studientyp:</b> Registerstudie; Datenanalyse aus: prospective observational cohort study that enrolls patients with chronic airway disease, including COPD</li> <li>• <b>Einschlusskriterien:</b> aged &gt; 40 years who smoked/had smoked <math>\geq 10</math> packs/year</li> <li>• <b>Ausschlusskriterien:</b> Participants who were not assessed either by SGRQ, the CAT, or the CCQ at the baseline visit</li> <li>• <b>primäre Endpunkte:</b> - assess whether the CCQ correlates</li> </ul>	<p>n=126</p> <p>The CCQ significantly correlated well with SGRQ, the CAT, and the mMRC (<math>r = 0.76, 0.69,</math> and <math>0.53,</math> respectively) (Fig 2). The CCQ showed a significant negative correlation with FEV1 and 6-min walk distance (<math>r = -0.40</math> and <math>-0.42,</math> respectively).</p> <p>A cutoff point of 1.4 showed the highest AUROC for identifying more symptomatic patients with <math>SGRQ \geq 25</math> (AUROC = 0.605, 0.633, 0.681, 0.762, and 0.711 for the CCQ cutoff points of 0.7, 1.0, 1.2, 1.4, and 1.6, respectively). The categorization based on the CCQ cutoff point of 1.4 showed the highest agreement with the SGRQ 25-based categorization (CCQ cutoff point = 0.7: agreement rate = 75.61% and <math>\kappa</math> value = 0.27; CCQ cutoff point = 1: agreement rate = 76.42% and <math>\kappa</math> value = 0.33; CCQ cutoff point = 1.4: agreement rate = 82.11% and <math>\kappa</math> value = 0.56) (Table 2). Even when adjusting for age, sex, body mass index, and FEV1, a CCQ score <math>\geq 1.4</math> was the good determinant of an SGRQ score <math>\geq 25</math> in the CART analysis (relative hazard risk, 1.23).</p> <p><b>&gt;&gt; CCQ cut-off von 1,4 entspricht eher SGRQ von <math>\leq 25</math> (für mehr symptomatische Patient*innen)</b></p>	<p>"Bias-Bewertung für nicht-vergleichende Studien; AWMF 2016:</p> <p><b>(I) prospektive Planung mit Protokoll:</b> retrospektiv angemeldete Studie; daher unklar</p> <p><b>(II) konsekutiver Patienteneinschluss:</b> nicht eindeutig beschrieben</p> <p><b>(II) transparentes, nicht-selektives Berichten in Bezug auf Patientencharakteristika, Intervention und Ergebnis:</b> ja</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	well with other health status measures, lung function, and exercise capacity in Korean COPD patients, - determine CCQ cutoff point that corresponds well with the SGRQ cutoff point of 25		
Smid DE. How to determine an impaired health status in COPD: Results from a population-based study. Neth J Med 2017; 75(4):151–7.  <a href="https://www.ncbi.nlm.nih.gov/pubmed/28522771">https://www.ncbi.nlm.nih.gov/pubmed/28522771</a>	<ul style="list-style-type: none"> <li>• <b>Niederlande</b></li> <li>• <b>Patient*innen:</b> mit und ohne COPD</li> <li>• <b>untersuchte Tests:</b> CAT, Spirometrie</li> <li>• <b>Studientyp:</b> subsample of "the Longitudinal Aging Study Amsterdam (LASA)", Dutch population-based study, multicenter</li> <li>• <b>Einschlusskriterien:</b> subjects aged between 55-65 years; no inclusion or exclusion criteria were outlined in the LASA study.</li> <li>• <b>primärer Endpunkt:</b> which cut-off value represents an abnormal CAT score for non-COPD subjects in a Dutch population</li> <li>• <b>sekundäre Endpunkte:</b> measure the impact of COPD on health status in a Dutch population, after stratification for work status</li> </ul>	<p>n=810</p> <p>When applying the CAT ≥ 10 cut-point, 50.0% of COPD subjects had an impaired health status and when using a CAT &gt; 18 cut-point 7.6% of COPD subjects had an impaired health status</p> <p>Subjects with CAT ≥ 10 points, n (%): 165 (22.8) Subjects with CAT &gt; 18 points, n (%): 28 (3.9)</p> <p><b>&gt;&gt; CAT &gt;18 entspricht besserem cut-off für Einschätzung: impaired health status</b></p>	<p>"Bias-Bewertung für nicht-vergleichende Studien; AWMF 2016:</p> <p><b>(I) prospektive Planung mit Protokoll:</b> nicht eindeutig beschrieben <b>(II) konsekutiver Patienteneinschluss:</b> (ja)</p> <p>(II) transparentes, nicht-selektives Berichten in Bezug auf Patientencharakteristika, Intervention und Ergebnis: ja</p>
Tsiligianni IG. Investigating sensitivity, specificity, and area under the curve of the Clinical COPD Questionnaire, COPD Assessment Test, and Modified Medical Research Council scale according to GOLD using St	<ul style="list-style-type: none"> <li>• <b>Deutschland, Niederlande</b></li> <li>• <b>Patient*innen:</b> mit COPD und Raucher (mind. 10 Jahre)</li> <li>• <b>untersuchte Tests:</b> SGRQ, CAT, CCQ, mMRC</li> <li>• <b>Studientyp:</b> Analyse zweier Datensets: study A, 238 patients from</li> </ul>	<p>n=238 + n= 101</p> <p>ROC analysis: In study A, the proportions of sensitivity, specificity, and AUC for the cutoff point SGRQ ≥ 25 were (respectively) 0.99, 0.43, and 0.96 for CCQ ≥ 1; 0.92, 0.48, and 0.89 for CAT ≥ 10; and 0.68, 0.91, and 0.91 for mMRC ≥ 2.</p> <p>In study B, these results were for the cutoff point SGRQ ≥ 25, and were (respectively) 0.87, 0.77, and 0.9 for CCQ ≥ 1; 0.76, 0.73, and 0.82 for CAT ≥ 10; and 0.21, 1, and 0.81 for mMRC ≥ 2 (Table 3). The maximal difference of high versus low CCQ or CAT scores based on the</p>	<p>"Bias-Bewertung für nicht-vergleichende Studien; AWMF 2016:</p> <p><b>(I) prospektive Planung mit Protokoll:</b> ja</p> <p><b>(II) konsekutiver Patienteneinschluss:</b> nicht beurteilbar</p>



Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>George's Respiratory Questionnaire cutoff 25 (and 20) as reference. Int J Chron Obstruct Pulmon Dis 2016; 11:1045–52.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/27274226">https://www.ncbi.nlm.nih.gov/pubmed/27274226</a></p>	<p>a pulmonary rehabilitation program; and study B, 101 patients from primary care.</p> <ul style="list-style-type: none"> <li>• <b>Einschlusskriterien:</b> Studie A: Participants with spirometry-confirmed COPD GOLD category II–IV Studie B: Patients 45 years of age and older with a smoking history of at least 10 years</li> <li>• <b>Ausschlusskriterien:</b> Studie A: Patients with a relevant hypercapnic respiratory failure (CO<sub>2</sub> partial pressure ≥ 50 mmHg in rest or indication for noninvasive breathing), linguistic and cognitive limitations, and lack of motivation Studie B: concomitant asthma, unstable cardiovascular disease, or any respiratory disease other than COPD</li> <li>• <b>primärer Endpunkt:</b> investigate the criterion validity of the CCQ, CAT, and mMRC scale cutoff points in differentiating between high- and low-symptom groups using the suggested cutoff point of the SGRQ as the gold standard,</li> </ul>	<p>changing SGRQ cutoff of 15–30 was 2.01 for the CCQ and 11.5 for the CAT, both at the SGRQ cutoff point of 20.</p> <p>When the SGRQ cutoff point was adjusted to ≥20, the proportions of sensitivity, specificity, and AUC were (respectively) 0.99, 0.73, and 0.99 for CCQ ≥1; 0.91, 0.73, and 0.94 for CAT ≥10; and 0.66, 0.95 and 0.94 for mMRC ≥2. In study B, these results were 0.8, 0.89, and 0.89 for CCQ ≥1; 0.69, 0.78, and 0.8 for CAT ≥10; and 0.18, 1, and 0.81 for mMRC ≥2.</p> <p><b>&gt;&gt; vergleicht Kompatibilität zwischen den Cut-offs von CAT, mMRC, CCQ im Vergleich zu SGRQ</b> <b>&gt;&gt; ein Cut-off des SGRQ von ≥ 20 stimmt besser mit den anderen Cut-offs der Tests überein, als der von ≥ 25</b> <b>&gt;&gt; Beweis: verschiedene Cut-offs der 4 Tests sind nicht 1:1 übertragbar</b></p>	<p><b>(II) transparentes, nicht-selektives Berichten in Bezug auf Patientencharakteristika, Intervention und Ergebnis: ja</b></p>
<p>Huang W-C. Features of COPD patients by comparing CAT with mMRC: A retrospective, cross-sectional study. NPJ Prim Care Respir Med 2015; 25:15063.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/26538368">https://www.ncbi.nlm.nih.gov/pubmed/26538368</a></p>	<ul style="list-style-type: none"> <li>• <b>Taiwan</b></li> <li>• <b>Patient*innen mit COPD</b></li> <li>• <b>Studienstart:</b> 11/2012</li> <li>• <b>Studienende:</b> 8/2013</li> <li>• <b>untersuchte Tests:</b> CAT, mMRC</li> <li>• <b>Studientyp:</b> Datenanalyse einer large-scale, cross sectional, multi-centre, observational, retrospective study</li> </ul>	<p>n=757 subjects included in analysis</p> <p>Based on the cut-points CAT score ≥ 10 and mMRC scale ≥ 2 recommended by the GOLD 2011, classifying patients by CAT resulted in 30.6, 17.3, 22.2 and 29.6% of participants in groups A, B, C and D, whereas by mMRC resulted in 22.2, 26.0, 1.9 and 35.9%, respectively.</p> <p>The best agreement of group assignment emerged when the cut-point CAT score ≥ 10 corresponded to the cut-point mMRC ≥ 3 (kappa = 0.55, P = 0.000), whereas the worst agreement emerged when the cut-point CAT score ≥ 10 corresponded to the cut-point mMRC ≥ 1 (kappa = 0.36, P = 0.000)</p>	<p>"Bias-Bewertung für nicht-vergleichende Studien; AWMF 2016:</p> <p><b>(I) prospektive Planung mit Protokoll:</b> nicht eindeutig beschrieben</p> <p><b>(II) konsekutiver Patientenein-schluss:</b> nicht eindeutig beschrieben</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<p>of the TOLD consortium</p> <ul style="list-style-type: none"> <li>• <b>Einschlusskriterien:</b> patients aged <math>\geq 40</math> years with a confirmed diagnosis of COPD based on the GOLD 2011 recommendation and a spirometry within the previous 1 year before enrollment</li> <li>• <b>Ausschlusskriterien:</b> participated in interventional clinical trials in the previous 1 year, had a history of asthma or, for the purpose of this study, did not complete both the CAT and mMRC</li> <li>• <b>primäre Endpunkte:</b> clarify how different patient characteristics influence the differences, to determine the relationships between CAT and mMRC and to characterise COPD patients by both CAT and mMRC</li> </ul>	<p>In contrast to the GOLD 2011 recommendation, COPD patients with a lower CAT score, less severe airway obstruction and less severe airflow limitation were associated with discordant group assignments and should evaluate their symptoms with both CAT and mMRC simultaneously. We did not find any optimal cut-point for mMRC to correspond to the cut-point CAT score <math>\geq 10</math>.</p> <p><b>&gt;&gt; We did not find any optimal cut-point for mMRC to correspond to the cut-point CAT score <math>\geq 10</math></b>  <b>--&gt; jedoch kein Vorschlag für neue Cut-Offs</b></p>	<p><b>(II) transparentes, nicht-selektives Berichten in Bezug auf Patientencharakteristika, Intervention und Ergebnis:</b> ja</p>
<p>Rhee CK. Discrepancies between modified Medical Research Council dyspnea score and COPD assessment test score in patients with COPD. Int J Chron Obstruct Pulmon Dis 2015; 10:1623–31.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/26316736">https://www.ncbi.nlm.nih.gov/pubmed/26316736</a></p>	<ul style="list-style-type: none"> <li>• <b>Korea</b></li> <li>• <b>Patient*innen:</b> mit COPD</li> <li>• <b>Studienstart:</b> initiated in April 2012</li> <li>• <b>untersuchte Tests:</b> CAT, mMRC</li> <li>• <b>Studientyp:</b> Datenanalyse: data obtained from the Korean COPD Subgroup Study cohort (KOCOSS), multicenter</li> <li>• <b>Einschlusskriterien:</b> n.a.</li> <li>• <b>Ausschlusskriterien:</b> n.a.</li> <li>• <b>primäre Endpunkte:</b> - examine the discrepancy between the mMRC and CAT scores in patients with COPD,</li> </ul>	<p>n=790</p> <p>There was a significant correlation between the CAT and mMRC scores (<math>P &lt; 0.01</math>). However, the correlation was not strong (<math>R = 0.49</math>).</p> <p>An ROC curve was used to identify the CAT score that was best correlated with the mMRC score. For an mMRC score of 2, a CAT score of 15 showed the maximum value of Youden's index with a sensitivity and specificity of 0.70 and 0.66, respectively (area under the ROC curve [AUC] 0.74; 95% confidence interval [CI], 0.70–0.77; <math>P, 0.01</math>). For an mMRC score of 1, a CAT score of 10 showed the maximum value of Youden's index with a sensitivity and specificity of 0.77 and 0.65, respectively (AUC 0.77; 95% CI, 0.72–0.83; <math>P, 0.01</math>; Figure 3).</p> <p>CAT score of 15 was the best cutoff point for an mMRC score of 2, and a CAT score of 10 was the best cutoff point for an mMRC score of 1. Among four different combinations of CAT and mMRC scores, a CAT score of 10 was most concordant with an mMRC score of 1 when classifying patients with COPD into GOLD groups A–D. However, a discrepancy remains between the CAT and mMRC scores. The results of the present study suggest that the GOLD committee needs to consider whether to lower the mMRC cutoff point to 1 or even to discard mMRC.</p>	<p>"Bias-Bewertung für nicht-vergleichende Studien; AWMF 2016:</p> <p><b>(I) prospektive Planung mit Protokoll:</b> nicht eindeutig beschrieben</p> <p><b>(II) konsekutiver Patientenein-schluss:</b> nicht eindeutig beschrieben</p> <p><b>(II) transparentes, nicht-selektives Berichten in Bezug auf Patientencharakteristika, Intervention und Ergebnis:</b> ja</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<ul style="list-style-type: none"> <li>- identify the ideal CAT score that exhibits minimal discrepancy with the mMRC score,</li> <li>- extent of agreement between the mMRC and the CAT scores in different settings</li> </ul>	<p>&gt;&gt; <b>höherer cut-off beim CAT von &gt;15 entspricht eher dem vom mMRC von &gt;2 zur Klassifizierung höher symptomatischer Patient*innen</b></p>	
<p>Xie G. New disease severity classification of patients with stable chronic obstructive pulmonary disease in Shanghai. Chin Med J (Engl) 2014; 127(17):3046–50.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/25189943">https://www.ncbi.nlm.nih.gov/pubmed/25189943</a></p>	<ul style="list-style-type: none"> <li>• <b>Shanghai</b></li> <li>• <b>Patient*innen mit stabiler COPD</b></li> <li>• <b>Studienstart/Studienende:</b> 1/2013–6/2013</li> <li>• <b>untersuchte Tests:</b> CAT, mMRC (assessment of symptom level)</li> <li>• <b>Studientyp :</b> clinical study, multicenter</li> <li>• <b>Einschlusskriterien:</b> met the diagnostic criteria for COPD and had recovered for at least 12 weeks since the last exacerbation</li> <li>• <b>Ausschlusskriterien:</b> (1) patients with reading and communication disorders; and (2) patients unable to complete lung function tests</li> <li>• <b>primärer Endpunkt:</b> To evaluate the clinical value of GOLD 2011 classification, a multicenter clinical study was conducted in patients with stable COPD</li> </ul>	<p>n=848</p> <p>Results of Kappa test showed that using mMRC grade=1 and CAT score=10 as cutoff points, the coincidence rate of COPD symptom assessment was 86.6% (734/848, <math>\kappa=0.706</math>), whereas using mMRC grade=2 and CAT score=10 as cutoff points, the coincidence rate of COPD symptom assessment was 77.9% (661/848, <math>\kappa=0.60</math>). The above results indicate that the assessment of COPD symptom level with mMRC grade=1 and CAT score=10 as cutoff points was more consistent compared with MRC grade=2 as cutoff point.</p> <p>&gt;&gt; <b>mMRC=1 korrespondiert besser mit CAT = 10 bei der Symptomschwereabschätzung von Patienten mit COPD</b></p>	<p>"Bias-Bewertung für nicht-vergleichende Studien; AWMF 2016:</p> <p><b>(I) prospektive Planung mit Protokoll:</b> nicht eindeutig beschrieben</p> <p><b>(II) konsekutiver Patienteneinschluss:</b> nein</p> <p><b>(II) transparentes, nicht-selektives Berichten in Bezug auf Patientencharakteristika, Intervention und Ergebnis:</b> ja</p>
<p>Price DB. Real-world characterization and differentiation of the Global Initiative for Chronic Obstructive Lung Disease strategy classification. Int</p>	<ul style="list-style-type: none"> <li>• <b>multicenter:</b> Patients were recruited in France (254, 15.3%), Germany (454, 27.3%), Italy (209, 12.6%), Spain (302, 18.2%), UK (52, 3.13%), and the US (388, 23.39%).</li> <li>• <b>Patient*innen:</b> mit COPD</li> </ul>	<p>n=1659</p> <p><b>GOLD-recommended cut point</b></p> <p>Out of the total 1,659 patients, there were 890 (53.65%) movers under the GOLD recommended cut points (GOLD-recommended mMRC cut point <math>\geq 2</math> versus the GOLD-recommended CAT cut point of <math>\geq 10</math>), three (0.34%) patients moved left, from mMRC higher symptomatic</p>	<p>"Bias-Bewertung für nicht-vergleichende Studien; AWMF 2016:</p> <p><b>(I) prospektive Planung mit Protokoll:</b> nicht beschrieben</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>J Chron Obstruct Pulmon Dis 2014; 9:551–61.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/24920893">https://www.ncbi.nlm.nih.gov/pubmed/24920893</a></p>	<ul style="list-style-type: none"> <li>• <b>Studiendauer:</b> 9/2012 - 12/2012</li> <li>• untersuchte Tests: CAT, mMRC</li> <li>• <b>Studientyp:</b> retrospektive Datenanalyse: of COPD patient data from the 2012 Adelphi Respiratory Disease Specific Program (cross-sectional surveys)</li> <li>• <b>Einschlusskriterien für die Grundstudie:</b> the next six consulting patients of 40 years of age and older, with a history of smoking and with a confirmed diagnosis of COPD (COPD-only or with mixed COPD and asthma).</li> <li>• <b>Ausschlusskriterien für diese Analyse:</b> with a mixed asthma diagnosis</li> <li>• <b>primärer Endpunkt:</b> the degree of CAT and mMRC alignment given the cut points recommended by GOLD</li> <li>• <b>sekundäre Endpunkte:</b> characterize the patients who have a different GOLD classification depending on which instrument is used – the movers – and to determine a CAT cut point that would more closely align the two populations</li> </ul>	<p>GOLD groups B and D to the lower CAT-defined symptomatic GOLD groups of A and C. Conversely, 887 (99.66%) patients moved right from mMRC lower symptomatic GOLD groups A and C to the higher CAT defined symptomatic GOLD groups of B and D</p> <p><b>ROC-recommended cut point</b> Of the total number of patients who moved under the ROC-recommended cut point of <math>\geq 24</math> (429), 170 (39.63%) moved left from mMRC higher symptomatic groups B and D to the newly defined CAT A and C lower symptomatic groups. The majority of patients, 259 (60.37%), still moved to the right from mMRC lower symptomatic groups A and C to the higher symptomatic ROC CAT-defined groups B and D, albeit to a lesser degree</p> <p><b>Kappa statistic-recommended cut point</b> Of the total number of patients who moved under the kappa statistic-recommended cut point of <math>\geq 26</math> (403), 230 (57.07%) patients moved left from mMRC higher symptomatic groups B and D to the newly defined CAT lower symptomatic groups A and C. Fewer patients 173 (42.92%) moved to the right from mMRC lower symptomatic groups A and C to the higher symptomatic groups of B and D defined by kappa statistic</p> <p><b>&gt;&gt; CAT von <math>\geq 24</math> oder <math>\geq 26</math> entspricht mMRC <math>\geq 2</math></b></p>	<p><b>(II) konsekutiver Patienteneinschluss:</b> ja</p> <p><b>(II) transparentes, nicht-selektives Berichten in Bezug auf Patientencharakteristika, Intervention und Ergebnis:</b> ja</p>
<p>Jones PW. Characteristics of a COPD population categorised using the GOLD framework by health status and exacerbations. Respir Med 2014; 108(1):129–35.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/24041746">https://www.ncbi.nlm.nih.gov/pubmed/24041746</a></p>	<ul style="list-style-type: none"> <li>• <b>France, Germany, Italy, Spain and the UK</b></li> <li>• <b>Patient*innen mit COPD</b></li> <li>• <b>Studiendauer:</b> 6/2011-9/2011</li> <li>• <b>untersuchte Tests:</b> CAT, mMRC</li> <li>• <b>Studientyp. Datenanalyse:</b> originated from the Adelphi Respiratory Disease Specific Programme (DSP),</li> </ul>	<p>n=1041</p> <p>Our data show a very similar picture, with an mMRC score of 2 being approximately equal to a CAT score of 22. The mMRC <math>\geq 2</math> cut-point (On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace) classified more patients as having low symptoms than using a CAT score <math>\geq 10</math>. With the latter, only 10% of patients were placed in the low symptom groups (GOLD groups A and C), compared to using the mMRC <math>\geq 2</math> which placed 51% of patients in these groups.</p> <p><b>&gt;&gt; CAT <math>\geq 22</math> entspricht mMRC <math>\geq 2</math></b></p>	<p>"Bias-Bewertung für nicht-vergleichende Studien; AWMF 2016:</p> <p><b>(I) prospektive Planung mit Protokoll:</b> keine Angaben</p> <p><b>(II) konsekutiver Patienteneinschluss:</b> ja</p> <p><b>(II) transparentes, nicht-selekti-</b></p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<p>an international, cross-sectional survey</p> <ul style="list-style-type: none"> <li>• <b>Einschlusskriterien:</b> patients with a spirometric assessment, and completed exacerbation history, CAT and mMRC in the last year</li> <li>• <b>primärer Endpunkt:</b> examine the distribution and clinical characteristics of COPD patients categorised according to the 2011 GOLD assessment framework using data from a combined European primary and secondary care routine clinical practice patient population.</li> </ul>	<p>&gt;&gt; keine überschneidende Patientenkohorte mit Ref. 28139, da anderer Studienzeitraum analysiert wurde</p>	<p>ves Berichten in Bezug auf Patientencharakteristika, Intervention und Ergebnis: ja</p>
<p>Jones PW. Comparisons of health status scores with MRC grades in COPD: Implications for the GOLD 2011 classification. Eur Respir J 2013; 42(3):647–54.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/23258783">https://www.ncbi.nlm.nih.gov/pubmed/23258783</a></p>	<ul style="list-style-type: none"> <li>• <b>Europe</b></li> <li>• <b>Patient*innen mit COPD</b></li> <li>• <b>Studiendauer:</b> n.a.</li> <li>• <b>untersuchte Tests:</b> CAT, mMRC, SGRQ, SF-12, FACIT</li> <li>• <b>Studientyp:</b> Datenanalyse der Health-Related Quality of Life in COPD in Europe Study (HEED) database (large, cross-sectional, observational study)</li> <li>• <b>Einschlusskriterien:</b> aged 40–80 years; post bronchodilator FEV1/forced vital capacity (FVC) ratio of ,70%; smoking pack history of o10 pack-years</li> <li>• <b>primärer Endpunkt:</b> test the equivalence, assumed by GOLD, between these two symptom cut-points, by examining the relationship between health status scores and mMRC grades</li> </ul>	<p>n=1817</p> <p>Patients in all four groups, as categorised by the mMRC <math>\geq 2</math> cut-point, had worse health status scores and more fatigue (encompassing tiredness, weakness and difficulty in conducting usual activities), compared with the equivalent group categorised by a CAT score <math>\geq 10</math>.</p> <p><u>Proportion of patients in each GOLD group using CAT score <math>\geq 10</math> and mMRC grade <math>\geq 2</math> symptom cutpoints (GOLD recommendation):</u> The proportion of patients categorised into groups A to D differed according to the use of a GOLD symptom cut-point of mMRC grade <math>\geq 2</math> or CAT score <math>\geq 10</math>. The mMRC classified 57.2% patients as having low symptoms (groups A and C), compared with 17.2% with the CAT. Concordance analysis comparing the frequencies of patients categorised by these two variables, the mMRC grade <math>\geq 2</math> and CAT score <math>\geq 10</math> cut-points, resulted in a weighted k-coefficient of 0.626.</p> <p><u>Proportion of patients in each GOLD group using CAT score <math>\geq 10</math> and mMRC grade <math>\geq 1</math> symptom cutpoints (amended criteria):</u> As an exploratory exercise, health status scores were investigated when patients were categorised using a mMRC cut-point of grade <math>\geq 1</math>. Using this cut-point, patients categorised by mMRC grade <math>\geq 1</math> had similar mean health status and fatigue scores to those found with a CAT score cut-point of <math>\geq 10</math>. Using this cut-point, the proportion of patients categorised in to groups A to D was similar to that with the CAT. mMRC grade <math>\geq 1</math> classified 18.9% of patients as having low symptoms (groups A and C) compared with 17.2% with the CAT. Concordance analysis comparing the frequencies of patients categorised by these two variables, the mMRC grade <math>\geq 1</math> and CAT</p>	<p>"Bias-Bewertung für nicht-vergleichende Studien; AWMF 2016:</p> <p><b>(I) prospektive Planung mit Protokoll:</b> nicht beschrieben</p> <p><b>(II) konsekutiver Patienteneinschluss:</b> nicht beschrieben</p> <p><b>(II) transparentes, nicht-selektives Berichten in Bezug auf Patientencharakteristika, Intervention und Ergebnis:</b> ja</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<ul style="list-style-type: none"> <li>• <b>sekundäre Endpunkte:</b> to compare the demographic and clinical characteristics and health status scores of patients grouped using the new GOLD combined assessment framework</li> </ul>	<p>score <math>\geq 10</math> cut-points, resulted in a weighted kcoefficient of 0.792; indicating that there was a higher degree of agreement between these variables and their respective cut-points than between the classification applying CAT <math>\geq 10</math> and mMRC <math>\geq 2</math>.</p> <p>&gt;&gt; CAT <math>\geq 10</math> entspricht mMRC <math>\geq 1</math></p>	

## Anhang 5.6 Angst/Depression

### Depression

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Matte DL. Prevalence of depression in COPD: A systematic review and meta-analysis of controlled studies. <i>Respir Med</i> 2016; 117:154–61.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/27492526">https://www.ncbi.nlm.nih.gov/pubmed/27492526</a></p>	<ul style="list-style-type: none"> <li>• Brasilien</li> <li>• Metaanalyse, n=8 controlled studies (Cross-sectional studies)</li> <li>• <b>Ziel:</b> this study aimed to perform a systematic review and meta-analysis of the literature on depression prevalence in COPD using stricter inclusion criteria for article selection than those described in previous metanalysis. We also sought to explore remaining causes of inter-study variability in the reported prevalence.</li> <li>• <b>Suchzeitraum:</b> inception - 01/01/2015</li> <li>• <b>Population:</b> Patient*innen mit stabiler COPD</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- controlled studies with a sample size &gt;100, outpatients with COPD diagnosed by spirometry (post-bronchodilator FEV1/FVC <math>\leq 0.7</math>) and, use of a validated depression screening instrument</li> <li>• depression determined by standardized and widely used criteria (e.g., SCID- DSM) or by a validated depression questionnaire (e.g., CES-D, GDS, HADS-D, SDS (Zung), HRSD)</li> </ul> </li> <li>• <b>Ausschlusskriterien:</b> <ul style="list-style-type: none"> <li>- Studies focused on subpopulations, such as patients on continuous oxygen therapy, included COPD patients recovering from an exacerbation and/or hospital admission at the time of evaluation, comprising convenience samples, focusing on pre-existing conditions that poten-</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Using stricter criteria for study selection reduced the variability of the depression prevalence in COPD and controls, which was 27.1% [25.9-28.3] in COPD subjects and 10.0% [9.2-10.8] in the control group. The pooled odds ratio and 95% CI was 3.74 [2.4-5.9]</li> <li>• <b>high heterogeneity across studies:</b> Possible explanatory factor included sample sizes, COPD/controls ratio, smoker's/nonsmokers ratio and qualitative differences (source of subjects, instruments to screen depression, COPD severity, smoking status, and comorbidities)</li> <li>• Subgroup analysis comparing the prevalence of depression in COPD subjects according to disease severity was described in all included studies. After adjustment for confounders <u>disease severity was associated with higher prevalence</u> of depression in five studies</li> <li>• <b>"authors conclusion":</b> The current systematic review of the literature, based on controlled well conducted studies, provides evidence suggesting that the use of stricter criteria reduces the variability of the estimates of depression prevalence in COPD subjects and controls. However, the observed lack in matching clinical variables that might increase the prevalence of depression and the absence of uniformity in choosing the instruments used to screen depression in COPD subjects indicate that standardization is critical to improve the accuracy of the estimates and to allow comparisons among studies.</li> </ul>	<p>ca-y-y-n-n-y-y-y-n-n</p> <p><b>AMSTAR-Score: 6/11</b></p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<p>tially could increase the risk for depression (such as living alone, having cancer)</p> <ul style="list-style-type: none"> <li>• <b>Body of Evidence</b> : n=8 controlled studies (n=5.552 COPD subjects and n=5.211 controls)</li> </ul>		

**Angst**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Willgoss TG. Anxiety disorders in patients with COPD: A systematic review. <i>Respir Care</i> 2013; 58(5):858–66.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/22906542">https://www.ncbi.nlm.nih.gov/pubmed/22906542</a></p>	<ul style="list-style-type: none"> <li>• United Kingdom</li> <li>• keine Metaanalyse, prospective studies</li> <li>• <b>Ziel:</b> The aim of this systematic review is to synthesize the available literature in order to estimate the prevalence of clinical anxiety and specific anxiety disorders in patients with COPD.</li> <li>• <b>Suchzeitraum:</b> 1966 - 31/01/2012</li> <li>• <b>Population:</b> Patient*innen mit COPD (im-patient &amp; out-patient)</li> <li>• <b>Einschlusskriterien:</b> prospective studies, had diagnosed anxiety disorders from a clinical interview using a recognized psychiatric format (eg, Diagnostic and Statistical Manual of Mental Disorders-IV or previous versions of DSM, or International Classification of Diseases, 10th Revision), published in English</li> <li>• <b>Body of Evidence:</b> n=10 studies (prospective studies = inclusion criterion), n=691 subjects</li> <li>• <b>Herkunft der Studien:</b> Nigeria, Turkey, New Zealand, US, Germany, Canada, Australia, UK</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Clinical Anxiety Disorder</b></li> <li>- The prevalence of clinical anxiety ranged from 10–55% (median 17%; n=8 studies)</li> <li>- clinical anxiety in <u>in-patients</u> varied from 10–55% (n=4 studies)</li> <li>- prevalence of clinical anxiety in <u>out-patient</u> ranged from 13–46% (n=4 studies)</li> </ul>	<p>n-y-y-n-n-y-n-n-na-n-n</p> <p><b>AMSTAR-Score: 3/10</b></p>

## Anhang 6 Evidenztabelle Tabakentwöhnung

### Anhang 6.1 Cochrane Review Tabakentwöhnung

Quelle	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
van-Eerd-Eva AM. Smoking cessation for people with chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2016;(8).	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To evaluate the effectiveness of behavioural or pharmacological smoking cessation interventions, or both, in smokers with COPD</li> <li>• <b>Body of Evidence:</b> <ul style="list-style-type: none"> <li>- n= 16 eingeschlossene RCTs (n=13.123 eingeschlossene Teilnehmer);</li> <li>- n=4 RCTs (n=1.540 Teilnehmer) für Metaanalyse</li> </ul> </li> <li>• <b>Suchzeitraum:</b> 03/2016</li> <li>• <b>Population:</b> smokers with COPD</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- RCTs reporting at least 6 months of follow-up abstinence rates</li> <li>- trials assessing the effectiveness of any behavioural or pharmacological treatment, or both, in smokers with COPD</li> </ul> </li> <li>• <b>Interventionen:</b> <ul style="list-style-type: none"> <li>&gt;&gt; categorised behavioural treatment as 'high' if more than one prescheduled counselling session of greater than 10 minutes was offered with at least one face-to-face counselling session; Otherwise we categorised the behavioural treatment as 'low'.</li> </ul> </li> <li>• Behavioural treatment vs. no treatment or usual care.</li> <li>• One form of behavioural treatment vs. a different form of behavioural treatment.</li> <li>• Pharmacological treatment vs. placebo.</li> <li>• Pharmacological treatment vs. a different pharmacological treatment.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- age: ranged from 48 to 66 years</li> </ul> </li> <li>• <b>Behavioural treatment vs. no treatment or usual care</b> <ul style="list-style-type: none"> <li>- <b>Prolonged abstinence at longest follow-up (6 month):</b> RR 25.38 (95% CI 8.03, 80.22; n=3562 participants; 1 study; 44/1000 vs. 2/1000, <b>GRADE: moderate</b>)</li> <li>&gt;&gt; high-intensity behavioural treatment increased abstinence rates when compared with usual care</li> <li>&gt;&gt; high-intensity behavioural treatment increased abstinence rates when compared to low-intensity behavioural treatment (17/42 vs. 8/43; RR 2.18 (95% CI 1.05 to 4.49)), 1 RCT, n=85 participants</li> </ul> </li> <li>• <b>One form of behavioural treatment vs. a different form of behavioural treatment</b> <ul style="list-style-type: none"> <li>- <b>Prolonged abstinence at longest follow-up (6-12 month):</b> Not estimable (n=739 participants; 4 studies) &gt;&gt; No pooling due to clinical and statistical heterogeneity. Individual RR were 2.18 (1.05, 4.49), RR 0.97 (0.47, 1.99), RR 1.09 (0.59, 2.04) , and RR not estimable. 3 of the 4 studies had a low risk of bias. 1 study had a high risk of bias due to poor adherence to the study protocol</li> </ul> </li> <li>• <b>Pharmacological treatment + behavioural treatment vs. placebo + behavioural treatment</b> <ul style="list-style-type: none"> <li>• <b>Gesamt</b> <ul style="list-style-type: none"> <li>- Prolonged abstinence at longest follow-up (6-12 month): RR 2.53 (95%CI 1.83, 3.50; n=1429 participants; 4 studies; 168/1000 vs. 66/1000, <b>GRADE: high</b>)</li> </ul> </li> <li>• <b>nicotine replacement therapy</b> <ul style="list-style-type: none"> <li>- Prolonged abstinence at longest follow-up (12 month): RR 2.60 (95%CI 1.29, 5.24; n=370 participants; 1 study; <b>GRADE: high</b>)</li> </ul> </li> <li>• <b>bupropion</b> <ul style="list-style-type: none"> <li>- Prolonged abstinence at longest follow-up (6 month): RR 2.03 (95%CI 1.26, 3.28; n=503 participants; 2 studies; <b>GRADE: moderate</b>)</li> </ul> </li> </ul> </li> </ul>	<p><b>AMSTAR-Score gesamt:</b> 11/11</p> <p>y-y-y-y-y-y-y-y-y-y</p>	<p>Als sekundärer Endpunkt wurde bei einigen Vergleichen auch die <i>Point prevalence abstinence at longest follow-up</i> dargestellt</p>



Quelle	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<ul style="list-style-type: none"> <li>• Comparison of different combinations of behavioural and pharmacological treatments.</li> <li>• <b>Primärer Endpunkt:</b> - Percentage of participants with continuous or prolonged abstinence over a period of six months or longer.</li> <li>• <b>Sekundärer Endpunkt:</b> - Percentage of participants with point prevalence abstinence over a period of six months or longer.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>varenicline</b> - Prolonged abstinence at longest follow-up (12 month): RR 3.34 (95%CI 1.88, 5.92; n=504 participants; 1 study; <b>GRADE: high</b>)</li> <li>• <b>nortriptyline</b> - Prolonged abstinence at longest follow-up (6 month): RR 2.54 (95%CI 0.87, 7.44; n=100 participants; 1 study; <b>GRADE: low</b>)</li> </ul> <p><b>Pharmacological treatment vs. a different pharmacological treatment</b> - Prolonged abstinence at longest follow-up (6-12 month): Not estimable (n=166 participants; 2 studies) &gt;&gt; No pooling due to clinical and statistical heterogeneity. - NRT vs bupropion RR 0.74 (95% CI 0.27, 2.05), - bupropion vs nortriptyline RR 1.29 (95% CI 0.63, 2.63). 1 study had a high risk of bias due to poor adherence to the study protocol. 1 study had an unclear risk of bias</p> <p><b>Combination interventions vs. different (combination) interventions or usual care</b> - Prolonged abstinence at longest follow-up (6-60 month): Not estimable (n=6431 participants; 4 studies) &gt;&gt; No pooling due to clinical and statistical heterogeneity. Individual RR 4.10 (3.36, 5.00) , RR 2.22 (1.06, 4.68) , RR 1.91 (0.65, 5.61), and RR not estimable. 3 studies had a low risk of bias, 1 study had a high risk of bias due to poor adherence to the study protocol</p>		

### Anhang 6.2 Suchupdate Cochrane Review Tabakentwöhnung

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Ellerbeck EF, Nollen N, Hutcheson TD, et al. Effect of Long-term Nicotine Replacement Therapy vs Standard Smoking Cessation for Smokers With Chronic Lung Disease: A Randomized Clinical Trial. JAMA network</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> To compare the effect of LT-NRT vs standard smoking cessation (SSC) on exposure to cigarette smoke, harm related to smoking, and cessation among smokers with COPD</li> <li>• <b>Studiendesign:</b> unblinded RCT</li> <li>• <b>Population:</b> Smokers with COPD (n=398)</li> <li>• <b>Intervention:</b> - Longterm nicotine replacement therapy</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, Geschlecht, Faktoren zur Einschätzung des Rauchverhaltens weitestgehend ausgeglichen</li> <li>- 59.8% female; mean [SD] age, 56.0 [9.3] years</li> <li>- mean (SD) CPD was 23.1 (12.3)</li> <li>- Participants completed assessments at baseline and 3, 6, and 12 months [...] received \$50 for each visit.</li> </ul> <p>At 12 months, <b>CO-verified 7-day point prevalence abstinence</b> occurred in <b>SSC:</b> 23 of 197 participants (11.7%) <b>LT-NRT:</b> in 24 of 197 participants(12.2%) (risk difference, 0.5%; 95% CI, -5.9% to</p>	<p><b>Selection bias</b> Randomisierung: <b>gering</b> Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>hoch</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>unklar</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>gering</b></p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>open 2018; 1(5):e181843. DOI: 10.1001/jamanetworkopen.2018.1843.</p> <p><a href="http://www.ncbi.nlm.nih.gov/pub-med/30646142">http://www.ncbi.nlm.nih.gov/pub-med/30646142</a>.</p>	<p>(LT-NRT) =12 months of NRT and 6 follow-up counseling sessions regardless of initial willingness to quit</p> <ul style="list-style-type: none"> <li>- Participants who set a quit date received a personalized quit plan, incorporating the use of NRT</li> <li>- <u>Regardless of whether participants set a quit date</u>, follow-up telephone counseling was provided at 1, 3, and 6 weeks and 9 months after baseline and in person at months 3 and 6.</li> </ul> <p>• <b>Vergleich:</b></p> <ul style="list-style-type: none"> <li>- standard smoking cessation (SSC)</li> <li>= 10 weeks of NRT and 4 follow-up counseling sessions for those willing to make a quit attempt</li> <li>- baseline session: motivational strategies to increase readiness to quit.</li> <li>- Participants who set a quit date received a personalized quit plan, incorporating the use of NRT</li> <li>- Participants <u>who set a quit date</u> were proactively contacted for telephone counseling 1, 3, 6, and 10 weeks after the baseline visit</li> </ul> <p>• <b>Beide Gruppen:</b> Combination NRT</p> <ul style="list-style-type: none"> <li>- nicotine patches (14-42 mg) plus 2 mg of nicotine gum and/or lozenges.</li> </ul> <p>• <b>Follow-up:</b> 12-month (completed 6.12.2016)</p> <p>• <b>Studienzeitraum:</b> 23.5.2014 - 30.11.2015</p> <ul style="list-style-type: none"> <li>• USA</li> </ul> <p>• <b>Definitionen:</b></p> <ul style="list-style-type: none"> <li>- cigarettes smoked per day (CPD)</li> </ul>	<p>6.9%).</p> <p><u>Self-reported smoking cessation</u> at 3, 6, and 12 months and 6-month sustained abstinence were not significantly different across treatment arms. In multivariate analyses, only increased age was associated with higher rates of cessation (odds ratio, 4.30; 95% CI, 2.25-8.19; P &lt; .001)</p> <p>12 months: among the <u>participants who continued to smoke</u>, both groups reported similar reductions relative to baseline in</p> <ul style="list-style-type: none"> <li>- self-reported CPD (LT-NRT group, -14.5; SSC group, -12.4 CPD)</li> <li>- expired CO level (LT-NRT group, -7.8 ppm; SSC group, -5.5 ppm)</li> <li>- NNAL excretion (LT-NRT group, -23.0%; SSC group, -21.7%).</li> </ul> <p>&gt;&gt; During the 12-month follow-up, these changes were significantly different from baseline, but did not differ significantly between groups.</p> <p><u>Secondary Outcomes</u></p> <p><b>CAT-Score</b></p> <ul style="list-style-type: none"> <li>- both groups experienced similar improvements in respiratory symptoms over time, with the mean COPD Assessment Test score improving by 4.6 points in the LT-NRT arm and 3.6 points in the SSC arm.</li> </ul> <p><b>Emergency department visits /hospitalizations</b></p> <ul style="list-style-type: none"> <li>- Similar numbers of participants in the 2 treatment arms had 1 or more respiratory-associated emergency department visits or hospitalizations during the 12 months of follow-up. Both groups reported similar frequency of quit attempts.</li> </ul> <p>• <b>Sicherheit:</b> The frequency of major adverse cardiac events was similar in both groups. During the course of the study, 17 major adverse cardiac events occurred, including 1 death. Nine events occurred in the SSC group and 8 in the LT-NRT group. Six events occurred while participants were receiving NRT and 11 occurred while not receiving NRT. Three noncardiac deaths were attributed to COPD complications, lung cancer, and pulmonary aspiration.</p>	<p>ITT-Analyse: durchgeführt</p> <p><b>Reporting bias</b></p> <p>selektive Ergebnisdarstellung: <b>gering</b></p> <p><b>Andere Biasursachen</b></p> <p>Baseline imbalance: <b>gering</b></p> <p><b>Interessenkonflikte/ Sponsoring:</b> grants from Patient-Centered Outcomes Research Institute (PCORI) and National Institutes of Health (NIH); investigator-initiated trial</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Zarghami M, Taghizadeh F, Sharifpour A, et al. Efficacy of Smoking Cessation on Stress, Anxiety, and Depression in Smokers with Chronic Obstructive Pulmonary Disease: A Randomized Controlled Clinical Trial. <i>Addiction &amp; health</i> 2018; 10(3):137–47. DOI: 10.22122/ahj.v10i3.600.</p> <p><a href="http://www.ncbi.nlm.nih.gov/pub-med/31105911">http://www.ncbi.nlm.nih.gov/pub-med/31105911</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> This study was aimed to investigate the effectiveness of smoking cessation on stress, anxiety, and depression in smokers with COPD.</li> <li>• <b>Studiendesign:</b> 3 block-RCT</li> <li>• <b>Population:</b> elderly adult Smokers with COPD</li> <li>• <b>Interventionen:</b> <ul style="list-style-type: none"> <li>- <u>guided self-change (GSC)</u> (n = 19)                             <ul style="list-style-type: none"> <li>-- 5 sessions: screening and assessment, deciding to change, discussing risky situations, identifying different solutions to action, and steps to the future.</li> <li>-- 5 one-hour sessions over 5 weeks</li> </ul> </li> <li>- <u>nicotine replacement therapy (NRT)</u> (n = 19)                             <ul style="list-style-type: none"> <li>-- Nicotine (Nicolife®) blisters (labeled 30 gums) included 2 mg nicotine in each gum</li> </ul> </li> <li>- <u>combined GSC-NRT</u> (n = 19)</li> </ul> </li> <li>• <b>Follow-up:</b> 29 weeks</li> <li>• Iran</li> <li>• <b>Messmethoden:</b> <ul style="list-style-type: none"> <li>- Transtheoretical Model (TTM) questionnaire,</li> <li>- Fagerstrom Test for Nicotine Dependence (FTND),</li> <li>- Depression Anxiety Stress Scale (DASS),</li> <li>- the Beck Depression Inventory-II (BDI-II),</li> <li>- Hospital Anxiety and Depression Scale (HADS)</li> <li>- exhaled carbon monoxide (CO)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, sozialen Faktoren, täglichem Zigarettenkonsum, Angst und Depressions-Einschätzungen keine signifikanten Unterschiede</li> <li>- mean of 23 daily cigarette (range of 5-60)</li> <li>- Mean duration of smoking: 32.9 years (range of 9-59)</li> <li>- 57 men (mean age of 53.60 ± 8.43)</li> </ul> <p><b>Smoking cessation</b>  GSC: A total of 9 (47.4%) participants in the GSC, 9 (47.4%) participants in combined groups, and 4 (21.1%) participants in the NRT group stated complete abstinence from smoking by the end of 29 weeks.</p> <p>--&gt; keine OR je Gruppe angegeben  --&gt; gesamt: the mean exhaled CO reduced from 22.6 ± 1.5 to 12.8 ± 0.9 and 8.6 ± 0.7 ppm (P = 0.001) during the baseline, 12, and 29 weeks.</p> <p>&gt;&gt;OR of smoking cessation in GSC and GSC-NRT groups decreased more than NRT group. In addition, DASS, FTND, and the exhaled CO in GSC and GSC-NRT groups showed a better performance compared with the NRT group.</p> <p><b>&gt;&gt; Änderung zum Protokoll</b></p> <ul style="list-style-type: none"> <li>- laut IRCT Register: primärer Endpunkt: Smoking Cessatio Rate; alle anderen Endpunkte als sekundär deklariert</li> <li>- in Publikation: depression, anxiety, and stress changes, smoking cessation rate als primäre Endpunkte beschrieben</li> </ul>	<p><b>Selection bias</b>  Randomisierung: <b>gering</b>  Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b>  Verblindung von Teilnehmern und Personal: <b>hoch</b></p> <p><b>Detection bias</b>  Verblindung der Ergebnisevaluation: <b>unklar</b></p> <p><b>Attrition bias</b>  Verlust von Studienteilnehmern/ fehlende Daten: <b>unklar</b>  ITT-Analyse: durchgeführt; Studie gepowert</p> <p><b>Reporting bias</b>  selektive Ergebnisdarstellung: <b>hoch</b></p> <p><b>Andere Biasursachen</b>  Baseline imbalance: <b>gering</b>  Interessenkonflikte/ Sponsoring: no Col  <b>weiteres:</b> Änderung im Protokoll vs. Publikation (siehe Kommentar)</p>

Anhang 6.3 Besprechung von Lungenfunktion oder CO-Werten (aus [17])

Erster Autor	Titel (gekürzt)	EG	Studientyp	Intervention	N	Effekt	AE	Qualität	Finanzierung	Kommentar
Kotz D, 2011	Smoking cessation and development of respiratory health in smokers screened with normal spirometry	3b	Längsschnittuntersuchung, Nachbeobachtung 2,4 Jahre	Bei Rauchern mit normaler Lungenfunktion wurde eine Lufu durchgeführt	255	Bei normaler Lufu keine Reduktion der Quit-Rate	nein	Keine Intervention, lediglich Beobachtung	öffentlich	Non-smoking was validated by carbon monoxide. Long follow up. Allerdings keine Intervention daher auch keine Randomisierung
Toljamo T, 2010	Early detection of COPD combined with individualized counselling for smoking cessation: a two-year prospective study.	3b	Bei Rauchern wurde TE (motivational Interviewing) und Lufu durchgeführt. Lufu wurde allerdings nicht erläutert	bei "gesunden" Rauchern mit > 20 PY wurde eine Lufu durchgeführt	584	in multivariater Analyse war Obstruktion in Lufu nicht prädiktiv für quitting, Pharmakotherapie sehr	nein	mäßig, da Lufu nicht als Intervention	öffentlich	Lufu nicht besprochen. Kein RCT
Sundblad BM, 2010	Lung function testing influences the attitude toward smoking cessation.	2b	Längsschnittuntersuchung, 3 Monate. Fragen zum Aufhörwunsch vor und nach Lufu	smokers, of whom 77 had COPD, answered a questionnaire before, shortly after, and 3 months after performing a lufu	513	Nach Lufu mehr Aufhörwillige (52% vs 9%; p<0.0001). Quit rate nach 3 Monaten 30 vs 14%; p=0,02)	nein	gut, random sample, aber nicht randomisiert	öffentlich	Prospektiv, Vergleichsgruppe, allerdings keine Randomisation, und keine (kaum) COPD Patienten
Kotz D, 2009	Efficacy of confronting smokers with airflow limitation for smoking cessation.	1b	RCT, Effekt der Intervention nach 1 Jahr untersucht	Raucher mit Obstruktion in Lufu wurde randomisiert in control oder confronting with Lufu Number randomised: n= 296  Behavioural treatment A. Experimental Individual counselling, lung minimal intervention strategy (L-MIS), by respiratory nurse, CONFRONTATION with spirometry. FC1: day 1 (40 minutes) ; FC2: day 8 (40 minutes); TQD: day 14; FC3: day 15 (40 minutes); FC4: day	296	OR für biochemisch-validierte Langzeitabstinenz (12 Monate) der Gruppen mit vs. ohne Lufu Konfrontation war 0.96 (0.43–2.18), p=0.961 Only the experimental group was confronted with their abnormal spirometry (mean forced expiratory volume in one second (FEV1) post-bronchodilator 80.5% predicted, mean FEV1/forced vital capacity post bronchodilator 62.5%).	nein	gut aber sample size mäßig. RCT.	öffentlich	RCT mit guter Methodik. Durch follow up von 1 Jahr Ergebnisse klinisch relevant. Jedoch Verlust von power.

Erster Autor	Titel (gekürzt)	EG	Studientyp	Intervention	N	Effekt	AE	Qualität	Finanzierung	Kommentar
				<p>22 (40 minutes). Telephone counselling day 15 (5 to 15 minutes)</p> <p>B. Control 1 Individual counselling, L-MIS, by respiratory nurse, NOCONFRONTATION with spirometry. FC1: day 1 (40 minutes); FC2: day 8 (40 minutes); TQD: day 14; FC3: day 15 (40 minutes); FC4: day 22 (40 minutes). Telephone counselling day 15 (5 to 15 minutes)</p> <p>C. Control 2 Referral to GP for usual care, NO CONFRONTATION with spirometry</p> <p>Pharmacological treatment</p> <p>A. Experimental Nortriptyline, 25 mg day 1 to 3; 50 mg day 4 to 7, 75 mg day 8 to end of treatment period</p> <p>B. Control 1 Nortriptyline, 25 mg day 1 to 3; 50 mg day 4 to 7, 75 mg day 8 to end of treatment period</p> <p>C. Control 2 Nortriptyline, 25 mg day 1 to 3; 50 mg day 4 to 7, 75 mg day 8 to end of treatment period</p>		<p>&gt;&gt; no difference in cotinine-validated prolonged abstinence rate between the experimental group (11.2%) and control group 1 (11.6%) from week 5–52 (OR (95% CI) 0.96, 0.43–2.18.</p> <p>&gt;&gt; conclusion: The present study did not provide evidence that the confrontational approach increases the rate of long-term abstinence from smoking compared with an equally intensive treatment in which smokers were not confronted with spirometry. The high failure rates (o88%) highlight the need for treating tobacco addiction as a chronic relapsing disorder.</p>				
van der Aalst CM, 2010	Lung cancer screening and smoking abstinence: 2 year follow-up data from the Dutch-Belgian randomised controlled	2b	historischer Vergleich, RCT	CT screening	1284	16,6% der Studienteilnehmer haben aufgehört zu rauchen (historischer Vergleich 3-7%)	kein	gut, großer RCT	öffentlich	CT-screening wird in der o.g. Empfehlung nicht (mehr) abgebildet. Nur historischer Vergleich der Rauchstopp-Raten.

Erster Autor	Titel (gekürzt)	EG	Studientyp	Intervention	N	Effekt	AE	Qualität	Finanzierung	Kommentar
	lung cancer screening trial.									
Schook RM, 2010	The finding of premalignant lesions is not associated with smoking cessation in chemoprevention study volunteers.	2b	Retrospective Auswertung einer Chemopreventionsstudie		188	Univariate regression demonstrated that smoking cessation was only associated with male gender.	nein	Lediglich Regressionanalyse		
Parkes G, 2008	Effect on smoking quit rate of telling patients their lung age: the Step2quit randomised controlled trial.	1b	RCT with 5 GP in UK	Lung age vs FEV1	561	13.6% and 6.4% (difference 7.2%, P=0.005, 95% confidence interval 2.2% to 12.1%; number needed to tr	nein	Sehr gut, 12 Monate Nachbeobachtung	öffentlich	Exzellenter britischer RCT. Objektiv verifizierter Endpunkt. Intervention war besonders effektiv bei denen mit schlechter Lufu. Allerdings wurde eine Patientengruppe aus Hausarztpraxen in die Studie eingeschlossen, die relativ jung war und überwiegend eine normale Lungenfunktion hatte (FEV1 89-90%, FEV1/FVC 73-75%), also keine COPD-Patientengruppe. Zudem spielt Selektionsbias eine Rolle, weil nur Patienten an der Studie teigegenommen hatten, mit Interesse an einer Lungenfunktionsmessung.
Bize R, 2007	Effectiveness of biomedical risk assessment as an aid for smoking cessation: a systematic review.	3a	Metaanalyse von 2007 mit Lit. bis 2004		8	für einzelne Interventionen wie CO Bestimmung oder Lufu keine Signifikanz		Gut, aber älter (von 2007) und hat daher wichtige Studien nicht erfasst		Aktuelle RCT nicht in Metaanalyse erfasst

Erster Autor	Titel (gekürzt)	EG	Studientyp	Intervention	N	Effekt	AE	Qualität	Finanzierung	Kommentar
					Qualität					
Carpenter MJ, 2007	Does genetic testing result in behavioral health change? Changes in smoking behavior following testing for alpha-1 antitrypsin deficiency.	2b	Nicht randomisierte prospektive Intervention	Testen auf alpha AT mangel bei Rauchern	n=199	Smokers who tested severely AAT deficient were significantly more likely to report a 24-hr quit atte			Alpha 1 foundation	Besprechung der Lufu war hier nicht die Intervention.
Taylor KL, 2007	Lung cancer screening as a teachable moment for smoking cessation.	3b	Lung cancer screening wohl retrospectiv ausgewertet		two samples: n=144 n=169	At 1-month follow-up, more ready to stop smoking (p < .05). Other sample: in younger participants				Besprechung der Lufu war hier nicht die Intervention.
van der Aalst, 2011	The impact of a lung cancer computed tomography screening result on smoking abstinence.	1b	RCT	CT screening	990	prolonged abstinence rate in smokers receiving a negative test (46 (8.9%) out of 519 subjects)	kein	gut	öffentlich	Besprechung der Lufu war hier nicht die Intervention.

Ergänzt durch Leitliniengruppe NVL COPD.

### Anhang 6.4 E-Zigaretten Schadenspotential

Autor/ Titel	Studientyp	Abstract	Schadenspotential
Cardenas VM, Fischbach LA, Chowdhury P. The use of electronic nicotine delivery systems during	Systematic Review	<p><b>INTRODUCTION</b> Use of electronic nicotine delivery systems (ENDS) among pregnant women is of great concern. To our knowledge the current literature provides conflicting views regarding the uncertainties of the effects of ENDS use during pregnancy on the health of the fetus.</p> <p><b>METHODS</b> We searched PubMed, CINAHL, and EMBASE, for the period</p>	<ul style="list-style-type: none"> <li>• electronic nicotine delivery systems = ENDS</li> <li>- In a mailed survey of US providers, 53% reported screening pregnant women at intake for use of ENDS and other emerging tobacco product use all or some of the time. Of these providers, 14% reported <b>that ENDS use had no adverse health effects</b> [England LJ, Anderson BL, Tong VT, et al. Screening practices</li> </ul>

Autor/ Titel	Studientyp	Abstract	Schadenspotential
<p>pregnancy and the reproductive outcomes: A systematic review of the literature. Tobacco induced diseases 2019; 17:52. DOI: 10.18332/tid/104724. <a href="http://www.ncbi.nlm.nih.gov/pub-med/31582941">http://www.ncbi.nlm.nih.gov/pub-med/31582941</a>.</p>		<p>2007 to October 2017 for terms to identify publications on ENDS use during pregnancy and the reproductive outcomes. We updated the search for the period November 2017 to November 2018 using Ovid Medline. We obtained full text of articles and present a summary of the contents.  <b>RESULTS</b> We found no studies of pregnant women exposed to ENDS use and its effect on their fetus or neonates. However, there is a growing body of experimental studies in animals that suggest that nicotine in ENDS alters DNA methylation, induces birth defects, reduces the birth weight, and affects the development of the heart and lungs of their offspring. A large population-based cohort study in the United States estimated that 5% of pregnant women were current ENDS users in 2014; most of them also smoked cigarettes. Surveys conducted among practitioners indicate that there is a need to screen and counsel pregnant women. Systematic reviews and meta-analysis of studies of women who used smokeless tobacco during pregnancy suggest that prenatal nicotine alone is a risk factor for low birth weight, premature delivery, and stillbirth.  <b>CONCLUSIONS</b> There were no previous studies assessing the reproductive effects of ENDS use during pregnancy. However, prenatal exposure to nicotine is known to be harmful to the fetus and the pregnancy.</p>	<p>and attitudes of obstetricians-gynecologists toward new and emerging tobacco products. Am J Obstet Gynecol. 2014;211(6):695.e1-695.e7. doi:10.1016/j.ajog.2014.05.041]</p> <p>- <b>CONCLUSIONS:</b> Since there are no current studies on the effects that ENDS use has on pregnancy outcomes, one can only hypothesize, based on existing studies on the reproductive effects of smokeless tobacco, that ENDS use by pregnant women is not safe for their fetuses.</p>
<p>Carpenter MJ, Heckman BW, Wahlquist AE, et al. A Naturalistic, Randomized Pilot Trial of E-Cigarettes: Uptake, Exposure, and Behavioral Effects. Cancer Epidemiol Biomarkers Prev 2017; 26(12):1795–803. DOI: 10.1158/1055-9965.EPI-17-0460. <a href="http://www.ncbi.nlm.nih.gov/pub-med/29127080">http://www.ncbi.nlm.nih.gov/pub-med/29127080</a>.</p>	<p>Naturalistic, Randomized Pilot Trial</p>	<p><b>Background</b>—Most studies of electronic nicotine delivery systems (ENDS) compare self-selected users vs. non-users. The few randomized studies to date generally support a positive impact on reducing smoking behavior, but these studies are focused on guided ENDS use. This study presents a randomized naturalistic trial of ENDS with prospective outcomes of uptake and behavioral changes in smoking.  <b>Methods</b>—Adult smokers with minimal ENDS history were randomized in a 2:1 ratio to receive product for 3 weeks (n=46), or not (n=22). Changes in nicotine delivery (16mg vs. 24mg), midway through the study allowed a compelling opportunity to examine two ENDS products compared to control group. Primary outcomes, assessed via daily diaries during sampling period and in-person lab visits over 4 months, included uptake and usage of ENDS, cessation-related outcomes, and exposure to smoke constituents.  <b>Results</b>—All ENDS participants tried product at least once, with 48% of 24mg and 30% of 16mg using their assigned product for the entire sampling period. Within 24mg ENDS group, 57% made an independent purchase of ENDS, vs. 28% of 16mg, and 14% of control participants (p=.01). Smokers in both ENDS groups significantly reduced their smoking, whereas control participants did not (p=.03). Cessation behaviors (quit attempts, biologically verified abstinence) numerically but not statistically favored ENDS participants.  <b>Conclusions</b>—Results suggest that cigarette smokers are willing to use ENDS with trends towards reduced cigarette smoking and positive changes in cessation-related behaviors.</p>	<p><b>Adverse Events</b>  During the course of the study, 11 24mg ENDS participants (52%) reported a total of 21 adverse events, compared with 9 16mg ENDS participants (36%) who reported 17 adverse events, and compared with 8 control participants (36%) who reported a total of 29 events. Collapsed across both ENDS groups, the most common side effects reported were <b>cough (32%), nausea (24%) and mouth/throat irritation (16%)</b>, and in the control group, headache (24%), cough (21%) and mouth/throat irritation (17%). None of the adverse events resulted in study termination, or, amongst ENDS participants, early discontinuation of sampling.</p>



Autor/ Titel	Studientyp	Abstract	Schadenspotential
<p>D'Ruiz CD, Graff DW, Yan XS. Nicotine delivery, tolerability and reduction of smoking urge in smokers following short-term use of one brand of electronic cigarettes. BMC Public Health 2015; 15:991. DOI: 10.1186/s12889-015-2349-2. <a href="http://www.ncbi.nlm.nih.gov/pub-med/26424091">http://www.ncbi.nlm.nih.gov/pub-med/26424091</a>.</p>	<p>randomized, partially single-blinded, 6-period crossover clinical study</p>	<p><b>Background:</b> This randomized, partially single-blinded, 6-period crossover clinical study of adult smokers compared the nicotine pharmacokinetics, impacts on smoking urge and tolerability of various formulations of one brand of e-cigarettes with that of a tobacco cigarette.</p> <p><b>Methods:</b> Five e-cigarettes with different e-liquid formulations containing 1.6 % and 2.4 % nicotine and a conventional tobacco cigarette were randomized among 24 subjects under two exposure sessions consisting of a 30-min controlled and a one-hour ad lib use period to assess plasma nicotine levels, impacts on smoking urge and adverse events. The 30-min controlled use session comprised an intensive use of the e-cigarettes with a total of 50 puffs taken every 30 s for comparison to a single conventional cigarette having a typical machine-measured nicotine yield (~0.8 mg). Ad lib product use conditions provided insight into more naturalistic product use behaviors and their accompanying smoking urge reductions. Adverse events (AEs) were assessed by the Principal Investigator.</p> <p><b>Results:</b> Significant (<math>p &lt; 0.05</math>) increases in plasma nicotine concentrations occurred within 10 min of controlled e-cigarette use and significant (<math>p &lt; 0.001</math>) reductions from baseline smoking urge were observed within 5 min. E-cigarette and cigarette nicotine plasma levels were comparable for up to one hour of use. After both sessions (90 min), nicotine exposure was the highest for the cigarette, with all e-cigarettes showing 23 % to 53 % lower plasma concentrations. During controlled use, peak reduction in smoking urge for e cigs occurred later than for the cigarette. After completion of both sessions, significant smoking urge reduction persisted for most of the tested e-cigarettes, albeit at levels lower than that provided by the tobacco cigarette. Nicotine content, vehicle differences, and the presence of menthol did not significantly affect smoking urge reduction by the e-cigarettes. No subjects were discontinued due to AEs. The most frequently reported AEs events included cough, throat irritation, headache, and dizziness.</p> <p><b>Conclusions:</b> Blood plasma nicotine levels obtained from short-term use of e-cigarettes containing 1.6 % and 2.4 % nicotine were significant, but lower than those of conventional tobacco cigarettes, yet the reduction in craving symptoms were broadly comparable. The types of AEs were consistent with other research studies of longer duration that have reported that use of e-cigarettes by adult smokers is well tolerated.</p> <p>Trial Registration: <a href="http://ClinicalTrials.gov">http://ClinicalTrials.gov</a> identifier: NCT02210754. Registered 8 August 2014.</p>	<p><u>• Tolerability and reported adverse events</u>                      During the course of the study, a total of 38 subjects were exposed to one or more of the study products. There were no serious adverse events reported and no subjects were discontinued due to AEs. Mild product-use emergent AEs were reported by 18 of 38 subjects provided a study product (including the lead-in period). The number of subjects reporting AEs was similar among products, ranging from 3 to 10 subjects each, with slightly fewer subjects experiencing AEs following use of the menthol-flavored product. The <b>most frequent AE was cough</b>, reported 20 times by 11 subjects (more commonly with use of an e-cigarette product than the tobacco cigarette), followed by <b>throat irritation</b> (8 reports by 5 subjects) and <b>headache</b> (6 reports by 5 subjects), and dizziness (5 reports by 4 subjects). All AEs resolved without sequelae. The observed acute effects of the study products on blood pressure, heart rate and CO levels were previously reported by the authors under a separate publication [24] where it was noted that heart rate and systolic and diastolic blood pressure were significantly elevated after the use of the tobacco cigarette, but the elevation was less after use of most of the e-cigarettes. Furthermore, it was also observed that the use of the e-cigarettes produced no increase the exhaled CO levels, whereas the cigarette significantly increased the exhaled CO more than eight (8) times above the baseline.</p>
<p>D'Ruiz CD, Graff DW, Robinson E. Reductions in biomarkers of</p>	<p>randomized into one of six study groups</p>	<p><b>Background:</b> Electronic cigarettes (e-cigarettes) are popular alternatives to conventional cigarettes among adult smokers wishing to reduce their exposure to harmful smoke constituents. However, little information exists on the relative</p>	<p><u>• Tolerability and adverse events</u>                      Overall, 72 mild product-use adverse events were experienced by 30 % of sub-</p>

Autor/ Titel	Studientyp	Abstract	Schadenspotential
<p>exposure, impacts on smoking urge and assessment of product use and tolerability in adult smokers following partial or complete substitution of cigarettes with electronic cigarettes.                      BMC Public Health 2016; 16:543. DOI: 10.1186/s12889-016-3236-1.  <a href="http://www.ncbi.nlm.nih.gov/pub-med/27401980">http://www.ncbi.nlm.nih.gov/pub-med/27401980</a>.</p>		<p>internal exposures resulting from the exclusive or dual use of e-cigarettes.  <b>Methods:</b> Measurements of product use; adverse events; changes in smoking urge; and blood, urine and exhaled breath biomarkers of exposure (BoE) representing toxicants believed to contribute to smoking related diseases were made at baseline and after five days of product use in 105 clinically-confined smokers randomized into groups that partially or completely substituted their usual brand combustible cigarette with commercial e-cigarettes, or discontinued all nicotine and tobacco products.  <b>Results:</b> Subjects switching to e-cigarettes had significantly lower levels (29 %–95 %) of urinary BoEs after 5 days. Nicotine equivalents declined by 25 %–40 %. Dual users who substituted half of their self-reported daily cigarette consumption with e-cigarettes experienced 7 %–38 % reductions, but had increases (1 %–20 %) in nicotine equivalents. Blood nicotine biomarker levels were lower in the cessation (75 %–96 %) and e-cigarette use groups (11 %–83 %); dual users had no significant reductions. All groups experienced significant decreases in exhaled CO (27 %–89 %). Exhaled NO increases (46 %–63 %) were observed in the cessation and e-cigarette use groups; dual users had minimal changes. By Day 5, all groups had greater reductions in smoking urge compared to cessation. However, reductions were larger in the dual use group. No serious adverse events were observed.  <b>Conclusions:</b> Exposures to harmful smoke toxicants were observed to be lower in smokers who completely or partially replaced their cigarettes with e-cigarettes over five days. Keywords: Electronic cigarettes, Clinical trial, Biomarkers of</p>	<p>jects. The number of subjects reporting adverse events ranged from 2 to 7 subjects each across groups receiving study products and only 1 subject in the cessation group. The most frequently reported adverse event was <b>headache</b>, reported 15 times by 12 subjects across study groups. There were no individual clinically significant laboratory and post product administration physical examination findings and/or vital sign adverse events. Moreover, there were no serious adverse events and no subjects were discontinued due to adverse events.</p>
<p>El Dib R, Suzumura EA, Akl EA, et al. Electronic nicotine delivery systems and/or electronic non-nicotine delivery systems for tobacco smoking cessation or reduction: A systematic review and meta-analysis. BMJ open 2017; 7(2):e012680. DOI: 10.1136/bmjopen-2016-012680.  <a href="http://www.ncbi.nlm.nih.gov/pub-med/27401980">http://www.ncbi.nlm.nih.gov/pub-med/27401980</a></p>	<p>Systematic Review</p>	<p><b>Objective:</b> A systematic review and meta-analysis to investigate the impact of electronic nicotine delivery systems (ENDS) and/or electronic non-nicotine delivery systems (ENNDS) versus no smoking cessation aid, or alternative smoking cessation aids, in cigarette smokers on long-term tobacco use.  <b>Data sources:</b> Searches of MEDLINE, EMBASE, PsycInfo, CINAHL, CENTRAL and Web of Science up to December 2015.                      Study selection: Randomised controlled trials (RCTs) and prospective cohort studies.  <b>Data extraction:</b> Three pairs of reviewers independently screened potentially eligible articles, extracted data from included studies on populations, interventions and outcomes and assessed their risk of bias. We used the Grading of Recommendations Assessment, Development and Evaluation approach to rate overall certainty of the evidence by outcome.  <b>Data synthesis:</b> Three randomised trials including 1007 participants and nine cohorts including 13 115 participants proved eligible. Results provided by only two RCTs suggest a possible increase in tobacco smoking cessation with ENDS in comparison with ENNDS (RR 2.03, 95% CI 0.94 to 4.38; p=0.07;</p>	<p><b>Adverse effects</b>                      Synthesised results from RCTs The Bullen 2013 study reported serious side effects in 27 out of 241 participants in the 16 mg ENDS group and 5 out of 57 for the ENNDS group followed at 6 months; results failed to show a difference between these groups with a very wide CI (OR 1.31, 95% CI 0.48 to 3.57; p=0.59). Results suggested possible increase in side effects in the 21 mg nicotine patches group (14 of 215) in comparison with ENDS (OR 1.81, 95% CI 0.92 to 3.55; p=0.08).                      - Serious side effects include death (n=1, in nicotine e-cigarettes group), life threatening illness (n=1, in nicotine e-cigarettes group), admission to hospital or prolongation of hospital stay (12% of all events in nicotine e-cigarettes group, 8% in patches group and 11% in placebo e-cigarettes group), persistent or significant disability or incapacity and other medically important events (6% of all events in nicotine e-cigarettes group, 4% in patches group and 3% placebo e-cigarettes group).                      - Adriaens 2014 study reported no serious adverse events in ENDS groups as well as in the e-liquid group at 8 months of follow-up; however at 1 week from start of intervention there were three cases of non-serious adverse events in the</p>

Autor/ Titel	Studientyp	Abstract	Schadenspotential
<p><a href="https://pubmed.ncbi.nlm.nih.gov/28235965">ih.gov/pub-med/28235965</a>.</p>		<p>I2=0%, risk difference (RD) 64/1000 over 6 to 12 months, low-certainty evidence).</p> <p>Results from cohort studies suggested a possible reduction in quit rates with use of ENDS compared with no use of ENDS (OR 0.74, 95% CI 0.55 to 1.00; p=0.051; I2=56%, very low certainty).</p> <p><b>Conclusions:</b> There is very limited evidence regarding the impact of ENDS or ENNDS on tobacco smoking cessation, reduction or adverse effects: data from RCTs are of low certainty and observational studies of very low certainty. The limitations of the cohort studies led us to a rating of very low-certainty evidence from which no credible inferences can be drawn. Lack of usefulness with regard to address the question of e-cigarettes' efficacy on smoking reduction and cessation was largely due to poor reporting. This review underlines the need to conduct well-designed trials measuring biochemically validated outcomes and adverse effects.</p>	<p>ENDS groups.</p> <ul style="list-style-type: none"> <li>- Caponnetto 2013 mentioned that no serious adverse events occurred during the study and authors found a significant reduction in frequency of reported symptoms compared with baseline.</li> </ul> <p><b>Synthesised results from cohort studies</b></p> <ul style="list-style-type: none"> <li>- Manzoli reported no significant differences in selfreported serious side effects, but observed four cases of pneumonia, four COPD exacerbations, three myocardial infarctions and one angina as possibly related serious side effects: two among the ENDS users (both switched to tobacco smoking during follow-up); six among tobacco smokers (three quit all smoking) and four among tobacco and ENDS smokers.</li> <li>- Hajek 2015 reported one leak irritating a participant's mouth and some reports of irritation at the back of the throat and minor coughing. The remaining studies did not report adverse effects.</li> </ul>
<p>Farsalinos KE, Gillman G. Carbonyl Emissions in E-cigarette Aerosol: A Systematic Review and Methodological Considerations. <i>Front Physiol</i> 2017; 8:1119. DOI: 10.3389/fphys.2017.01119. <a href="http://www.ncbi.nlm.nih.gov/pub-med/29375395">http://www.ncbi.nlm.nih.gov/pub-med/29375395</a>.</p>	<p>Systematic Review</p>	<p>Carbonyl emissions from tobacco cigarettes represent a substantial health risk contributing to smoking-related morbidity and mortality. As expected, this is an important research topic for tobacco harmreduction products, in an attempt to compare the relative risk of these products compared to tobacco cigarettes. In this study, a systematic review of the literature available on PubMed was performed analyzing the studies evaluating carbonyl emissions from e-cigarettes. A total of 32 studies were identified and presented. We identified a large diversity of methodologies, with substantial discrepancies in puffing patterns, aerosol collection and analytical methods as well as reported units of measurements. Such discrepancies make comparisons difficult, and in some cases the accuracy of the findings cannot be determined. Importantly, control for the generation of dry puffs was not performed in the vast majority of studies, particularly in studies using variable power devices, which could result in testing conditions and reported carbonyl levels that have no clinical relevance or context. Some studies have been replicated, verifying the presence of dry puff conditions. Whenever realistic use conditions were ensured, carbonyl emissions from e-cigarettes were substantially lower than tobacco cigarette smoke, while newer generation (bottom-coil, cotton wick) atomizers appeared to emit minimal levels of carbonyls with questionable clinical significance in terms of health risk. However, extremely high levels of carbonyl emissions were reported in some studies, and all these studies need to be replicated because of potentially important health implications.</p>	<p>The main ingredients in e-cigarette liquids, propylene glycol (PG) and glycerol (VG) are known to be oxidized to carbonyls (Bekki et al., 2014; Spencer and Lauterbach, 2015). [...]</p> <ul style="list-style-type: none"> <li>- Some studies produced contradictory results.</li> <li>-- Kosmider et al. (2014) found that VG liquids emitted lower carbonyl emissions compared to PG liquids.</li> <li>-- Geiss et al. (2015) found that VG liquids remitted higher carbonyl levels compared to mixed PG/VG liquids</li> <li>-- Wang et al. (2017) found higher levels of carbonyls in VG compared to PG liquids. VG has higher viscosity compared to PG and, unless diluted with water, it is possible that this might adversely affect the liquid supply rate to the coil and, thus, create overheating conditions.</li> </ul> <p>In a study that generated a lot of publicity, Jensen et al. (2015) tested a "tank system" e-cigarette with a commercial ecigarette liquid (Halo "café mocha" flavor, 6 mg/mL nicotine concentration) for the presence of formaldehyde hemiacetals. [...] Despite mentioning that the behavior of formaldehyde hemiacetals in the respiratory tract are unknown, they assumed that the risk is similar to formaldehyde and reported that the <b>cancer risk of long term vaping</b> was "5 times as high. . . or even 15 times as high. . . as the risk associated with long term smoking" when comparing 3mL liquid consumption with 20 tobacco cigarettes.</p>
<p>Fernández E, Ballbè M, Sureda X, et al. Particulate Matter</p>	<p>Systematic Review and</p>	<p><b>Objectives</b> The aim of this study is to review the literature on the composition of aerosols from electronic cigarettes (ecigarettes) originated by human vaping and to describe the emission of particulate matter ≤2.5 µm in diameter (PM2.5)</p>	<p>emissions from ecigarettes can <b>contain potential toxic compounds such as nicotine, carbonyls, metals, and organic volatile compounds, besides particulate matter.</b></p>

Autor/ Titel	Studientyp	Abstract	Schadenspotential
from Electronic Cigarettes and Conventional Cigarettes: A Systematic Review and Observational Study. Current environmental health reports 2015; 2(4):423–9. DOI: 10.1007/s40572-015-0072-x. <a href="http://www.ncbi.nlm.nih.gov/pub-med/26452675">http://www.ncbi.nlm.nih.gov/pub-med/26452675</a> . Study	Observational Study	from conventional and e-cigarettes at home in real-use conditions. <b>Methods</b> We conducted a systematic literature search in PubMed and Web of Science. We measured PM2.5 in four different homes: one from a conventional cigarette smoker, one from an e-cigarette user, and two from non-smokers. <b>Results</b> The review identified eight previous investigations on the composition of aerosols from e-cigarettes originated by human vaping and indicated that emissions from ecigarettes can contain potential toxic compounds such as nicotine, carbonyls, metals, and organic volatile compounds, besides particulate matter. In the observational study, the PM2.5 median concentration was 9.88 µg/m3 in the e-cigarette user home and 9.53 and 9.36 µg/m3 in the smoke-free homes, with PM2.5 peaks concurrent with the e-cigarette puffs. <b>Conclusion</b> Both the literature review and the observational study indicate that e-cigarettes used under real-conditions emit toxicants, including PM2.5. Further research is needed to characterize the chemicals emitted by different types of ecigarettes and to assess secondhand exposure to e-cigarette aerosol using biological markers.	- In the observational study, the PM2.5 median concentration was 9.88 µg/m3 in the e-cigarette user home and 9.53 and 9.36 µg/m3 in the smoke-free homes, with PM2.5 peaks concurrent with the e-cigarette puffs.
Ferrari M, Zanasi A, Nardi E, et al. Short-term effects of a nicotine-free e-cigarette compared to a traditional cigarette in smokers and non-smokers. BMC Pulm Med 2015; 15:120. DOI: 10.1186/s12890-015-0106-z. <a href="http://www.ncbi.nlm.nih.gov/pub-med/26459355">http://www.ncbi.nlm.nih.gov/pub-med/26459355</a> .	laboratory-based study; randomized; cross-over design	<b>Background:</b> A few studies have assessed the short-term effects of low-dose nicotine e cigarettes, while data about nicotine-free e-cigarettes (NF e-cigarettes) are scanty. Concerns have been expressed about the use of NF e-cigarettes, because of the high concentrations of propylene glycol and other compounds in the e-cigarette vapor. <b>Methods:</b> This laboratory-based study was aimed to compare the effects of ad libitum use of a NF e-cigarette or and a traditional cigarette for 5 min in healthy adult smokers (n = 10) and non-smokers (n = 10). The main outcome measures were pulmonary function tests, fraction of exhaled nitric oxide (FeNO) and fractional concentration of carbon monoxide (FeCO) in exhaled breath. <b>Results:</b> The traditional cigarette induced statistically significant increases in FeCO in both smokers and non-smokers, while no significant changes were observed in FeNO. In non-smokers, the traditional cigarette induced a significant decrease from baseline in FEF75 (81 % ± 35 % vs 70.2 % ± 28.2 %, P = 0.013), while in smokers significant decreases were observed in FEF25 (101.3 % ± 16.4 % vs 93.5 % ± 31.7 %, P = 0.037), FEV1 (102.2 % ± 9.5 % vs 98.3 % ± 10 %, P = 0.037) and PEF (109.5 % ± 14.6 % vs 99.2 % ± 17.5 %, P = 0.009). In contrast, the only statistically significant effects induced by the NF e-cigarette in smokers were reductions in FEV1 (102.2 % ± 9.5 % vs 99.5 ± 7.6 %, P = 0.041) and FEF25 (103.4 % ± 16.4 % vs 94.2 % ± 16.2 %, P = 0.014). <b>Discussion:</b> The present study demonstrated that the specific brand of NF e-cigarette utilized did not induce any major acute effects. In contrast, several studies have shown that both traditional cigarettes and nicotine-containing e-cigarettes have acute effects on lung function. Our study expands on previous	<ul style="list-style-type: none"> <li>• several studies have shown that both traditional cigarettes and nicotine-containing e-cigarettes have acute effects on lung function</li> <li>• nicotine-free e-cigarettes (NF e-cigarettes): The short-term use of the specific brand of NF e-cigarette assessed in this study had no immediate adverse effects on non-smokers and only small effects on FEV1 and FEF25 in smokers. The long term health effects of NF e-cigarette use are unknown but worthy of further investigations.</li> <li>• Diskussion: One of the concerns of using NF e-cigarettes is that the devices contain high concentrations of glycol, which is a known irritant when inhaled. Other potentially dangerous ingredients that may be found in NF e-cigarettes are solvents, genotoxins and various other chemicals</li> </ul>

Autor/ Titel	Studientyp	Abstract	Schadenspotential
		<p>observations on the effects of NF e-cigarettes, but also for the first time describes the changes induced by smoking one traditional cigarette in a group of never smokers.</p> <p>Conclusions: The short-term use of the specific brand of NF e-cigarette assessed in this study had no immediate adverse effects on non-smokers and only small effects on FEV1 and FEF25 in smokers. The long term health effects of NF e-cigarette use are unknown but worthy of further investigations</p>	
<p>Flach 2019</p> <p>E-cigarettes and head and neck cancers: A systematic review of the current literature</p>	<p>Systematic Review</p>	<p><b>Background:</b> Cigarette smoking is a well-established risk factor for head and neck (HN) cancers. Use of electronic cigarettes (e-cigarettes) is gaining popularity, being advertised as benign alternatives to tobacco. A wide variety of potentially harmful chemical components with variable quantity have been identified in e-liquids and aerosols of e-cigarettes. However, use of e-cigarettes remains controversial due to conflicting evidence.</p> <p><b>Objectives:</b> We aimed to assess the association between e-cigarettes and HN cancers. We conducted a systematic review to evaluate the literature for evidence on carcinogenic effects of e-cigarettes in the pathogenesis of HN cancers.</p> <p><b>Type of review:</b> Qualitative systematic review.</p> <p><b>Search strategy:</b> A PubMed/MEDLINE, Cochrane, CINAHL Plus, Trip Medical Database and Web of Science search was done for studies on e-cigarettes and HN cancer. <b>Evaluation method:</b> Abstract review of all articles, full article revision of included studies, data extraction and quality assessment were performed by two independent assessors.</p> <p><b>Results:</b> The literature search resulted in the identification of 359 articles. Eighteen articles were selected for inclusion into the systematic review. The majority were laboratory-based studies, followed by several cohort and case studies, representing low-level evidence. A few reports suggested DNA damage following exposure to ecigarettes potentially due to increased oxidative stress. Flavoured e-liquids appear to be more harmful. There is variable evidence from clinical studies.</p> <p><b>Conclusions:</b> Our review outlines potential dangers associated with the use of ecigarettes and their role in HN cancers. More longitudinal and controlled studies are needed to assess the possible link between e-cigarettes and HN cancers.</p>	<p>The current literature on the association between e-cigarettes and HN cancer pathogenesis is poor. There is limited evidence that e-cigarettes are <b>harmful and potentially carcinogenic for the head and neck</b>, with some reports stating that e-cigarettes can lead to in vitro damage and that flavoured e-liquids are particularly damaging. There is currently no good-quality evidence to conclude that e-cigarettes are less harmful than conventional cigarettes.</p>
<p>Gentry S, Forouhi NG, Nolley C. Are Electronic Cigarettes an Effective Aid to Smoking Cessation</p>	<p>Systematic Review</p>	<p><b>Introduction:</b> Smoking prevalence remains high in some vulnerable groups, including those who misuse substances, have a mental illness, are homeless, or are involved with the criminal justice system. E-cigarette use is increasing and may support smoking cessation/reduction.</p>	<p>No serious adverse events were identified. Some side effects were reported, commonly <b>cough, headache, and throat irritation</b>. O'Brien et al. compared adverse events/month among e-cigarette users with and without mental illness and found no significant difference (0.05 events/month in both groups (p = .592, IRR = 0.89, 95% CI = 0.59 to 1.35)). Adverse</p>

Autor/ Titel	Studientyp	Abstract	Schadenspotential
<p>or Reduction Among Vulnerable Groups? A Systematic Review of Quantitative and Qualitative Evidence. Nicotine &amp; tobacco research official journal of the Society for Research on Nicotine and Tobacco 2019; 21(5):602–16. DOI: 10.1093/ntr/nty054. <a href="http://www.ncbi.nlm.nih.gov/pub-med/29608714">http://www.ncbi.nlm.nih.gov/pub-med/29608714</a>.</p>		<p><b>Methods:</b> Systematic review of quantitative and qualitative data on the effectiveness of e-cigarettes for smoking cessation/reduction among vulnerable groups. Databases searched were MEDLINE, EMBASE, PsychINFO, CINAHL, ASSIA, ProQuest Dissertations and Theses, and Open Grey. Narrative synthesis of quantitative data and thematic synthesis of qualitative data.</p> <p><b>Results:</b> 2628 records and 46 full texts were screened; 9 studies were identified for inclusion. Due to low quality of evidence, it is uncertain whether e-cigarettes are effective for smoking cessation in vulnerable populations. A moderate quality study suggested that e-cigarettes were as effective as nicotine replacement therapy. Four studies suggested significant smoking reduction; however, three were uncontrolled and had sample sizes below 30. A prospective cohort study found no differences between e-cigarette users and nonusers. No significant adverse events and minimal side effects were identified. Qualitative thematic synthesis revealed barriers and facilitators associated with each component of the COM-B (capability, opportunity, motivation, and behavior) model, including practical barriers; perceptions of effectiveness for cessation/reduction; design features contributing to automatic and reflective motivation; smoking bans facilitating practical opportunity; and social connectedness increasing social opportunity.</p> <p><b>Conclusion:</b> Further research is needed to identify the most appropriate device types for practicality and safety, level of support required in e-cigarette interventions, and to compare e cigarettes with current best practice smoking cessation support among vulnerable groups.</p> <p><b>Implications:</b> Smoking prevalence among people with mental illness, substance misuse, homelessness, or criminal justice system involvement remains high. E-cigarettes could support cessation. This systematic review found limited quantitative evidence assessing effectiveness. No serious adverse events were identified. Qualitative thematic synthesis revealed barriers and facilitators mapping to each component of the COM-B (capability, opportunity, motivation, and behavior) model, including practical barriers; perceived effectiveness; design features contributing</p>	<p>event counts were similar between nicotine e-cigarette, placebo e-cigarette, and NRT but small numbers prohibited significance testing. Caponetto et al. reported side effects experienced among people with mental illness resolved over time, but no data beyond 52 weeks were available.</p>
<p>Glasser AM, Collins L, Pearson JL, et al. Overview of Electronic Nicotine Delivery Systems: A Systematic Review. Am J Prev Med 2017; 52(2):e33-e66. DOI: 10.1016/j.amepre.2016.10.036.</p>	<p>Systematic Review</p>	<p><b>Context</b>—Rapid developments in e-cigarettes, or electronic nicotine delivery systems (ENDS), and the evolution of the overall tobacco product marketplace warrant frequent evaluation of the published literature. The purpose of this article is to report updated findings from a comprehensive review of the published scientific literature on ENDS.</p> <p><b>Evidence acquisition</b>—The authors conducted a systematic review of published empirical research literature on ENDS through May 31, 2016, using a detailed search strategy in the PubMed electronic database, expert review, and additional targeted searches. Included studies presented empirical findings and were coded to at least one of nine topics: (1) Product Features; (2)</p>	<p>There have been 116 articles that examine the impact of vaping on human health and 13 on animal health. Studies address physiologic and cognitive effects of vaping, adverse events associated with vaping, exposure to secondhand vapor, and cytotoxicity of ENDS.</p> <p>- Human exposure to some potentially harmful chemicals is significantly lower for ENDS than for cigarettes. Laboratory studies (n=20) find <b>modest increases in nicotine biomarkers</b> after vaping.</p> <p>- Some studies (n=13) have examined cardiovascular measures associated with vaping, with the majority finding an <b>increase in heart rate</b>, but three finding no</p>

Autor/ Titel	Studientyp	Abstract	Schadenspotential
<a href="http://www.ncbi.nlm.nih.gov/pub-med/27914771">http://www.ncbi.nlm.nih.gov/pub-med/27914771</a> .		<p>Health Effects; (3) Consumer Perceptions; (4) Patterns of Use; (5) Potential to Induce Dependence; (6) Smoking Cessation; (7) Marketing and Communication; (8) Sales; and (9) Policies; reviews and commentaries were excluded. Data from included studies were extracted by multiple coders (October 2015 to August 2016) into a standardized form and synthesized qualitatively by topic.</p> <p><b>Evidence synthesis</b>—There were 686 articles included in this systematic review. The majority of studies assessed patterns of ENDS use and consumer perceptions of ENDS, followed by studies examining health effects of vaping and product features.</p> <p><b>Conclusions</b>—Studies indicate that ENDS are increasing in use, particularly among current smokers, pose substantially less harm to smokers than cigarettes, are being used to reduce/quit smoking, and are widely available. More longitudinal studies and controlled trials are needed to evaluate the impact of ENDS on population-level tobacco use and determine the health effects of longer-term vaping.</p>	<p>change after use.</p> <p><b>Adverse events</b></p> <ul style="list-style-type: none"> <li>- The Food and Drug Administration received 35 adverse event reports (<b>respiratory symptoms, eye irritation, headache, nausea, sore throat/irritation, dizziness, racing/irregular heart rate</b>) of <b>passive vapor exposure</b> between January 2012 and December 2014.</li> <li>- Other studies report the most common adverse events associated with vaping as <b>mouth and throat irritation, nausea, headache, and dry cough</b>.</li> <li>- From 2012 to 2015, there were 92 reported <b>overheating/fire/explosion</b> events in the U.S., and about half resulted in injuries (i.e., <b>thermal burns, lacerations, or smoke inhalation</b>).</li> </ul>
Gualano MR, Passi S, Bert F, et al. Electronic cigarettes: Assessing the efficacy and the adverse effects through a systematic review of published studies. J Public Health (Oxf) 2015; 37(3):488–97. DOI: 10.1093/pub-med/fdu055. <a href="http://www.ncbi.nlm.nih.gov/pub-med/25108741">http://www.ncbi.nlm.nih.gov/pub-med/25108741</a> .	Systematic Review	<p><b>Background</b> To investigate the efficacy and the adverse effects (AEs) of the electronic cigarette, we performed a systematic review of published studies.</p> <p><b>Methods</b> We selected experimental and observational studies examining the efficacy (as reduction of desire to smoke and/or number of cigarettes smoked and/or quitting or as reduction of nicotine withdrawal symptoms) and the safety of EC (AEs self-reported or clinical/laboratory). The following search engines were used: PubMed, ISIWeb of Knowledge and Cochrane Controlled Trials Register.</p> <p><b>Results</b> Finally, six experimental studies and six cohort studies were included. In the prospective 12-month, randomized controlled trial, smoking reduction was documented in 22.3 and 10.3% at Weeks 12 and 52, respectively (P, 0.001 versus baseline). Moreover, two cohort studies reported a reduction in the number of cigarette/day (from 50 to 80%) after the introduction of the EC. 'Mouth and throat irritation', 'nausea', 'headache' and 'dry cough' were the most frequently AEs reported.</p> <p><b>Conclusions</b> The use of the EC can reduce the number of cigarettes smoked and withdrawal symptoms, but the AEs reported are mainly related to a short period of use. Long-term studies are needed to evaluate the effects of the EC usage after a chronic exposure.</p>	<p>'Mouth and throat irritation', 'nausea', 'headache' and 'dry cough' were the most frequently AEs reported.</p> <p><u>Short-term adverse effects</u></p> <ul style="list-style-type: none"> <li>- Mouth (20.6%) and throat (32.4%) irritation, dry cough (32.4%) and nausea (14.4%) were the most frequently AEs reported by the EC smokers and diminished substantially. (n=3 studies)</li> <li>- The same AEs are reported by smokers enrolled in the trial ECLAT where before using e-cigarettes, at baseline, the most frequently reported AEs were dry cough (26%; average for all study groups combined), mouth irritation (22%), shortness of breath (20%), throat irritation (17%) and headache (17%). For all the investigated AEs, compared with baseline, a significant reduction in frequency of reported symptoms was observed at Week 52: dry cough (12% average for all study groups combined), mouth irritation (11%), shortness of breath (6%), throat irritation (13%) and headache (3%)</li> <li>- Finally, the RCT by Bullen et al. identified no significant differences in adverse events between the three arms, with 137 events in the nicotine e-cigarettes group, 119 events in the patches group and 36 events in the placebo e-cigarettes group.</li> </ul>
Hajek P, Phillips-Waller A, Przulj D, et al. A Randomized Trial of E-Cigarettes ver-	RCT	<p><b>BACKGROUND</b> E-cigarettes are commonly used in attempts to stop smoking, but evidence is limited regarding their effectiveness as compared with that of nicotine products approved as smoking-cessation treatments.</p> <p><b>METHODS</b> We randomly assigned adults attending U.K. National Health Service stop-smoking services to either nicotine-replacement products of their</p>	<p>There were 27 serious adverse events in the e-cigarette group and 22 in the nicotine-replacement group. No serious adverse event in either group was classified by the trial clinician as being related to product use, but we noted 1 respiratory event in the nicotine-replacement group and 5 in the e-cigarette group (2 in</p>

Autor/ Titel	Studientyp	Abstract	Schadenspotential
<p>sus Nicotine-Replacement Therapy. N Engl J Med 2019; 380(7):629–37. DOI: 10.1056/NEJMoa1808779. <a href="http://www.ncbi.nlm.nih.gov/pub-med/30699054">http://www.ncbi.nlm.nih.gov/pub-med/30699054</a>.</p>		<p>choice, including product combinations, provided for up to 3 months, or an e-cigarette starter pack (a secondgeneration refillable e-cigarette with one bottle of nicotine e-liquid [18 mg per milliliter]), with a recommendation to purchase further e-liquids of the flavor and strength of their choice. Treatment included weekly behavioral support for at least 4 weeks. The primary outcome was sustained abstinence for 1 year, which was validated biochemically at the final visit. Participants who were lost to follow-up or did not provide biochemical validation were considered to not be abstinent. Secondary outcomes included participant-reported treatment usage and respiratory symptoms.</p> <p><b>RESULTS</b> A total of 886 participants underwent randomization. The 1-year abstinence rate was 18.0% in the e-cigarette group, as compared with 9.9% in the nicotine-replacement group (relative risk, 1.83; 95% confidence interval [CI], 1.30 to 2.58; P&lt;0.001). Among participants with 1-year abstinence, those in the e-cigarette group were more likely than those in the nicotine-replacement group to use their assigned product at 52 weeks (80% [63 of 79 participants] vs. 9% [4 of 44 participants]). Overall, throat or mouth irritation was reported more frequently in the e-cigarette group (65.3%, vs. 51.2% in the nicotine-replacement group) and nausea more frequently in the nicotine replacement group (37.9%, vs. 31.3% in the e-cigarette group). The e-cigarette group reported greater declines in the incidence of cough and phlegm production from baseline to 52 weeks than did the nicotine-replacement group (relative risk for cough, 0.8; 95% CI, 0.6 to 0.9; relative risk for phlegm, 0.7; 95% CI, 0.6 to 0.9). There were no significant between-group differences in the incidence of wheezing or shortness of breath.</p> <p><b>CONCLUSIONS</b> E-cigarettes were more effective for smoking cessation than nicotine-replacement therapy, when both products were accompanied by behavioral support.</p>	<p>participants who were smoking and not vaping, 2 in participants who were smoking and vaping, and 1 in a participant whose status with respect to smoking and vaping was not known).</p> <p><u>prespecified adverse reactions of interest</u></p> <ul style="list-style-type: none"> <li>- <b>nausea</b> was reported more frequently in the nicotine-replacement group (37.9%, vs. 31.3% in the e-cigarette group) and</li> <li>- <b>throat or mouth irritation</b> more frequently in the e-cigarette group (65.3%, vs. 51.2% in the nicotine-replacement group).</li> <li>- participants reporting <b>severe nausea</b> (6.6% in the e-cigarette group and 6.5% in the nicotine-replacement group) or <b>severe throat or mouth irritation</b> (5.9% and 3.9%, respectively)</li> </ul>
<p>Hess I, Lachireddy K, Capon A. A systematic review of the health risks from passive exposure to electronic cigarette vapour. Public health research &amp; practice 2016; 26(2):e2621617. DOI: 10.17061/phrp2621617. <a href="http://www.ncbi.nlm.nih.gov/pub-med/30699054">http://www.ncbi.nlm.nih.gov/pub-med/30699054</a>.</p>	<p>Systematic Review</p>	<p><b>Objectives:</b> Electronic cigarettes (ECs) have recently become popular around the world, and their safety is being widely discussed in the scientific literature. Previous studies have examined the chemicals in e-liquids and vapour, and demonstrated that the aerosol from ECs can contain toxic chemicals that are harmful to health. However, little is known about the potential adverse health effects of passive exposure to EC vapour. The aim of this paper is to summarise and review all studies that have examined potential adverse health effects of passive exposure from inhaling EC vapour. Specifically, our research objectives were to describe 1) the absolute impact of passive exposure from inhaling vapour when compared with background, and 2) the relative impact of passive exposure from inhaling vapour when compared with passive exposure from inhaling conventional cigarette smoke.</p> <p><b>Methods:</b> A systematic review was conducted to identify articles published from 1996 to 10 September 2015 from Embase, Ovid MEDLINE and PreMED-</p>	<ul style="list-style-type: none"> <li>• We reviewed 16 studies, with varying designs, investigating potential adverse health effects of passive exposure to EC vapours.</li> <li>- Studies (n=9) examining the composition of EC vapour or some of its aspects found that <b>ECs are not emission-free</b>.</li> <li>- The majority of studies (n=10) concluded that <b>passive exposure to EC vapour may pose a health risk to bystanders</b>.</li> <li>- n=2 studies did not comment on the passive exposure risk and n=4 concluded that their investigation showed no risk to bystanders.</li> </ul> <p>&gt;&gt; It is noted that those studies undertaken by tobacco employees or funded by the National Vapers Club concluded no apparent risk from ECs to bystanders. Those who did not declare a conflict of interest were more likely to draw conclusions that were more precautionary and/or suggested a potential risk from passive exposure to ECs, highlighting potential biases in the current literature.</p>



Autor/ Titel	Studientyp	Abstract	Schadenspotential
<p><a href="https://pubmed.ncbi.nlm.nih.gov/27734060">ih.gov/pub-med/27734060</a>.</p>		<p>LINE. Papers eligible for inclusion had to be written in English, study health effects from passive exposure to EC vapour in animals or humans, test or analyse the EC vapour directly or in the ambient air (with an inference made about passive or second-hand vapour exposure). The review was conducted using the PRISMA guidelines for reporting on systematic reviews. We identified 312 studies, and 16 were relevant for inclusion in our review.</p> <p><b>Results:</b> A variety of study designs were used to investigate potential health risks from passive exposure to EC vapour. These included direct exposure studies involving humans and animals, and indirect exposure studies using volunteer EC users or smoking machines. The majority of studies determined that passive exposure to EC vapour may pose a health risk to bystanders. All papers encountered a number of limitations.</p> <p><b>Conclusion:</b> Our review found that the absolute impact from passive exposure to EC vapour has the potential to lead to adverse health effects. The risk from being passively exposed to EC vapour is likely to be less than the risk from passive exposure to conventional cigarette smoke.</p>	
<p>Khoudigian S, Devji T, Lytvyn L, et al. The efficacy and short-term effects of electronic cigarettes as a method for smoking cessation: A systematic review and a meta-analysis. Int J Public Health 2016; 61(2):257–67. DOI: 10.1007/s00038-016-0786-z. <a href="http://www.ncbi.nlm.nih.gov/pub-med/26825455">http://www.ncbi.nlm.nih.gov/pub-med/26825455</a>.</p>	<p>Systematic Review</p>	<p><b>Objectives</b> E-cigarettes are increasingly popular as smoking cessation aids. This review assessed the efficacy of e-cigarettes for smoking cessation as well as desire to smoke, withdrawal symptoms, and adverse events in adult smokers.</p> <p><b>Methods</b> A systematic review was conducted. Studies comparing e-cigarettes to other nicotine replacement therapies or placebo were included. Data were pooled using meta-analysis.</p> <p><b>Results</b> Of 569 articles, 5 were eligible. Study participants were more likely to stop smoking when using nicotine e-cigarettes (43/489, 9 %) versus placebo e-cigarettes (8/173, 5 %); however, this difference was not statistically significant (RR 2.02; 95 % CI 0.97, 4.22). The pooled effect estimates for the desire to smoke (RR -0.22; 95 % CI -0.80, 0.36), irritability (RR -0.03; 95% CI -0.38, 0.31), restlessness (RR -0.03; 95 % CI -0.42, 0.35), poor concentration (RR -0.01; 95 % CI -0.35, 0.32), depression (RR -0.01; 95 % CI -0.22, 0.20), hunger (RR -0.01; 95 % CI -0.32, 0.30), and average number of non-serious adverse events (RR -0.09; 95 % CI -0.28, 0.46) were not statistically significantly different. Only one study reported serious adverse events with no apparent association with e-cigarette use.</p> <p><b>Conclusions</b> Limited low-quality evidence of a non-statistically significant trend toward smoking cessation in adults using nicotine e-cigarettes exists compared with other therapies or placebo. Larger, high-quality studies are needed to inform policy decisions.</p>	<p>Only one study reported serious adverse events with no apparent association with e-cigarette use.</p> <p>- Serious adverse events, reported in the Bullen et al. (2013) study, were slightly higher in the nicotine e-cigarette group (27/137, 19.7 %) than in the placebo e-cigarette group (5/36, 13.9 %). Serious events by convention included death (n = 1, in nicotine e-cigarette group), life-threatening illness (n = 1, in nicotine e-cigarette group), admission to hospital or prolongation of hospital stay (n = 17 and n = 4, in nicotine and placebo e-cigarette groups, respectively), persistent or significant disability or incapacity, congenital abnormality (n = 8 and n = 1, in the nicotine and placebo e-cigarette groups, respectively).</p> <p>--&gt; not associated with the use of e-cigarettes.</p>
<p>Liu X, Lu W, Liao S, et al. Efficiency and</p>	<p>Systematic Review</p>	<p><b>Background:</b> Electronic cigarettes (e-cigarettes) are a prevalent smoking cessation aid worldwide; however, a consensus regarding their efficacy and safety</p>	<p><u>Adverse events of e-cigarettes.</u></p> <p>- The dominant adverse events of e-cigarettes were reported as <b>cough, mouth</b></p>

Autor/ Titel	Studientyp	Abstract	Schadenspotential
<p>adverse events of electronic cigarettes: A systematic review and meta-analysis (PRISMA-compliant article). <i>Medicine (Baltimore)</i> 2018; 97(19):e0324. DOI: 10.1097/MD.00000000000010324. <a href="http://www.ncbi.nlm.nih.gov/pub-med/29742683">http://www.ncbi.nlm.nih.gov/pub-med/29742683</a>.</p>		<p>has yet to be reached.  <b>Methods:</b> We conducted a systematic review of the literature from related studies written in English or Chinese and published between January 1, 2003, and July 30, 2017. Eligible studies reporting the number of smokers who reduced or quit smoking and suffered from adverse events after e-cigarette use were selected according to predefined criteria; pertinent data were then extracted for a meta-analysis.  <b>Results:</b> Our search produced 198 articles; of these publications, 14 including 35,665 participants were analyzed. The pooled efficacy rate of e-cigarettes ranged from 48.3% to 58.7% for smoking reduction and from 13.2% to 22.9% for smoking cessation. The pooled rate of adverse events associated with e-cigarettes ranged from 49.1% to 51.6% based on 11 studies including 16,406 participants. The most prevalent adverse events were mouth or throat irritation, anxiety, depressed mood, nausea, and insomnia. No significant differences in overall CO<sub>2</sub> exhalation (eCO) levels were observed after e cigarette use according to the data from 5 studies.  <b>Conclusion:</b> Our findings suggest that e-cigarettes are moderately effective with regard to smoking reduction and smoking cessation. eCO levels are unreliable for evaluating the efficacy of e-cigarettes. E cigarette related adverse events frequently occur, especially due to high-dose nicotine-containing cartridges.</p>	<p><b>or throat irritation, anxiety, depressed mood, nausea, and insomnia</b> (n=11 studies; 16,406 participants)                      - Among them, approximately 12.9% claimed to be anxious or nervous, 6.18% complained of having a depressed or sad mood, and 4.57% felt hungry or were concerned about weight gain.                      - participants who smoked ecigarettes more than 3cartridges/day had a high incidence of adverse events (pooled rate, 63.8%).                      - Smokers who used ecigarettes less than 12 months also had a high rate of adverse events (pooled rate, 55.0%).</p>
<p>Oncken CA, Litt MD, McLaughlin LD, et al. Nicotine concentrations with electronic cigarette use: Effects of sex and flavor. <i>Nicotine &amp; tobacco research official journal of the Society for Research on Nicotine and Tobacco</i> 2015; 17(4):473–8. DOI: 10.1093/ntr/ntu232. <a href="http://www.ncbi.nlm.nih.gov/pub-med/25762758">http://www.ncbi.nlm.nih.gov/pub-med/25762758</a>.</p>	<p>randomized, crossover</p>	<p><b>Introduction:</b> This study examined overall changes in nicotine concentrations when using a popular e-cigarette and 18 mg/mL nicotine e-Juice, and it further explored effects of sex and flavorings on these concentrations.  <b>Methods:</b> We recruited nontreatment-seeking smokers who were willing to try e cigarettes for 2 weeks and abstain from cigarette smoking. Subjects were randomized to either menthol tobacco or non-menthol tobacco-flavored e-cigarette use for 7–10 days, and the next week they were crossed over to the other condition. On the last day of e-cigarette use of each flavor, subjects completed a laboratory session in which they used the e-cigarette for 5 min ad libitum. Nicotine concentrations were obtained 5 min before and 5, 10, 15, 20, and 30 min after the onset of e cigarette use.  <b>Results:</b> Twenty subjects completed at least 1 monitoring session. Nicotine concentrations significantly increased from baseline to 5 min by 4 ng/mL at the first laboratory session (p &lt; .01) and by 5.1 ng/mL at the second laboratory session (p &lt; .01). Combining sessions, there were no main effects of sex or preferred flavor (based on smoking history) on changes in nicotine concentrations. After adding preferred flavor, sex, and visit order to the model, there was a significant preferred flavor by sex interaction (p &lt; .01), such that women who received nonpreferred flavors had lower nicotine concentrations and rated their e-cigarette as less likeable (p &lt; .01).  <b>Conclusion:</b> We found nicotine concentrations significantly increase after e-</p>	<p>• 27 participants (n=18 completed study):                      - Moderate adverse events included <b>cough in 19% (5/27) subjects, mouth/throat irritation in 15% (4/27) subjects, nausea in 4% (1/27) subject, headache in 4% (1/27) subjects, and “other” in 4% (1/27) subjects (irritability, stomach cramps)</b>.                      - <b>One severe adverse event (itchy throat and cough)</b> occurred in one subject. This subject had a history of childhood asthma, but no current history of asthma. The subject was discontinued from e-cigarettes use and symptoms resolved.                      - No serious adverse events occurred in the study.</p>

Autor/ Titel	Studientyp	Abstract	Schadenspotential
<p>Ramôa CP, Hiler MM, Spindle TR, et al. Electronic cigarette nicotine delivery can exceed that of combustible cigarettes: A preliminary report. <i>Tob Control</i> 2016; 25(e1):e6-9. DOI: 10.1136/tobaccocontrol-2015-052447. <a href="http://www.ncbi.nlm.nih.gov/pub-med/26324250">http://www.ncbi.nlm.nih.gov/pub-med/26324250</a>.</p>	<p>controlled trial</p>	<p>cigarette use for 5 min, and flavor may impact nicotine concentrations with e-cigarette use in women.</p> <p><b>Introduction</b>—Electronic cigarettes (ECIGs) aerosolize a liquid that usually contains propylene glycol and/or vegetable glycerin, flavorants, and the dependence producing drug nicotine in various concentrations. This laboratory study examined the relationship between liquid nicotine concentration on plasma nicotine concentration and puffing behavior in experienced ECIG users.</p> <p><b>Methods</b>—Sixteen ECIG-experienced participants used a 3.3-Volt ECIG battery attached to a 1.5-Ohm dual-coil “cartomizer” loaded with 1 ml of a flavored propylene glycol/vegetable glycerin liquid to complete four sessions, at least 2 days apart, that differed by nicotine concentration (0, 8, 18, or 36 mg/ml). In each session, participants completed two 10-puff ECIG use bouts (30-sec puff interval) separated by 60 minutes. Venous blood was sampled to determine plasma nicotine concentration. Puff duration, volume, and average flow rate were measured.</p> <p><b>Results</b>—Immediately after bout 1, mean plasma nicotine concentration was 5.5 ng/ml (SD=7.7) for 0 mg/ml liquid, with significantly (<math>p&lt;0.05</math>) higher mean concentrations observed for the 8 (mean=17.8 ng/ml, SD=14.6), 18 (mean=25.9 ng/ml, SD=17.5), and 36 mg/ml (mean=30.2 ng/ml; SD=20.0) concentrations; a similar pattern was observed for bout 2. For bout 1, at 36 mg/ml, the mean post- minus pre-bout difference was 24.1 ng/ml (SD=18.3). Puff topography data were consistent with previous results and revealed few reliable differences across conditions.</p> <p><b>Discussion</b>—This study demonstrates a relationship between ECIG liquid nicotine concentration and user plasma nicotine concentration in experienced ECIG users. Nicotine delivery from some ECIGs may exceed that of a combustible cigarette. The rationale for this higher level of nicotine delivery is uncertain.</p>	<p>n=16 participants</p> <p>[...]Thus, some ECIGs are so efficient at delivering nicotine that they appear capable of exceeding the nicotine delivery profile of a combustible tobacco cigarette. We speculate that this <b>excessive nicotine delivery may be harmful if it leads to a greater level of nicotine dependence</b>, which could make ECIG cessation difficult if users eventually choose to try to quit their ECIG use.</p>
<p>Riley HE, Berry-Bibee E, England LJ, et al. Hormonal contraception among electronic cigarette users and cardiovascular risk: A systematic review. <i>Contraception</i> 2016; 93(3):190–208. DOI: 10.1016/j.contraception.2015.11.003.</p>	<p>Systematic Review</p>	<p><b>Background:</b> Women who use combined hormonal contraceptives and cigarettes have an increased risk for cardiovascular (CV) events. We reviewed the literature to determine whether women who use hormonal contraceptives (HC) and electronic cigarettes (e-cigarettes) also have an increased risk.</p> <p><b>Study Design:</b> Systematic review.</p> <p><b>Methods:</b> We searched for articles reporting myocardial infarction (MI), stroke, venous thromboembolism, peripheral arterial disease or changes to CV markers in women using e-cigarettes and HC. We also searched for indirect evidence, such as CV outcomes among e-cigarette users in the general population and among HC users exposed to nicotine, propylene glycol or glycerol.</p> <p><b>Results:</b> No articles reported on outcomes among e-cigarette users using HC.</p>	<p>We identified no evidence on CV outcomes among e-cigarette users using HC. Limited data reporting mostly acute outcomes suggested that CV events are rare among e-cigarette users in the general population and that e-cigarettes may affect heart rate and blood pressure less than conventional cigarettes.</p>

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<p><a href="http://www.ncbi.nlm.nih.gov/pub-med/26546021">http://www.ncbi.nlm.nih.gov/pub-med/26546021</a>.</p>		<p>Among the general population, 13 articles reported on heart rate or blood pressure after e-cigarette use. These markers generally remained normal, even when significant changes were observed. In three studies, changes were less pronounced after e-cigarette use than cigarette use. One MI was reported among 1012 people exposed to ecigarettes in these studies. One article on nicotine and HC exposure found both exposures to be significantly associated with acute changes to heart rate, though mean heart rate remained normal. No articles on propylene glycol or glycerol and HC exposure were identified.  <b>Conclusion:</b> We identified no evidence on CV outcomes among e-cigarette users using HC. Limited data reporting mostly acute outcomes suggested that CV events are rare among e-cigarette users in the general population and that e-cigarettes may affect heart rate and blood pressure less than conventional cigarettes. There is a need for research assessing joint HC and e-cigarette exposure on clinical CV outcomes.</p>	
<p>Skotsimara G, Antonopoulos AS, Oikonomou E, et al. Cardiovascular effects of electronic cigarettes: A systematic review and meta-analysis. Eur J Prev Cardiol 2019; 26(11):1219–28. DOI: 10.1177/2047487319832975.  <a href="http://www.ncbi.nlm.nih.gov/pub-med/30823865">http://www.ncbi.nlm.nih.gov/pub-med/30823865</a>.</p>	<p>Systematic Review</p>	<p><b>Aims:</b> The electronic cigarette is marketed as a safe alternative to tobacco smoking, but electronic cigarette cardiovascular effects remain largely unknown. We systematically reviewed and meta-analysed published literature to investigate the cardiovascular effects and associated risk from electronic cigarette use.  <b>Methods and results:</b> We searched PubMed from January 2000 to November 2017 for published studies assessing the cardiovascular effects of the electronic cigarette. Evidence suggests that the electronic cigarette negatively affects endothelial function, arterial stiffness and the long-term risk for coronary events, but these findings are from single study reports and have not been confirmed in additional studies. Conflicting evidence exists on the effects of the electronic cigarette on heart rate and blood pressure, which is mainly based on non-randomized clinical studies of moderate quality. The meta-analysis of 14 studies (N=441 participants) suggested that despite the negative acute effects of the electronic cigarette on heart rate (pooled mean difference (MD)=2.27, 95% confidence interval (CI): 1.64 to 2.89, p&lt;0.001), diastolic (pooled MD=2.01 mmHg, 95% CI: 0.62 to 3.39, p=0.004) and systolic blood pressure (pooled MD=2.02 mmHg, 95% CI: 0.07 to 3.97, p=0.042), benefits may be observed in terms of blood pressure regulation when switching from tobacco smoking to chronic electronic cigarette use (systolic blood pressure pooled MD= 7.00, 95% CI: 9.63 to 4.37, p&lt;0.001; diastolic blood pressure pooled MD= 3.65, 95% CI: 5.71 to 1.59, p=0.001).  <b>Conclusions:</b> The existing evidence on the cardiovascular effects of the electronic cigarette is concerning, with several unexplored issues. Unless supported by stronger evidence, the electronic cigarette should not be labelled as</p>	<ul style="list-style-type: none"> <li>• Evidence suggests that the <b>electronic cigarette negatively affects endothelial function, arterial stiffness and the long-term risk for coronary events</b>, but these findings are from single study reports and have not been confirmed in additional studies.</li> <li>• Conflicting evidence exists on the effects of the electronic cigarette on heart rate and blood pressure, which is mainly based on non-randomized clinical studies of moderate quality.</li> <li>• meta-analysis of 14 studies (N=441 participants) suggested that despite the <b>negative acute effects of the electronic cigarette on</b> <ul style="list-style-type: none"> <li>- <b>heart rate</b> (pooled mean difference (MD)=2.27, 95% confidence interval (CI): 1.64 to 2.89, p&lt;0.001),</li> <li>- <b>diastolic blood pressure</b> (pooled MD=2.01 mmHg, 95% CI: 0.62 to 3.39, p=0.004) and</li> <li>- <b>systolic blood pressure</b> (pooled MD=2.02 mmHg, 95% CI: 0.07 to 3.97, p=0.042),</li> <li>- benefits may be observed in terms of blood pressure regulation when switching from tobacco smoking to chronic electronic cigarette use (systolic blood pressure pooled MD= 7.00, 95% CI: 9.63 to 4.37, p&lt;0.001; diastolic blood pressure pooled MD= 3.65, 95% CI: 5.71 to 1.59, p=0.001).</li> </ul> </li> </ul>

Autor/ Titel	Studientyp	Abstract	Schadenspotential
<p>Tseng T-Y, Ostroff JS, Campo A, et al. A Randomized Trial Comparing the Effect of Nicotine Versus Placebo Electronic Cigarettes on Smoking Reduction Among Young Adult Smokers. <i>Nicotine &amp; tobacco research official journal of the Society for Research on Nicotine and Tobacco</i> 2016; 18(10):1937–43. DOI: 10.1093/ntr/ntw017. <a href="http://www.ncbi.nlm.nih.gov/pub-med/26783292">http://www.ncbi.nlm.nih.gov/pub-med/26783292</a>.</p>	<p>two-arm; double-blind RCT</p>	<p>a cardiovascular safe product. Future studies should delineate whether electronic cigarette use is less hazardous to cardiovascular health than conventional cigarette smoking.</p> <p><b>Introduction:</b> Electronic cigarette (EC) use is growing dramatically with use highest among young adults and current smokers. One of the most common reasons for using ECs is interest in quitting or reducing cigarettes per day (CPD); however there are few randomized controlled trials (RCT) on the effect of ECs on smoking abstinence and reduction.</p> <p><b>Methods:</b> We conducted a two-arm; double-blind RCT. Subjects were randomized to receive 3-weeks of either disposable 4.5% nicotine EC (intervention) or placebo EC. The primary outcome was self-reported reduction of at least 50% in the number of CPDs smoked at week 3 (end of treatment) compared to baseline. Study subjects (n = 99) were young adult (21–35), current smokers (smoked ≥ 10 CPDs) living in NYC.</p> <p><b>Results:</b> Compared with baseline, a significant reduction in CPDs was observed at both study time periods (1 and 3 weeks) for intervention (P &lt; .001) and placebo (P &lt; .001) groups. Between-group analyses showed significantly fewer CPDs in the intervention group compared to the placebo group at week 3 (P = .03), but not at any other follow-up periods. The logistic regression analysis showed that using a greater number of ECs, treatment condition and higher baseline readiness to quit were significantly associated with achieving at least 50% reduction in CPDs at the end of treatment.</p> <p><b>Conclusion:</b> A diverse young adult sample of current everyday smokers, who were not ready to quit, was able to reduce smoking with the help of ECs. Further study is needed to establish the role of both placebo and nicotine containing ECs in increasing both reduction and subsequent cessation.</p> <p><b>Implications:</b> Despite the critical need for well-designed clinical trials on the effect of ECs on cessation and cigarette reduction, the majority of studies have been observational or noncomparative intervention designs. Only three RCTs studying ECs as a cessation or reduction intervention have been published, and none were conducted in the United States. The current study adds knowledge to current literature on the feasibility of using ECs to aid smoking reduction among young smokers in US urban populations.</p>	<ul style="list-style-type: none"> <li>• There was no difference in reported side effects between groups (34.1% for intervention and 17.5% for placebo group at week 1, P = .09; 22.5% for intervention and 10.3% for placebo group at week 3, P = .14; chi-square test) or between study time points in each group (P = .39 for intervention and P = .63 for placebo group; McNemar test).</li> <li>• Common side effects included <b>mouth or throat irritation, cough, insomnia or difficulty sleeping, abnormal dreams, headache and fatigue.</b></li> </ul>

### Anhang 6.5 Selektiv eingebrachte Literatur

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Osei AD, Mirbolouk M, Orimoloye OA, et al.</p>	<p>• <b>Aim:</b> this study examines the association between e-cigarette use</p>	<p>• <b>Baseline-Patientencharakteristika:</b> n= 705159 participants (with complete information on all key variables)</p>	<p>Strobe (<a href="https://www.strobe-statement.org/fileadmin/Strobe/up-">https://www.strobe-statement.org/fileadmin/Strobe/up-</a></p>	<p>Selektiv eingebrachte Literatur</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Association Between E-Cigarette Use and Chronic Obstructive Pulmonary Disease by Smoking Status: Behavioral Risk Factor Surveillance System 2016 and 2017. Am J Prev Med 2020; 58(3):336–42. DOI: 10.1016/j.amepre.2019.10.014.</p> <p><a href="http://www.ncbi.nlm.nih.gov/pub-med/31902685">http://www.ncbi.nlm.nih.gov/pub-med/31902685</a>.</p>	<p>and self-reported chronic bronchitis, emphysema, or COPD across differing combustible cigarette smoking use patterns in the Behavioral Risk Factor Surveillance System (BRFSS) (=public data set)</p> <ul style="list-style-type: none"> <li>• <b>Studiendesign:</b> representative, annual, cross-sectional, telephone-based survey</li> <li>• <b>Population:</b> U.S. adult participants aged ≥18 years</li> <li>• <b>Intervention:</b> Fragestellungen</li> <li>• <b>Studienzeitraum:</b> pooled 2016 and 2017 data from the Behavioral Risk Factor Surveillance System; All the analyses were conducted in 2019.</li> <li>• USA</li> </ul>	<p>- 25175 (3,6%) were current e-cigarette users,                      - 64792 (9,2%) current, combustible cigarette smokers,                      - 207905 (29,5%) former combustible cigarette smokers,                      - 432462 (61,3%) never combustible cigarette smokers, and                      - 14036 (2,0%) dual users of e-cigarettes and combustible cigarettes.</p> <p>- median age group of current e-cigarette users was 30–34 years</p> <ul style="list-style-type: none"> <li>• <b>Ergebnisse:</b>                              Among never combustible cigarette smokers, current e-cigarette use was associated with 75% higher odds of chronic bronchitis, emphysema, or chronic obstructive pulmonary disease compared with never e-cigarette users (OR=1.75, 95% CI=1.25, 2.45), with daily users of e-cigarettes having the highest odds (OR=2.64, 95% CI=1.43, 4.89).</li> </ul> <p>Among former combustible cigarette smokers, current e-cigarette users had higher odds of COPD compared with never e-cigarette users (OR=2.13, 95% CI=1.82, 2.50).</p> <p>In the additional analysis with never combustible cigarette smokers who never used e-cigarette as the sole reference group, dual users of combustible cigarette and e-cigarettes had the highest odds of the outcome of interest (OR=6.89, 95% CI=6.29, 7.55).</p> <ul style="list-style-type: none"> <li>• <b>authors conclusion:</b> The results suggest possible e-cigarette-related pulmonary toxicity across all the categories of combustible cigarette smoking status, including those who had never smoked combustible cigarettes.</li> </ul>	<p><a href="#">loads/checklists/STROBE_checklist_v4_cross-sectional.pdf</a></p> <ol style="list-style-type: none"> <li>Title and abstract: y</li> <li>Background/ rationale: y</li> <li>Objectives: y</li> <li>Study design: y</li> <li>Setting: y</li> <li>Participants: y</li> <li>Variables: py</li> <li>Data sources/Measurement: y</li> <li>Bias: n</li> <li>Study size: y</li> <li>Quantitative variables: y</li> <li>Statistical methods: a) y, b) na, c) na, d) na, e) na</li> <li>Participants: y</li> <li>Descriptive data: na</li> <li>Outcome data: y</li> <li>Main results: py</li> <li>Other analyses: na</li> <li>Key results: y</li> <li>Limitations: y</li> <li>Interpretation: y</li> <li>Generalisability: n</li> <li>Funding: y</li> </ol>	<p>Zusammenhang zwischen E-Zigaretten und Vorkommen von COPD (Odds)</p> <p><b>Limitationen:</b> [...] In addition, the authors cannot exclude the possibility that reverse causation may have contributed to the finding of the highest odds of COPD among dual users when compared with never combustible cigarette smokers who never use e-cigarettes. For example, current and former combustible cigarette smokers with the outcome of interest are potentially more likely to report using ecigarette as a smoking-cessation strategy. [...]</p> <p><b>Methodische Qualität:</b> angelehnt an STROBE (Reporting; nicht für qualitative Einschätzung)</p>
<p>Bhatta DN, Glantz SA. Association of E-Cigarette Use With Respiratory Disease Among Adults: A Longitudinal Analysis. Am J Prev Med 2020; 58(2):182–90. DOI: 10.1016/j.amepre.2019.07.028.</p>	<ul style="list-style-type: none"> <li>• <b>Aim:</b> This study determines the longitudinal associations between e-cigarette use and respiratory disease controlling for combustible tobacco use.</li> <li>• <b>Studiendesign:</b> nationally representative, population-based, longitudinal study</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b>                              - adult (aged ≥18 years)                              Wave 1: n = 32320                              - Respiratory disease: Yes 15.1%, No 84.9%                              - E-cigarette user: Never 82.3%, Former 12.2%, Current 5.5%                              - Combustible tobacco smoker: Never 28.6%, Former 45.4%, Current 26.0%                              - Cigarette smoker: Never 33.2%, Former 45.4%, Current 21.4%</li> <li>• <b>Ergebnisse:</b></li> </ul>	<p>Strobe (<a href="https://www.strobe-statement.org/fileadmin/Strobe/uploads/checklists/STROBE_checklist_v4_cross-sectional.pdf">https://www.strobe-statement.org/fileadmin/Strobe/uploads/checklists/STROBE_checklist_v4_cross-sectional.pdf</a>)</p> <ol style="list-style-type: none"> <li>Title and abstract: y</li> <li>Background/ rationale: y</li> <li>Objectives: y</li> <li>Study design: y</li> <li>Setting: y</li> <li>Participants: y</li> </ol>	<p>Selektiv eingebrachte Literatur</p> <p>Zusammenhang zwischen E-Zigaretten und Entwicklung einer chronischen Lungenerkrankung</p> <p><b>Methodische Qualität:</b> L. Tooth Quality of reporting of observational longitudinal research_2005</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p><a href="http://www.ncbi.nlm.nih.gov/pub-med/31859175">http://www.ncbi.nlm.nih.gov/pub-med/31859175</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Population:</b> adult Population Assessment of Tobacco and Health Waves 1, 2, and 3.</li> <li>• <b>Intervention:</b> Fragestellungen - Wave I: Has a doctor or other health professional ever told you that you had any of the following lung or respiratory conditions? (yes or no): COPD, chronic bronchitis, emphysema, and asthma. - Wave II + III: In the past 12 months, has a doctor, nurse, or other health professional told you that you had any of the following lung or respiratory conditions? (yes or no): COPD, chronic bronchitis, emphysema, and asthma. &gt;&gt; + use of e-cigarettes and/or conventional cigarettes asked</li> <li>• <b>Studienzeitraum:</b> Data were collected in 2013–2016 and analyzed in 2018–2019. (Waves 1 (September 2013 to December 2014), 2 (October 2014 to October 2015), and 3 (October 2015 to October 2016)) • San Francisco, California</li> </ul>	<p><u>Wave 1:</u> The risk of having had respiratory disease was significantly associated with former e-cigarette use (AOR=1.34, 95% CI=1.23, 1.46) and current e-cigarette use (AOR=1.32, 95% CI=1.17, 1.49). The risk of having had respiratory disease was also significantly associated with former combustible tobacco smoking (AOR=1.29, 95% CI=1.14, 1.47) and current combustible tobacco smoking (AOR=1.61, 95% CI=1.42, 1.82).</p> <p>Among people who did not report respiratory disease at Wave 1, the longitudinal analysis revealed statistically significant associations between former e-cigarette use (AOR=1.31, 95% CI=1.07, 1.60) and current e-cigarette use (AOR=1.29, 95% CI=1.03, 1.61) at Wave 1 and having incident respiratory disease at Waves 2 or 3 adjusting for combustible tobacco smoking, demographic, and clinical variables. Current combustible tobacco smoking (AOR=2.56, 95% CI=1.92, 3.41) was also significantly associated with having respiratory disease at Waves 2 or 3.</p> <p>The total odds of developing respiratory disease for a current dual user is (odds of respiratory disease among current combustible tobacco smoker) x (odds of respiratory disease among current e-cigarette user) = 2.56 x 1.29 = 3.30 compared with a never smoker who never used e-cigarettes</p> <ul style="list-style-type: none"> <li>• <b>authors conclusion:</b> Use of e-cigarettes is an independent risk factor for respiratory disease in addition to combustible tobacco smoking. Dual use, the most common use pattern, is riskier than using either product alone.</li> </ul>	<p>7. Variables: y 8. Data sources/Measurement: y 9. Bias: n 10. Study size: y 11. Quantitative variables: y 12. Statistical methods: a) y, b) na, c) na, d) na, e) na 13. Participants: y 14. Descriptive data: na 15. Outcome data: y 16. Main results: py (adjusted OR used) 17. Other analyses: y 18. Key results: y 19. Limitations: y 20. Interpretation: y 21. Generalisability: y 22. Funding: y</p>	<p>(<a href="https://pub-med.ncbi.nlm.nih.gov/15671260/">https://pub-med.ncbi.nlm.nih.gov/15671260/</a>) nicht validiert &gt;&gt; deswegen angelehnt an STROBE (Reporting; nicht für qualitative Einschätzung)</p>

## Anhang 7 Evidenztabellen Nicht-medikamentöse Therapie und Rehabilitation

### Anhang 7.1 Cochrane Reviews Nicht-medikamentöse Therapie

ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
27016	Zainuldin R. Optimal intensity and type of leg exercise training for people with	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=3 bzw. 8 eingeschlossene RCTs für Metaanalyse ( n=231 bzw. 367 eingeschlossene Patienten)</li> <li>• <b>Suchzeitraum:</b> current as of 6/2011</li> </ul>	<p><b>Interval training compared with continuous training</b> <u>Functional exercise capacity:</u> Six-minute walk distance (m), n= 287 (6 studies); <b>GRADE: Low</b> - Continuous: The mean change in 6MWD ranged across continuous training</p>	<p>AMSTAR-Score: 9/11 y-y-y-y-y-y-y-y-n-n</p>

ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<p>chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2011;(11).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008008.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008008.pub2/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- participants were diagnosed with COPD defined by best post-bronchodilator forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) ratio &lt; 0.7</li> <li>- Trials of lower limb exercise training of 12 sessions or more</li> </ul> </li> <li>• <b>Ausschlusskriterien:</b> studies that compared exercise training with no exercise training</li> <li>• <b>Interventionen:</b> <ol style="list-style-type: none"> <li>1. higher training intensity to lower training intensity (n=3, 231 subjects)</li> <li>2. continuous training to interval training (n=8, 367 subjects)</li> </ol> </li> <li>• <b>Primäre Endpunkte:</b> <ol style="list-style-type: none"> <li>1. Peak exercise</li> <li>2. Isowork or isotime</li> <li>3. Endurance time of constant work rate exercise test</li> <li>4. Functional exercise capacity</li> </ol> </li> <li>• <b>Sekundäre Endpunkte:</b> <ol style="list-style-type: none"> <li>1. Symptom scores: dyspnoea or leg fatigue at end of peak exercise, and at isowork or isotime</li> <li>2. Health-related quality of life (HRQoL): (SGRQ) or (CRQ) or SF-12 or SF-36</li> <li>3. Muscle strength</li> </ol> </li> </ul>	<p>groups from 32 to 46 m</p> <ul style="list-style-type: none"> <li>- Interval: The mean change in 6MWD in the interval training groups was 4.4m longer (10.1 shorter to 18.9m longer)</li> <li>- 6MWD: MD -3,10m; 95% CI -17,88 – 11,69; I<sup>2</sup> =0.0%</li> </ul> <p>Health-related Quality of Life: Dyspnoea domain of the CRQ, n=212 (4 studies), GRADE: Moderate</p> <ul style="list-style-type: none"> <li>- Continuous: The mean change in the CRQ dyspnoea score ranged across continuous training groups from 3.7 to 8.4 points</li> <li>- Interval: The mean change in the CRQ dyspnoea score for the interval training groups was 1. 26 lower (0.01 lower to 2.54 points higher)</li> <li>- Total CRQ: MD 2,51; 95% CI -1,32 – 6,34; I<sup>2</sup> =0.0%</li> </ul> <p><u>Dyspnoea:</u> The SMD for peak dyspnoea was in favour of the interval group, but the effect size was small and not significant (SMD 0.09; 95% CI -0.18 to 0.35)</p> <p><b>Higher intensity versus lower intensity</b></p> <p><u>Dyspnoea:</u> The treatment effect for peak dyspnoea was -1.40 points in favour of the higher-intensity group and was significant (95% CI -2.30 to -0.50)</p> <p><u>HrQoL:</u> Total CRQ score (MD 2.51; 95% CI -1.32 to 6.34), Dyspnoea domain score (MD 1.26; 95%CI -0.01 to 2.54), Fatigue domain score(MD-0.27; 95%CI -1.72 to 1.18), Emotional domain score (MD 0.59; 95% CI -1.30 to 2.47) and Mastery domain score (MD -0.02; 95% CI -1.65 to 1.61) were not significantly different between continuous and interval training.</p>	
27035	<p>McKeough ZJ. Upper limb exercise training for COPD. Cochrane Database of Systematic Reviews 2016;(11)</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858">http://onlinelibrary.wiley.com/doi/10.1002/14651858</a></p>	<p>.</p> <ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=12 eingeschlossene RCTs für Metaanalyse ( n= eingeschlossene Patienten)</li> <li>• <b>Suchzeitraum:</b> inception to 9/2016</li> <li>• <b>Population:</b> Patient*innen mit stabiler COPD</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- any age or disease severity. Participants' COPD was stable (that is optimal and stable respiratory medications with no exacerbation or hospital admission within the previous month), although oxygen supplementation during training could have been used.</li> <li>- included inpatient, outpatient, and home-based training</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- mean age: ranging from 57 to 72 years</li> <li>- mean FEV1: 27% to 60%predicted, indicating moderate to very severe disease</li> </ul> </li> <li>• <b>Upper limb training vs No upper limb training</b></li> <li>• <u>Symptoms of dyspnoea</u> assessed with: Chronic Respiratory Disease Questionnaire Dyspnoea Score., n=129 (4 RCTs), GRADE: Moderate</li> <li>• No upper limb training: The mean symptoms of dyspnoea was 4.2 points.</li> <li>• Upper limb training: The mean symptoms of dyspnoea in the intervention group was <b>0.37 points higher</b> (0.02 to 0. 72 points)</li> </ul>	<p>AMSTAR-Score: 11/11</p> <p>y-y-y-y-y-y-y-y-y-y</p>



ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	CD011434.pub2/abstract	<p>programmes.</p> <ul style="list-style-type: none"> <li>• <b>Interventionen:</b> (at least four weeks' duration)                     <ol style="list-style-type: none"> <li>1. upper limb training only (endurance or resistance training, or both) versus no training or sham intervention;</li> <li>2. combined upper limb training and lower limb training versus lower limb training alone; and</li> <li>3. upper limb training versus another type of upper limb training.</li> </ol> </li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Dyspnoea</li> <li>- Health-related quality of life</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ol style="list-style-type: none"> <li>1. Peak upper limb exercise capacity</li> <li>2. Endurance upper limb exercise capacity</li> <li>3. Upper limb strength</li> <li>4. Respiratory muscle strength</li> <li>5. Physical activity level</li> <li>6. Activities of Daily Living (ADL)</li> <li>7. Psychological status</li> <li>8. Healthcare utilisation recorded as hospitalisation or length of stay.</li> </ol> </li> </ul>	<p>(Comment: Higher value post-intervention is favourable indicating improvement in dyspnoea. The MID for dyspnoea component of the chronic respiratory disease questionnaire is 0.5)</p> <ul style="list-style-type: none"> <li>- CRQ dyspnoea: MD 0.37; 95% CI 0,02 – 0,72</li> </ul> <p><u>Health-Related Quality of Life</u> assessed with: Chronic Respiratory Disease Questionnaire Total Score, n=126 (4 RCTs), <b>GRADE: Moderate</b></p> <p>No upper limb training: The mean health-related quality of life was 5.3 points. Upper limb training: The mean health-related quality of life in the intervention group was <b>0.05 points higher</b> (0.3 points lower to 0.36 points higher)</p> <ul style="list-style-type: none"> <li>- CRQ total: SMD 0,05; 95% CI –0,31 – 0,40)</li> </ul> <p><u>Activities of daily living</u></p> <p>n=1 study showed no between- group differences on the duration of a blackboard/grocery shelving/dishwashing task (SMD 0.67, 95% CI –0.12 to 1.47, 28 participants)</p> <p>&gt;&gt; when arm training was compared to no arm training or a sham intervention in people with COPD, there was a small improvement in breathlessness. However, this improvement was not evident when the studies of combined arm and leg training were compared to leg training alone. No studies have examined whether breathlessness improves more with different types of arm training. Arm training had no effect on quality of life in any of the three comparisons. When endurance arm training was specifically examined, there was an improvement seen in the capacity of the arms to move and lift light weights compared to no training. These effects were not seen with arm strength training.</p>	
27025	<p>McNamara RJ. Water-based exercise training for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2013;(12).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858">http://onlinelibrary.wiley.com/doi/10.1002/14651858</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=5 eingeschlossene randomised or quasi-randomised controlled trials für Metaanalyse (n=176 eingeschlossene Patienten)</li> <li>• <b>Suchzeitraum:</b> inception to 8/2013</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b> The COPD should be stable (i.e. optimal and stable respiratory medications with no exacerbation or hospital admission within the previous month), and supplemental oxygen may be used. Swimming interventions were excluded.</li> <li>• <b>Interventionen:</b> water-based exercise training, supervised or unsupervised</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- mean age: ranged from 57 to 73 years</li> <li>- exercise training programmes lasted from four to 12 weeks</li> </ul> </li> </ul> <p><b>Water-based exercise training compared with no exercise training</b></p> <p><u>Exercise capacity - functional.</u> Six-minute walk test, n=99 (3 studies), <b>GRADE: Moderate</b></p> <p>No exercise training: Mean change in six-minute walk distance ranged across control groups from -39 metres to -16 metres</p> <p>Water-based exercise training: Mean change in six-minute walk distance in the intervention groups was <b>62 metres higher</b> (44 metres to 80 metres higher)</p> <ul style="list-style-type: none"> <li>-6MWD ( MD 62,1m; 95% CI 44,3 – 79,9m; I<sup>2</sup> =27%</li> </ul>	<p>AMSTAR-Score: 10/11</p> <p>y-y-y-y-y-y-y-n-y-y</p>

ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	CD008290.pub2/abstract	<p>vs. no exercise training</p> <ul style="list-style-type: none"> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Exercise capacity (functional or maximal)</li> <li>- Quality of life</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Pulmonary function</li> <li>- Respiratory muscle strength</li> <li>- Upper and lower limb strength</li> <li>- Oxygen saturation</li> <li>- Symptoms</li> <li>- Level of activity</li> <li>- Psychological status</li> <li>- Self management/self efficacy</li> <li>- Healthcare utilisation</li> <li>- Cost-effectiveness</li> <li>- Adverse events</li> <li>- Withdrawal</li> <li>- Body composition</li> <li>- Attendance</li> <li>- Exercise training mode preference</li> <li>- Arterial blood gases</li> </ul> </li> </ul>	<p><u>Quality of life</u> St George's Respiratory Questionnaire (total score) (Lower value post intervention is favourable, indicating improvement in QoL), n=19 (1 study), <b>GRADE: Low</b></p> <p>No exercise training: Mean change in St George's Respiratory Questionnaire total score in the control group was +6 points</p> <p>Water-based exercise training: Mean change in St George's Respiratory Questionnaire total score in the intervention group was <b>10 points lower</b> (1 point to 19 points lower)</p> <p>- SMD -0,97; 95% CI -0,37 – (-) 1,57; I<sup>2</sup> =0.0%</p> <p>&gt;&gt; Two studies reported on adverse events; one minor adverse event was documented (from 20 people participating in water-based exercise training).</p>	
27085	<p>Hill K. Neuromuscular electrostimulation for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2013;(11).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010821/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010821/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=16 eingeschlossene RCTs für Metaanalyse ( n=267 eingeschlossene Patienten)</li> <li>• <b>Suchzeitraum:</b> inception - 03/2018</li> <li>• <b>Population:</b> Erwachsene mit COPD</li> <li>• <b>Einschlusskriterien:</b> Adults with a diagnosis of COPD regardless of their clinical stability</li> <li>• <b>Ausschluss:</b> randomised crossover trials</li> <li>• <b>Interventionen:</b> <ol style="list-style-type: none"> <li>1. Neuromuscular electrostimulation (NMES) vs. Usual care (n=7) or</li> <li>2. Neuromuscular electrostimulation + conventional exercise training vs. conventional exercise training alone (n=9)</li> </ol> </li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Peripheral muscle force</li> <li>- Peripheral muscle endurance/fatigability</li> <li>- Thigh muscle size</li> <li>- Serious adverse events (e.g. mortality; for these muscle-</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- mean age: range 56 to 76 years</li> <li>- men=179 (67%)</li> <li>- mean FEV1: range 15% to 50% of the predicted value</li> </ul> </li> <li>• <b>NMES vs. Usual care</b></li> <li>• <u>Exercise capacity</u> assessed with 6MWD (m): n=72 (2 RCTs); <b>GRADE: Low</b></li> <li>Usual care: The mean change in 6MWD in the control group ranged from -5.70 m to 0.80 m.</li> <li>NMES: <b>MD 39.26 m more</b> (95% CI 16.31 to 62.22)</li> <li>• <u>Functional performance:</u></li> <li>None of the studies reported on functional performance.</li> <li>• <u>Symptoms of dyspnoea</u> reported on completion of an exercise test assessed with Borg score: n=32 (3 RCTs), <b>GRADE: Very low</b></li> <li>Usual care: The mean change in dyspnoea reported on completion of an exercise test ranged from - 0.50 to 0.40.</li> <li>NMES: <b>MD 1.03 less dyspnoea</b> (95% CI 2.13 less to 0.06 more)</li> </ul>	<p>AMSTAR-Score: 11/11</p> <p>y-y-y-y-y-y-y-y-y-y</p>

ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
		specific outcomes) • <b>Sekundäre Endpunkte:</b> - Exercise capacity - Functional performance - Symptoms of dyspnoea and fatigue - Health-related quality of life - Minor adverse events (for secondary outcomes)	<p><u>Health- related quality of life</u> assessed with: SGRQ; n=72 (2 RCTs), <b>GRADE: Very low</b>                      Usual care: The mean change in HRQoL ranged from -2. 00 to 0.07                      NMES: <b>MD 4.12 better</b> (95% CI 12.60 better to 4.35 worse)</p> <p><u>Minor adverse events assessed:</u> related to intervention only (e.g. redness), n=139 (5 RCTs), <b>GRADE: Low</b>                      Usual care: 5970 per 100,000                      NMES: 0 per 100,000 (95% CI -418 to 418)</p> <p>- quadriceps endurance: SMD 1,36; 95% CI 0,59 – 2,12; Datenqualität niedrig                      - peripheral muscle force SMD 0,34; 95% CI 0,02 - 0.65; Datenqualität niedrig</p> <p><b>NMES + training vs. training alone</b>  <u>Exercise capacity</u> assessed with 6MWD (m), n=138 (6 RCTs), <b>GRADE: Very low</b>                      Exercise: The mean change in 6MWD ranged from 10. 30 m to 94.00 m                      NMES + exercise: <b>MD 25.87 m more</b> (1.06 more to 50.69 more)</p> <p><u>Functional performance</u> assessed with: time (days) until first sit out of bed, n=44 (2 RCTs), <b>GRADE: Very low</b>                      Exercise: The mean time until first sit out of bed ranged from 12.60 to 14.33 days                      NMES + exercise: <b>MD 4.98 fewer days</b> (8.55 to 1.41 fewer)</p> <p><u>Symptoms of dyspnoea</u> reported on completion of an exercise test assessed with: Borg score, n=44 (2 RCTs), <b>GRADE: Very low</b>                      Exercise: The mean change in dyspnoea reported on completion of an exercise test ranged from - 0.62 units to 1.00 units                      NMES + exercise: <b>MD 0.44 less dyspnoea</b> (2.27 less to 1.38 more)</p> <p><u>Health- related quality of life</u> assessed with: any validated questionnaire, n=122 (5 RCTs), <b>GRADE: Very low</b>                      Exercise: - - -                      NMES + exercise: <b>SMD 0.56 SD better</b> (1.27 better to 0.15 worse)</p> <p><u>Minor adverse events</u> assessed: related to intervention only (e.g. redness), n=144 (6 RCTs), <b>GRADE: LOW</b>                      Exercise: 0 per 1000                      NMES + exercise: 0 per 1000 (0 to 0)</p>	

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			<p><u>Days out of bed</u> combined with conventional exercise reduced the time taken for participants to first sit out of bed (4.98 days; 95% CI -8,55 – (-)1,41; I<sup>2</sup> =60%; <b>GRADE: Very low</b>, 2 RCT, n = 22</p>	
26998	<p>Ngai-Shirley PC. Tai Chi for chronic obstructive pulmonary disease (COPD). Cochrane Database of Systematic Reviews 2016;(6).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009953.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009953.pub2/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=12 eingeschlossene RCTs für Metaanalyse ( n=811 eingeschlossene Patienten)</li> <li>• <b>Suchzeitraum:</b> from inception to 9/2015</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b> No exclusions were based on age, gender, disease severity or smoking history.</li> <li>• <b>Interventionen:</b> Tai Chi alone or Tai Chi in addition to another intervention vs.usual care or another intervention identical to that used in the Tai Chi group</li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Level of dyspnoea: All measures related to dyspnoea were considered (e.g. Borg Scale, Modified Medical Research Council (MMRC) Dyspnoea Scale, Dyspnoea Visual Analogue Scale (DVAS)).</li> <li>- Functional capacity or aerobic capacity</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Pulmonary function</li> <li>- Quality of life status                             <ul style="list-style-type: none"> <li>◦ Generic health-related quality of life</li> <li>◦ Disease-specific health-related quality of life</li> </ul> </li> <li>- Quadriceps or other muscle strength</li> <li>- Balance</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- mean age: ranged from 61 to 74 years</li> <li>- Programmes lasted for six weeks to one year</li> </ul> </li> <li>• <b>Tai Chi versus usual care</b> <u>Level of dyspnoea</u> Assessed with Modified Borg Scale, n=137 (1 RCT); <b>GRADE: Low</b> <ul style="list-style-type: none"> <li>- Usual care: 2.1 units</li> <li>- Tai Chi: <b>0.2 unit lower</b> (95%CI -0.67 to 0.27 unit)</li> </ul> </li> <li>• <u>Functional capacity</u> Assessed with 6-minute walk test (metre), n=318 (6 RCTs), <b>GRADE: Very low</b> <ul style="list-style-type: none"> <li>- Usual care: Mean 317.38 metres</li> <li>- Tai Chi: <b>29.64 metres farther</b> (95% CI 10.52 to 48.77 metres)</li> <li>- 6MWD (MD 29,64 m; 95% CI 10,52 - 48,77 m; I<sup>2</sup> = 59%;</li> </ul> </li> <li>• <u>Functional capacity</u> Assessed with endurance shuttle walk test (second), n=38 (1 RCT), <b>GRADE: Low</b> <ul style="list-style-type: none"> <li>- Usual care: Mean 430 seconds</li> <li>- Tai Chi: <b>373 seconds longer</b> (95%CI 135.42 to 610.58 seconds)</li> </ul> </li> <li>• <u>Quality of life (SGRQ)</u>, n=233 (3 RCTs), <b>GRADE: Very low</b> <ul style="list-style-type: none"> <li>- Usual care: Mean 48.93 units</li> <li>- Tai Chi: <b>7.85 units lower</b> (95%CI -16.53 to 0.83 unit)</li> </ul> </li> <li>• <u>Quality of life (CRQ)</u>, n=248 (2 RCTs), <b>GRADE: Low</b> <ul style="list-style-type: none"> <li>- Usual care: Mean 4.75 units</li> <li>- Tai Chi: <b>0.41 unit higher</b> (95%CI -0.54 to 1.35 units)</li> </ul> </li> </ul> <p>&gt;&gt; No adverse events were reported, implying that Tai Chi is safe to practise in people with COPD.</p>	<p>AMSTAR-Score: 9/11</p> <p>y-n-y-y-y-y-y-y-n-y</p>

ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
27074	<p>Gendron LM. Active mind-body movement therapies as an adjunct to or in comparison to pulmonary rehabilitation for people with chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2018;(10).</p> <p><a href="https://www.cochraneli-brary.com/cdsr/doi/10.1002/14651858.CD012290.pub2/full">https://www.cochraneli-brary.com/cdsr/doi/10.1002/14651858.CD012290.pub2/full</a></p>	<p>• <b>Body of Evidence:</b> n=10 eingeschlossene RCTs für Metaanalyse (n= 762 eingeschlossene Patienten)</p> <p>• <b>Suchzeitraum:</b> inception to 07/2017; updated 07/2018</p> <p>• <b>Population:</b> patients with COPD</p> <p>• <b>Einschlusskriterien:</b></p> <ul style="list-style-type: none"> <li>- clinical diagnosis of COPD as defined by GOLD 2018</li> <li>- best recorded FEV /FVC ratio &lt; 0.7</li> <li>- ≥ 18 years of age</li> <li>- RCTs comparing AMBMT vs. PR or AMBMT + PR vs. PR</li> </ul> <p>• <b>Interventionen:</b></p> <p><u>Active mind-body movement therapies</u> (AMBMT)</p> <ul style="list-style-type: none"> <li>- including yoga, tai chi, qigong, pilates, others</li> <li>- i.e. controlled breathing and/or focused meditation/ attention interventions for which patients must actively move their joints and muscles for at least four weeks with no minimum intervention frequency</li> <li>- programmes of at least four weeks' duration with no minimum intervention frequency</li> </ul> <p>vs. <u>pulmonary rehabilitation</u> (PR)</p> <ul style="list-style-type: none"> <li>- any inpatient or outpatient, community-based or home-based rehabilitation programme lasting at least four weeks, with no minimum intervention frequency, that included conventional exercise training with or without education or psychological support</li> <li>- Exercise training: any continuous endurance or interval exercise or upper limb or lower limb training in the form of walking (groundbased or on a treadmill) and cycling with or without resistance/ strength training, flexibility training, or inspiratory muscle training</li> </ul> <p>• <b>Primäre Endpunkte:</b></p> <ul style="list-style-type: none"> <li>- Disease-specific quality of life (all validated tools w, e.g. CRQ, SGRQ, CAT)</li> <li>- Generic health-related quality of life (e.g. Short Form (SF)- 36)</li> <li>- Dyspnoea (all validated tools, e.g. MRC Scale, BORG Scale, TDI, Dyspnoea domain of the CRQ)</li> <li>- Serious adverse events (all types)</li> </ul> <p>• <b>Sekundäre Endpunkte:</b></p>	<p>8/10 studies considered walking training as equal to PR and used this as conventional exercise training within PR --&gt; limits comparison of AMBMT and PR</p> <p><b>AMBMTs vs PR</b> (mainly unstructured walking training)</p> <p><b>disease-specific quality of life</b></p> <ul style="list-style-type: none"> <li>• <u>SGRQ total score:</u></li> <li>- statistically significant improvements;favoured AMBMT</li> <li>- MD -5.83, 95% CI -8.75 to -2.92; 3 trials; 249 participants; <b>low-quality evidence.</b></li> <li>• <u>COPD Assessment Test (CAT)</u></li> <li>- statistically significant improvements favouring AMBMT over PR, with scores exceeding the MCID of three</li> <li>- MD 6.58 units (95%CI -9.16 to - 4.00 units; one trial; 74 participants; <b>low-quality evidence)</b></li> </ul> <p><b>Dyspnoe</b></p> <p>&gt;&gt; no between-group differences with regard to dyspnoea measured by:</p> <ul style="list-style-type: none"> <li>• <u>modified Medical Research Council Scale:</u></li> <li>- MD 0.00 units, 95% CI -0.37 to 0.37; two trials; 127 participants; <b>very low-quality evidence</b></li> <li>• <u>Borg Scale:</u></li> <li>- MD 0.44 units, 95% CI -0.88 to 0.00; one trial; 139 participants; very low-quality evidence)</li> <li>• <u>Chronic Respiratory Questionnaire (CRQ) Dyspnoea Scale:</u> MD -0.21, 95% CI -2.81 to 2.38; one trial; 11 participants; <b>very low-quality evidence</b></li> </ul> <p>• <b>Sicherheit:</b> keine Adverse Events berichtet (n=490, 8 RCTs)</p> <p><b>AMBMT + PR vs. PR alone</b> (mainly unstructured walking training)</p> <ul style="list-style-type: none"> <li>• <u>generic QoL</u></li> <li>&gt;&gt; significant improvements measured by Short Form (SF)-36 for both the:</li> <li>- SF-36 general health summary score (MD 5.42, 95% CI 3.82 to 7.02; one trial; 80 participants; <b>very low-quality evidence)</b></li> <li>- the SF-36 mental health summary score (MD 3.29, 95% CI 1.45 to 4.95; one trial; 80 participants; <b>very low-quality evidence).</b></li> <li>• <u>disease-specific QoL</u></li> <li>&gt;&gt; no significant improvement with addition of AMBMT to PR versus PR alone</li> <li>- SGRQtotal score:MD-2.57, 95%CI -7.76 to 2.62 units; one trial; 192 participants;</li> </ul> <p><b>moderate-quality evidence</b></p> <ul style="list-style-type: none"> <li>- CRQ Dyspnoea Scale score: MD 0.04, 95% CI -2.18 to 2.26 units; one trial;</li> </ul>	<p><u>AMSTAR-Score:</u> 11/11</p> <p>y-y-y-y-y-y-y-y-y-y</p> <p><u>AMSTAR II-Score:</u> Moderate</p>

ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
		<ul style="list-style-type: none"> <li>- Exercise capacity (Maximal exercise performance, Functional exercise capacity)</li> <li>• Pulmonary function (FEV and FEV predicted, %; FVC, FEV /FVC ratio)</li> <li>• Limb muscle function (muscle strength, endurance, and fatigue)</li> <li>• Exacerbations</li> <li>• Adherence (ratio between participants analysed and participants who received intervention)</li> </ul>	<p>80 participants; <b>very low quality evidence</b>).</p> <ul style="list-style-type: none"> <li>• Sicherheit: keine Adverse Events berichtet (n=272, 2 RCTs)</li> </ul>	
02198	<p>Ashworth NL. Home versus center based physical activity programs in older adults. Cochrane Database of Systematic Reviews 2005;(1).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004017.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004017.pub2/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n= 2 (für COPD-Subgruppe, mit 68 eingeschlossenen Patient*innen)</li> <li>• <b>Suchzeitraum:</b> until 09/2002</li> <li>• <b>Population:</b> older adults (50 years or older); eine Subgruppe mit COPD</li> <li>• <b>Einschlusskriterien für COPD-Subgruppe:</b> Existing Chronic Obstructive Pulmonary Disease (COPD) and allied conditions plus pneumoconiosis and other lung diseases due to external agents</li> <li>• <b>Interventionen:</b> 'home based' vs. 'center based' exercise program</li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Measures of functional activity (ADLs, walking ability etc)</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Long-term maintenance of physical activity (e.g. activity log book, Community healthy activities model program for seniors-CHAMPS, etc)</li> <li>- Measures of Quality of Life (SF36, Sickness impact profile, etc)</li> <li>- Cost</li> <li>- Health Service utilization</li> </ul> </li> <li>• <b>Sekundäre Endpunkte COPD related:</b> <ul style="list-style-type: none"> <li>- Mortality</li> <li>- Lung function tests</li> <li>- Exercise capacity</li> </ul> </li> </ul>	<p><u>Physiological measures:</u> Two trials looked at older adults with COPD. In patients with COPD the evidence is conflicting. One study showed similar changes in various physiological measures at 3 months that persisted in the home based group up to 18 months but not in the center based group. The other study showed significantly better improvements in physiological measures in the center based group after 8 weeks but again the possibility of a training effect is high.</p> <p><u>Quality of life:</u> n=1 Studie: Compared with controls, significantly more participants in the exercise groups experienced 'better' general well-being at 3 months (80% for center, 73% for home versus 47% for control) and 18 months (62% for center, 64% for home versus 50% for control). There was no significant difference between home and center groups however.</p> <p><u>Methodische Qualität:</u> Allocation concealment was 'unclear' in all the studies. None of the participants in the included studies were blinded to the interventions (for obvious reasons). None of the investigators/assessors appeared to be blinded either however. Dropouts were well described and reached a maximum of approximately 16%. <b>Both studies were 'medium' quality.</b></p>	<p>AMSTAR-Score: 7/11</p> <p>n-n-y-y-y-y-n-y-y-n</p>

ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
26987	<p>Osadnik CR. Airway clearance techniques for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2012;(3).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008328.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008328.pub2/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=28 eingeschlossene RCTs und randomised cross-over trials ( n= 907 eingeschlossene Patient*innen); n= 12 für Metaanalyse</li> <li>• <b>Suchzeitraum:</b> inception to 10/ 2011 (PEDro 10/2009)</li> <li>• <b>Population:</b> individuals with AECOPD and stable COPD</li> <li>• <b>Interventionen:</b> <ul style="list-style-type: none"> <li>- any techniques applied with the primary purpose of clearing sputum from the airways (This included but was not restricted to 'conventional' techniques, breathing exercises, and PEP or mechanical devices, but excluded suctioning and breathing strategies for purposes of relaxation (e.g. relaxed controlled breathing) or respiratory muscle strengthening (e.g. inspiratory/ expiratory muscle training).</li> </ul> </li> <li>• <b>Control:</b> intervention, sham intervention or coughing alone</li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- beneficial effects on exacerbations, hospitalisation and HRQoL</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- effectiveness: airway clearance techniques</li> <li>- airway clearance techniques are safe for individuals with AECOPD and stable COPD.</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- mean age: ranging from 54 to 72</li> <li>- mean FEV1: from 29 to 58 % predicted</li> </ul> </li> <li>&gt;&gt; Ergebnisse für Patient*innen mit stabiler COPD:                     <ul style="list-style-type: none"> <li><u>exacerbations and hospitalisations</u> <ul style="list-style-type: none"> <li>- 1 PEP-based study (n=30= investigated the short-term effect of ACTs on the number of AECOPDs, finding no significant differences between groups at four weeks (OR 3.21, 95% CI 0.12 to 85.20).</li> <li>- 1 PEP-based study (n=50) investigated the effect of ACTs on respiratory-related hospital admissions, with long-term data revealing a significantly lower need for hospitalisation in favour of the ACT group (OR 0.27, 95% CI 0.08 to 0.95).</li> </ul> </li> <li><u>HRQoL</u> <ul style="list-style-type: none"> <li>1 study (n=15 participants) investigated the effect of a PEP-based ACT on HRQoL, with short-term data revealing significantly lower (better) SGRQ (St. George's Respiratory Questionnaire) total scores following one week of daily ACTs compared to a sham intervention (MD -6.10, 95% CI -8.93 to -3.27)</li> </ul> </li> <li><u>Symptoms</u> <ul style="list-style-type: none"> <li>- 1 study in quantitative analysis: Borg scores were significantly lower immediately following a PEP-based ACT plus inhaled bronchodilator therapy than after a sham ACT plus inhaled bronchodilator therapy (MD -0.30 points, 95% CI -0.53 to -0.07; Analysis 2.12)</li> </ul> </li> <li><u>mortality (all-cause)</u> <ul style="list-style-type: none"> <li>No data were available for analysis.</li> </ul> </li> <li><u>Safety</u> <ul style="list-style-type: none"> <li>- 5 Studies clearly reported no negative effects from ACTs</li> <li>- 1 study reported a clinically important adverse event (one participant vomited and two others felt uncomfortable during a sequence of postural drainage positions incorporating a head-down tilt)</li> <li>- Meta-analysis revealed no significant effect of ACTs during an AECOPD on mortality in the short term (OR 0.72, 95% CI 0.14 to 3.80) or long term (OR 0.82, 95% CI 0.26 to 2.63), however this outcome is likely to be underpowered.</li> </ul> </li> </ul> </li> </ul>	<p>AMSTAR-Score: 10/11</p> <p>y-y-y-y-y-y-y-y-y-n</p>
27013	<p>Holland AE. Breathing exercises for chronic obstructive</p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n= 16 eingeschlossene RCTs für Metaanalyse ( n= 1233 eingeschlossene Patient*innen)</li> <li>• <b>Suchzeitraum:</b> inception to 10/ 2011</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- mean age: ranging from 51 to 73 years</li> <li>- mean FEV1: 30% to 51% predicted</li> </ul> </li> </ul>	<p>AMSTAR-Score: 8/11</p> <p>y-y-y-y-y-y-y-ca-ca-n</p>

ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<p>pulmonary disease. Cochrane Database of Systematic Reviews 2012;(10).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008250.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008250.pub2/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Population:</b> Patient*innen mit stabiler COPD</li> <li>• <b>Einschlusskriterien:</b> Adults with a clinical diagnosis of COPD in a stable condition</li> <li>• <b>Interventionen:</b> <ol style="list-style-type: none"> <li>1. breathing exercises versus no breathing exercises;</li> <li>2. breathing exercises versus another intervention;</li> <li>3. breathing exercises combined with another intervention versus no breathing exercises.</li> </ol> </li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Dyspnoea</li> <li>- Functional or maximal exercise capacity</li> <li>- Health-related quality of life</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Gas exchange (e.g. PaO2, PaCO2).</li> <li>- Ventilation (e.g. minute ventilation, tidal volume).</li> <li>- Energy cost (e.g. oxygen consumption).</li> <li>- Breathing pattern (e.g. respiratory frequency, chest wall kinematics).</li> <li>- Adverse events.</li> </ul> </li> </ul>	<p><b>Pursed lip breathing compared to no breathing exercises</b>  <u>Dyspnoea during exercise:</u> Modified Borg Dyspnoea score; n=19 (1 RCT); <b>GRADE: Low</b>                      No breathing exercises: 4 units                      Pursed lip breathing: The mean dyspnoea score during exercise in the intervention groups was <b>1 unit lower</b> (2.1 lower to 0.1 higher)</p> <p><u>Dyspnoea during daily life:</u> University of California San Diego Shortness of Breath Questionnaire, n=19 (1 RCT), <b>GRADE: Low</b>                      No breathing exercises: 69 units                      Pursed lip breathing: The mean dyspnoea score during daily life in the intervention groups was <b>10 units lower</b> (28.89 lower to 8.89 higher)</p> <p><u>Walking capacity:</u> 6-minute walk distance (metres), n=30 (1 RCT), <b>GRADE: Low</b>                      No breathing exercises: 233 metres                      Pursed lip breathing: The mean walking distance in the intervention groups was <b>50.1 metres higher</b> (37.21m to 62.99m higher)</p> <p><u>Health-related quality of life:</u> Dyspnoea domain of Hiratsuka scale, n=60 (2 RCTs), <b>GRADE: Low</b>                      No breathing exercises: 46 units                      Pursed lip breathing: The mean quality of-life score in the intervention groups was <b>12.94 units better (lower)</b> (22.29 lower to 3.6 lower)</p> <p><b>Diaphragmatic breathing compared to no breathing exercises</b>  <u>Dyspnoea,</u> n=30 (1 RCT), <b>GRADE: Moderate</b>                      No breathing exercises: Decrease of 0.33 units                      Diaphragmatic breathing: The mean reduction in dyspnoea score in the intervention groups was <b>0.27 units greater</b> (0.76 greater to 0.22 smaller)  <u>Walking capacity,</u> n=30 (1 RCT), <b>GRADE: Moderate</b>                      No breathing exercises: Reduction of 8 metres                      Diaphragmatic breathing: The mean walking distance in the intervention groups was <b>34.67 metres greater</b> (4.05 higher to 65.29 higher)  <u>Health-related quality of life (SGRQ):</u> n=30 (1 RCT), <b>GRADE: Moderate</b>                      No breathing exercises: Increase of 0.8 units                      Diaphragmatic breathing: The mean change in quality of life score in the intervention groups was <b>10.51 units lower (better)</b></p> <p><b>Yoga compared to no breathing exercises</b>  <u>Dyspnoea intensity;</u> Modified Borg Scale, n=29 (1 RCT), <b>GRADE: Low</b></p>	



ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
			<p>No breathing exercises: 3.3 units                      Yoga: The mean dyspnoea intensity in the intervention group was <b>0.5 units higher</b> (0.99 lower to 1.99 higher)  <u>Dyspnoea distress</u>; Modified Borg scale, n=29 (1 RCT), <b>GRADE: Low</b>                      No breathing exercises: 1.4 units                      Yoga: The mean dyspnoea distress in the intervention group was <b>0.2 units higher</b> (0.97 lower to 1.37 higher)  <u>Walking capacity</u>, n=74 (2 RCTs), <b>GRADE: Moderate</b>                      No breathing exercises: Reduction of 6.38 m                      Yoga: The mean walking distance in the intervention groups was 44.51 m higher (28.47 higher to 60.55 higher)  <u>Health-related quality of life</u> (SGRQ), n=45 (1 RCT), <b>GRADE: Moderate</b>                      No breathing exercises: Reduction of 1.2 units                      Yoga: The mean quality of life score in the intervention group was <b>5.3 units lower</b> (7.82 lower to 2.78 lower)</p>	
27077	<p>McNamara RJ. Singing for adults with chronic obstructive pulmonary disease (COPD). Cochrane Database of Systematic Reviews 2016;(7).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012296/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012296/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=3 eingeschlossene RCTs für Metaanalyse ( n=112 eingeschlossene Patient*innen)</li> <li>• <b>Suchzeitraum:</b> inception - 08/2017</li> <li>• <b>Population:</b> Patient*innen mit stabiler COPD</li> <li>• <b>Einschlusskriterien:</b> adults with COPD of any age or disease severity. The COPD was required to be stable. We included participants with COPD who used supplemental oxygen.</li> <li>• <b>Interventionen:</b> <ol style="list-style-type: none"> <li>1. singing versus no intervention (usual care) or another control intervention</li> <li>2. singing plus pulmonary rehabilitation versus pulmonary rehabilitation alone</li> </ol> </li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Health-related quality of life</li> <li>- Dyspnoea</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Respiratory muscle strength</li> <li>- Pulmonary function</li> <li>- Psychological status</li> <li>- Functional exercise capacity</li> <li>- Peak exercise capacity</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- mean age: range 67 to 72 years</li> <li>- mean FEV1: range from 37% to 64% of predicted values</li> <li>- frequency of the singing intervention: ranged from 1 to 2 times a week over a 6 to 24 week period.</li> <li>- duration of the singing sessions: 60 minutes (conducted in groups led by a singing teacher)</li> </ul> </li> <li>• <u>Health- related quality of life (respiratory specific) SGRQ</u>, n=58 (2 RCTs), <b>GRADE: Low</b> <ul style="list-style-type: none"> <li>Control: The mean change in SGRQ (total score) ranged across control groups from -5.0 to -0.4</li> <li>Singing: The mean change in SGRQ (total score) in the intervention groups was <b>0.8 units higher</b> (3. 0 units lower to 4.7 units higher)</li> </ul> </li> <li>• <u>Health- related quality of life (generic) SF-36</u> (Physical Component Summary (PCS) score), n=52 (2 RCTs, I<sup>2</sup>=0%), <b>GRADE: Low</b> <ul style="list-style-type: none"> <li>Control: The mean change in SF-36 (PCS score) ranged across control groups from -3.8 to -2.5</li> <li>Singing: The mean change in SF-36 (PCS score) in the intervention groups was <b>12.6 units higher</b> (5.5 units higher to 19.8 units higher)</li> </ul> </li> <li>• <u>Health- related quality of life (generic) SF-36</u> (Mental Component Summary (MCS) score), n=52 (2 RCTs), <b>GRADE: Low</b> <ul style="list-style-type: none"> <li>Control: The mean change in SF-36 (MCS score) ranged across control groups from -3.2 to 4.3</li> </ul> </li> </ul>	<p>AMSTAR-Score: 11/11</p> <p>y-y-y-y-y-y-y-y-y-y</p>

ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
		<ul style="list-style-type: none"> <li>- Healthcare utilisation</li> <li>- Physical activity level</li> <li>- Adverse events/side effects</li> </ul>	<p>Singing: The mean change in SF-36 (MCS score) in the intervention groups was <b>5.4 units higher</b> (3.9 units lower to 14.7 units higher)</p> <ul style="list-style-type: none"> <li>• <b>Dyspnoea Basal Dyspnea Index (BDI) (score)</b>, n=30 (1 RCT), <b>GRADE: Very low</b> Control: The mean change in BDI (score) was 0.3 Singing: The mean change in BDI (score) in the intervention groups was <b>0.4 units higher</b> (0.7 units lower to 1.5 units higher)</li> <li>• <b>Psychological status</b>, n= 52 (2 RCT) There was no statistically significant improvement in the HADS anxiety score (MD -1.09, 95% CI - 3.02 to 0.83, n = 52) or HADS depression score (MD - 0.87, 95% CI -2.16 to 0.42, n = 52).</li> <li>• <b>Physical activity level</b>: n=24, (1 RCT) There were no statistically significant differences between the singing group and control group for sedentary time (minutes per day), but the confidence interval is wide (MD -8.60, 95%CI -88.33 to 71.13). There were statistically significant differences in the remaining measures of physical activity favouring the control group (steps (steps per day) MD -1774.00, 95% CI -2847.73 to -700.27; physical activity duration (minutes per day) MD -142.20, 95% CI -262.56 to -21.84; active energy expenditure (kJ per day) MD -373.00, 95% CI -625.28 to -120.72).</li> <li>- SF-36: MD 12,64; 95% CI 5,50 – 19,77</li> </ul> <p>No <u>adverse events/side effects</u> were reported by any of included studies,</p>	
27046	<p>Ferreira IM. Nutritional supplementation for stable chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2012;(12).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000998.pub3/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000998.pub3/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=17 eingeschlossene RCTs für Metaanalyse ( n= 632 eingeschlossene Patient*innen)</li> <li>• <b>Suchzeitraum:</b> current to 04/2012</li> <li>• <b>Population:</b> Patient*innen mit stabiler COPD</li> <li>• <b>Einschlusskriterien:</b> stable patients with COPD, among whom at least 75% of participants had a forced expired volume in one second (FEV1) less than 70% predicted, and less than 12% reversibility after use of a bronchodilator</li> <li>• <b>Interventionen:</b> - subjects received oral, enteral or parenteral nutritional support vs. (I) placebo</li> </ul>	<p><u>Anthropometric measures (Illustrative comparative risks* (95% CI)</u></p> <p><b>Weight</b> (mixed population) kg (Follow-up: 2 to 24 weeks; n=512 participants; 14 RCTs; <b>GRADE: moderate</b>)</p> <ul style="list-style-type: none"> <li>- The mean weight (mixed population) in the control groups was 56.43 kg</li> <li>- The mean weight (mixed population) in the intervention groups was 0.69 higher (0.86 lower to 2.24 higher)</li> </ul> <p><b>Weight</b> (undernourished) kg (Follow-up: 2 to 24 weeks; n=325 participants; 11 RCTs; <b>GRADE: moderate</b>)</p> <ul style="list-style-type: none"> <li>- The mean weight (undernourished) in the control groups was 60.34 kg</li> <li>- The mean weight (undernourished) in the intervention groups was 1.65 higher (0.14 to 3.16 higher)</li> </ul>	<p>AMSTAR-Score: 9/11</p> <p>y-y-y-y-y-y-y-n-n</p>

ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
		(ii) their usual diet or (iii) other treatment regimens such as anabolic substances  <b>• Primäre Endpunkte:</b> 1. Anthropometric measures (body weight, fat-free mass index, lean body mass, mid-arm muscle circumference (MAMC), skinfold measures). 2. Functional exercise (timed walk test).  <b>• Sekundäre Endpunkte:</b> 1. Pulmonary mechanics (lung volumes, respiratory muscle function). 2. Peripheral muscle function. 3. HRQoL derived from validated scales (e.g. SGRQ, CRQ, SF-36).	<b>Fat-free mass index</b> (mixed population) kg/m <sup>2</sup> (Follow-up: 3 to 4 months; n=93 participants; 3 RCTs; <b>GRADE: low</b> ) - The mean fat-free mass index (mixed population) in the control groups was 14.8 kg/m <sup>2</sup> - The mean fat-free mass index (mixed population) in the intervention groups was 0.08 higher (0.51 lower to 0.66 higher)  <b>Fat-free mass index</b> (undernourished patients) kg/m <sup>2</sup> (Follow-up: 3 to 4 months; n=62 participants; 2 RCTs; <b>GRADE: low</b> ) - The mean fat-free mass index (undernourished patients) in the control groups was 14.5 kg/m <sup>2</sup> - The mean fat-free mass index (undernourished patients) in the intervention groups was 0.31 higher (0.32 lower to 0.95 higher)  <u>Functional exercise</u> There was low-quality evidence (five RCTs, 142 participants) of no significant difference between groups in the six-minute walk distance (MD 14.05 m; 95% CI -24.75 to 52.84), 12-minute walk distance or in shuttle walking. However, the pooled change from baseline for the six-minute walk distance was significant (MD 39.96 m; 95% CI 22.66 to 57.26).  <u>Health-related quality of life</u> There was low-quality evidence (4 RCTs, 130 participants) of no significant difference in HRQoL total score (SMD -0.36; 95% CI -0.77 to 0.06) when pooling results from both the St George's Respiratory Questionnaire (SGRQ) and the Chronic Respiratory Questionnaire (CRQ).  Two trials (n=67) used the SGRQ to measure individual domains of activity, impact and symptoms. At the end of treatment, the pooled total SGRQ score was both statistically and clinically significant (MD 6.55; 95% CI -11.7 to -1.41). The 3 RCTs (n=123) that used the CRQ to measure the change in individual domains (dyspnoea, fatigue, emotion, mastery), found no significant difference between groups.  <b>&gt;&gt; This review of 17 studies (632 participants) that provided nutritional supplementation for patients with COPD for more than two weeks found growing evidence that nutritional supplementation improved body weight, respiratory muscle strength, walking and quality of life.</b>	
27080	Pollok J. Psychological therapies for the	<b>• Fragestellung:</b> To assess the effectiveness of psychological therapies for the treatment of depression in patients	<b>• Baseline-Charakteristika:</b> - depressive symptoms varied from no symptoms to severe depression	AMSTAR-II: moderate

ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<p>treatment of depression in chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2019;(3).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012347/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012347/abstract</a></p>	<p>with chronic obstructive pulmonary disease.</p> <ul style="list-style-type: none"> <li>• <b>Suchzeitraum:</b> June 2016 to 26 November 2018</li> <li>• <b>Population:</b> patients with COPD whose depressive symptoms were measured before or at baseline assessment.</li> <li>• <b>Interventionen:</b> <ul style="list-style-type: none"> <li>- psychological therapies vs.</li> <li>- either no intervention, education, or</li> <li>- psychological therapies combined with a co-intervention vs.</li> <li>- the same co-intervention</li> </ul> </li> <li>• <b>eingeschlossene Studien:</b> 13 RCTs, 1500 participants</li> </ul>	<p><u>depressive symptoms</u></p> <ul style="list-style-type: none"> <li>- small effect showing the effectiveness of psychological therapies in improving depressive symptoms when compared to</li> <li>-- no intervention (SMD 0.19, 95% CI 0.05 to 0.33; P = 0.009; 6 studies, 764 participants; <b>GRADE: very low</b>)</li> <li>-- education (SMD 0.23, 95% CI 0.06 to 0.41; P = 0.010; 3 studies, 507 participants; <b>GRADE: very low</b>)</li> </ul> <p>Change in Quality of life</p> <ul style="list-style-type: none"> <li>-- no intervention: standardised mean improvement in QoL from baseline in the psychological therapies group was 0.15 higher (0.09 lower to 0.38 higher) compared to no intervention (3 studies; 348 participants; <b>GRADE: very low</b>)</li> <li>-- education:                     <ul style="list-style-type: none"> <li>--- mean change from baseline in QoL, <u>emotional functioning</u> in the psychological therapies group was 2.98 units CRQ higher (9.15 lower to 3.19 lower) compared to education (2 studies; 460 participants; <b>GRADE: very low</b>)</li> <li>--- mean quality of life - CRQ - <u>dyspnoea</u> in the psychological therapies group was 1.84 units CRQ higher (5.94 lower to 2.26 higher) compared to education (2 studies; 458 participants; <b>GRADE: very low</b>)</li> </ul> </li> </ul> <p><u>psychological therapy combined with a PR programme</u></p> <ul style="list-style-type: none"> <li>- can reduce depressive symptoms more than a PR programme alone (SMD 0.37, 95% CI -0.00 to 0.74; P = 0.05; I<sup>2</sup>=0%, 2 studies, 112 participants; <b>GRADE: very low</b>)</li> </ul> <p>None of the included studies measured adverse events.</p>	
27054	<p>Usmani ZA. Psychological therapies for the treatment of anxiety disorders in chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2017;(3).</p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=3 eingeschlossene RCTs für Metaanalyse ( n= 319 eingeschlossene Patient*innen)</li> <li>• <b>Suchzeitraum:</b> to 8/2015</li> <li>• <b>Population:</b> Patient*innen mit COPD und Angststörung</li> <li>• <b>Einschlusskriterien:</b> &gt; 40 years, with COPD and coexisting anxiety disorders (as confirmed by recognised diagnostic criteria or a validated measurement scale) or anxiety symptom( s)</li> <li>• <b>Interventionen:</b></li> </ul>	<ul style="list-style-type: none"> <li>• All three studies assessed psychotherapy (CBT) with a co-intervention, versus the co-intervention alone</li> </ul> <p><u>Anxiety Becks Anxiety Inventory.</u> Scale f rom: 0 to 63. Follow-up: 3-12 months, n=319 (3 RCTs), <b>GRADE: Low</b>; I<sup>2</sup>=62%</p> <ul style="list-style-type: none"> <li>- Control: mean anxiety 15.51</li> <li>- Psychological therapies for anxiety: mean anxiety <b>4.41 lower</b> (8.28 to 0.53 lower)</li> <li>- Comment: Beneficial findings were observed in favour of the psychological</li> </ul>	<p>AMSTAR-Score: 11/11</p> <p>y-y-y-y-y-y-y-y-y-y</p>

ID	Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010673.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010673.pub2/abstract</a>	<p>psychological therapies vs. no intervention or education only</p> <ul style="list-style-type: none"> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Change in anxiety symptoms</li> <li>- Adverse events</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Change in quality of life</li> <li>- Difference in exercise tolerance</li> <li>- Change in dyspnoea scores</li> <li>- Change in length of stay or readmission rate</li> <li>- Change in forced expiratory volume in one second (FEV1)</li> </ul> </li> </ul>	<p>therapy group (p= 0.03), with levels of anxiety half that of the control population by final follow-up (Gillis 1995)</p> <p><u>Quality of life - physical composite</u> (SGRQ and SF36 Follow-up: 6-12 months), n=289 (2 RCTs); <b>GRADE: Low</b>, I<sup>2</sup>=61%</p> <ul style="list-style-type: none"> <li>- Control: mean QoL physical 45.08</li> <li>- Psychological therapies for anxiety: mean QoL was <b>0.40 standard deviations lower</b> (0.88 lower to 0.08 higher)</li> <li>- Comment: Subgroup analyses separating short-term (0 to 3 months; SMD -0.22, 95%CI -0.45 to 0.01; P = 0.06) and long-term follow-up (6 to 12 months; SMD -0.30, 95% CI -0.53 to -0.06; P = 0.01) resulted in better treatment outcomes longterm</li> </ul> <p><u>Quality of life - emotional composite</u> (SGRQ and SF36 Follow-up: 6-12 months), n=289 (2 RCTs), <b>GRADE: Low</b>, I<sup>2</sup>=82%</p> <ul style="list-style-type: none"> <li>- Control: mean QoL emotional 52.3</li> <li>- Psychological therapies for anxiety: mean QoL emotional was <b>0.30 standard deviations lower</b> (1.03 lower to 0.44 higher)</li> <li>- Comment: Subgroup analyses separating short-term (0 to 3 months; SMD 0.05, 95% CI -0.18 to 0.28) and long-term follow-up (6 to 12 months; SMD -0.09, 95% CI -0.32 to 0.14) resulted in better treatment outcomes long-term</li> </ul> <p><u>Exercise capacity</u> (6MWD Follow-up: 3-12 months), n=268 (2 RCTs), <b>GRADE: Low</b>; I<sup>2</sup>=80%</p> <p>Control: mean 839</p> <p>Psychological therapies for anxiety: mean exercise capacity was <b>2.78 lower</b> (58.49 lower to 52.94 higher)</p> <p><u>Adverse events:</u> No studies reported on adverse events</p>	

### Anhang 7.2 Cochrane Reviews Respiratorische Insuffizienz

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
Cranston JM. Domiciliary oxygen for chronic obstructive pulmonary disease. Cochrane	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To determine the effect of domiciliary oxygen therapy on survival and quality of life in patients with COPD.</li> <li>• <b>Suchzeitraum:</b> current as of 1/2007</li> <li>• <b>Population:</b> patients with hypoxaemia and COPD</li> </ul>	<p><b>Continuous oxygen therapy versus nocturnal oxygen therapy</b></p> <ul style="list-style-type: none"> <li>- Mortality at 12 months: Peto Odds Ratio (OR) 0,53 (95% KI 0,25; 1,11); 1 RCT, n = 203, JADAD 3</li> <li>- Mortality at 24 months: Peto OR 0,45 (95% KI 0,25; 0,81); 1 RCT, n = 203, JADAD 3</li> </ul>	<p>AMSTAR- I Score: 7/11</p> <p>y-n-y-y-y-y-y-ca-n-n</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Database of Systematic Reviews 2005;(4).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001744.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001744.pub2/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Interventionen:</b> long term domiciliary or home oxygen therapy (all forms of LTOT including provision of oxygen using cylinders, concentrators or liquid oxygen therapy)</li> <li>• <b>Vergleich:</b> control treatment (placebo air by the same method of delivery or no specific intervention)</li> <li>• <b>eingeschlossene Studien:</b> n=6 eingeschlossene RCTs für Metaanalyse</li> <li>• <b>RoB der eingeschlossenen Studien</b> (GRADE nicht durchgeführt):             <ul style="list-style-type: none"> <li>- methodological quality of the studies was scored as moderate (Jadad score 3) in five studies (NOTT 1980, MRC 1981, Fletcher 1992, Gorecka 1997, Chaouat 1999) and low (Jadad score 2) in the remaining trial (Haidl 2004).</li> </ul> </li> </ul>	<p><b>Long-term oxygen therapy versus no oxygen therapy in severe hypoxaemia</b></p> <ul style="list-style-type: none"> <li>- Mortality at 60 months: Peto OR 0,42 (95% KI 0,18; 0,98); 1 RCT, n = 87, JADAD 3</li> </ul> <p><b>Nocturnal oxygen therapy versus room air with mild to moderate hypoxaemia; change from baseline</b></p> <ul style="list-style-type: none"> <li>- Mortality at 36 months: Peto OR 0,97 (95% KI 0,41; 2,31); I<sup>2</sup>:0%, 2 RCT, n = 114, JADAD 3</li> </ul> <p><b>Long term oxygen therapy versus no oxygen therapy in mild to moderate hypoxaemia</b></p> <ul style="list-style-type: none"> <li>- Mortality: Peto OR 1,39 (95% KI 0,74; 2,59); I<sup>2</sup>:0%, 2 RCT, n = 163, JADAD 2-3</li> <li>- Mortality between oxygen &gt;15hrs per day and &lt;15hrs per day: Peto OR 1,67 (95% KI 0,62; 4,47); 1 RCT, n = 68, JADAD 3</li> <li>- End exercise dyspnoea score: Mean Difference - 1,20 (MD, 95% KI -2,47; 0,07), 1 RCT, n = 28, JADAD 2</li> <li>- Endurance time: MD 2,20 (95% KI (-0,73; 5;13), 1 RCT, n = 28, JADAD 2</li> </ul> <p>&gt;&gt; Long-term home oxygen therapy improved survival in a selected group of COPD patients with severe hypoxaemia (arterial PaO<sub>2</sub> less than 55 mm Hg (8.0 kPa)). Home oxygen therapy did not appear to improve survival in patients with mild to moderate hypoxaemia or in those with only arterial desaturation at night.</p>	
<p>Ameer F. Ambulatory oxygen for people with chronic obstructive pulmonary disease who are not hypoxaemic at rest. Cochrane Database of Systematic Reviews 2014;(6).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000</a></p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To determine the longer term efficacy of ambulatory oxygen therapy only in patients with COPD who do not meet the criteria for LTOT, with respect to improvement in exercise capacity, mortality, quality of life and other relevant measures of improvement.</li> <li>• <b>Suchzeitraum:</b> current as of 11/2012</li> <li>• <b>Population:</b> <ul style="list-style-type: none"> <li>- Patient*innen mit stabiler COPD</li> <li>- Participants had chronic hypoxaemia (resting PaO 55 to 59 mmHg) without cor pulmonale (failure of the right side of the heart caused by an increase in blood pressure in the pulmonary artery, the vessel that carries blood from the heart to the lungs) or PaO ≥ 60 mmHg, or they developed hypoxaemia on activity (PaO &lt; 60 mmHg or peripheral capillary oxygen de-saturation to &lt; 88% SpO ) with or without cor pulmonale with symptoms on exertion.</li> </ul> </li> <li>• <b>Einschlusskriterien:</b> participants with</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- mean age: 71 years</li> </ul> </li> </ul> <p><u>Mortality</u> (Follow-up: mean 12 weeks)</p> <ul style="list-style-type: none"> <li>- RR 4,17 (95% KI 0,48; 36,3); I<sup>2</sup>: 0%, 2 RCT, n = 179, <b>GRADE: moderat</b></li> <li>- Comment: Although deaths occurred only in the intervention arm of the study (n=3), they were not believed to be a direct result of the intervention</li> </ul> <p><u>Quality of life (dyspnoea)</u> on CRQ, the output is a number from 0 to 7, where higher on the scale is better)</p> <ul style="list-style-type: none"> <li>- MD 0,28 (95% KI 0,10; 0,45); I<sup>2</sup>: 0%, 4 RCT, n = 341, <b>GRADE: moderat</b></li> <li>- Control: Baseline risk in control groups ranged from 2.8 to 3.7 points</li> </ul> <p><u>Dyspnoea</u></p> <ul style="list-style-type: none"> <li>- Meta-analysis not possible; 3 RCT, n = 198, <b>GRADE: not applicable</b></li> </ul> <p><u>Adverse events</u> Follow-up: mean 12 weeks</p> <ul style="list-style-type: none"> <li>- Ambulatory oxygen: 117/1000 (35 to 325)</li> </ul>	<p>AMSTAR- I Score: 11/11</p> <p>y-y-y-y-y-y-y-y-y-y</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
238.pub2/abstract	<p>COPD who did not meet criteria for LTOT</p> <ul style="list-style-type: none"> <li>• <b>Interventionen:</b> ambulatory oxygen therapy provided through portable oxygen cylinders/battery powered devices or liquid oxygen canisters</li> <li>• <b>Vergleich:</b> placebo air cylinders, usual medical care or co-intervention</li> <li>• <b>eingeschlossene Studien:</b> n=4 eingeschlossene RCTs für Metaanalyse ( n=331 eingeschlossene Patient*innen)</li> </ul>	<p>- Control:146/1000 - OR 0,77 (95% KI 0,21; 2,81); I<sup>2</sup>: 1%, 2 RCT, n = 83, <b>GRADE: niedrig</b></p> <p><u>Hospitalisations:</u> No studies reported data on hospitalisations</p> <p>&gt;&gt; In patients with COPD with moderate hypoxia, current evidence on ambulatory oxygen therapy reveals improvements in dyspnoea post exercise and in the dyspnoea and fatigue domain of quality of life. However, evidence for the clinical utility and effectiveness of ambulatory oxygen in improving mortality and exercise capacity was not evident in this review.</p> <p>&gt;&gt; From this review, it is not possible to know whether ambulatory oxygen therapy should be provided during exercise or for day-to-day activities for patients with COPD who are not severely hypoxaemic at rest.</p>	
<p>Bradley JM. Short-term ambulatory oxygen for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2005;(4). <a href="http://online.library.wiley.com/doi/10.1002/14651858.CD004356.pub3/abstract">http://online.library.wiley.com/doi/10.1002/14651858.CD004356.pub3/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To determine the efficacy of ambulatory oxygen in patients with COPD using single assessment studies.</li> <li>• <b>Suchzeitraum:</b> current as of 3/2005</li> <li>• <b>Population:</b> Patient*innen mit stabiler COPD</li> <li>• <b>Einschlusskriterien:</b> Studies had to compare oxygen and placebo when administered to people with COPD who were undergoing an exercise test</li> <li>• <b>Interventionen:</b> ambulatory oxygen therapy (provided either via oxygen cylinders or a reservoir system)</li> <li>• <b>Vergleich:</b> intervention (Placebo) via air cylinders or a reservoir system</li> <li>• <b>eingeschlossene Studien:</b> n=31 eingeschlossene RCTs (cross-over indesign) für Metaanalyse ( n=534 eingeschlossene Patient*innen)</li> <li>• <b>RoB der eingeschlossenen Studien:</b> Overall, the methodological quality of the included studies as rated by the Jadad score was low (16 studies had score of 1; nine studies had a score of 2; 4 studies had a score of 3; and two studies had a score of 5).</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> - mean age: ranged from 47 to 73 years - mean PaO<sub>2</sub> ranged from 6.9 KPa to 11.3 KPa (52 mmHg to 85 mmHg)</li> </ul> <p><b>Endurance test studies: Exercise capacity</b> <u>Distance</u> With fixed effects modelling oxygen significantly improved exercise distance by 18,86 metres (95% KI 13,11; 24,61, 10 Studien, n = 238; 6MWT) and 18,61 metres (95% KI 12,83; 24,39, 10 Studien, n = 238; endurance walk)</p> <p><b>Maximal test studies: Exercise capacity</b> <u>Distance</u> There was a significant improvement in distance walked during oxygen versus placebo of 32 metres (95% KI 20,61; 43,38, 4 Studien, n = 70). There was a moderate level of heterogeneity between the studies. Random Effects modelling widened the confidence interval but the result remained significant (39,57 metres (95% KI 17,03; 62,11)).</p> <p><b>Endurance test isotimes studies:</b> <u>Breathlessness</u> Random Effects modelling gave a significant result in favour of oxygen (Somfay 2001 low dose: -1,46 (95% KI -2,30; -0,62); Somfay 2001 high dose: -1,51 (95% KI -2,41; -0,61); n = 44).</p> <p><b>Maximal test isotimes:</b> <u>Breathlessness</u> Data from 14 patients showed high dose oxygen significantly reduced breathlessness compared to placebo but no data was provided</p>	<p>AMSTAR- I Score: 9/11</p> <p>y-n-y-y-y-y-y-y-n</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
		>> This review provides some evidence from small, single assessment studies that ambulatory oxygen improves exercise performance in people with moderate to severe COPD. The results of the review may be affected by publication bias, and the small sample sizes in the studies.	
<p>Nonoyama M. Oxygen therapy during exercise training in chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2007;(2). <a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005372.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005372.pub2/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To determine how supplemental oxygen in comparison to control (compressed air or room air) during the exercise-training component of a pulmonary rehabilitation program affects exercise capacity, dyspnea and health-related quality of life in individuals with COPD.</li> <li>• <b>Suchzeitraum:</b> last search 6/2009</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b> &gt; 18 years, diagnosed with COPD and did not meet criteria for long-term oxygen therapy. No studies with mixed populations (pulmonary fibrosis, cystic fibrosis, etc) were included.</li> <li>• <b>Intervention:</b> supplemental oxygen during the exercise-training</li> <li>• <b>Vergleich:</b> control (compressed air or room air) during the exercise-training</li> <li>• <b>eingeschlossene Studien:</b> n=5 eingeschlossene RCTs für Metaanalyse ( n=31 (oxygen)/ n=32 (control) eingeschlossene Patient*innen)</li> </ul>	<p><b>Functional ex. capacity: 6 MWT distance</b> (2 studies) n = 22 O<sup>2</sup> + n= 22 control, <b>GRADE: Low</b> Effect: WMD (95% CI): -23.87 metres (-81.55 to 33.82)</p> <p><b>Functional ex. capacity: 6 MWT end-of-test Borg dyspnea</b> (2 studies) n = 22 O<sup>2</sup> + n = 22 control, <b>GRADE: Low</b> Effect: WMD (95% CI): 0.06 Borg units (-0.89 to 1.00)</p> <p><b>CRQ dyspnea</b> (2 studies) n = 26 O<sup>2</sup> + n = 27 control, <b>GRADE: Low</b> Effect: WMD (95% CI): 0.03 (-0.54 to 0.59)</p> <p>&gt;&gt; This review provides little support for oxygen supplementation during exercise training for individuals with COPD, but the evidence is very limited.</p>	<p>AMSTAR- I Score: 9/11</p> <p>y-n-y-y-y-y-y-y-n</p>
<p>Ekström M. Oxygen for breathlessness in patients with chronic obstructive pulmonary disease who do not qualify for home oxygen therapy. Cochrane Database of Systematic Reviews 2016;(11).</p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To determine the efficacy of oxygen versus air in mildly hypoxaemic or non-hypoxaemic patients with COPD</li> <li>• <b>Suchzeitraum:</b> to 7/2016</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b> people with COPD and mild or no hypoxaemia (partial pressure of oxygen (PaO<sub>2</sub>) &gt; 7.3 kPa) who were not already receiving LTOT; &gt; 18 years</li> <li>• <b>Intervention:</b> oxygen delivered through a non-invasive method</li> <li>• <b>Vergleich:</b> air delivered through the same non-invasive method</li> </ul>	<p><b>Breathlessness - all trials</b> (Lower score indicates improvement in breathlessness), n=865, 32 RCT, <b>GRADE: Low</b> - Effect: SMD <b>0.31, SD lower</b> (95% CI 0.43 lower to 0.2 lower) - Comment: This corresponds to 0. 65 points lower (0.90 lower to 0.42 lower) on a 0-10 NRS.*</p> <p><b>Health- related quality of life - all trials</b> (Higher scores indicate improved healthrelated quality of life), n=267, 5 RCT, <b>GRADE: Low</b> - Effect: SMD <b>0.12, SD higher</b> (95% CI 0.04 lower to 0.28 higher) - Comment: This corresponds to 0. 25 points higher (0.09 lower to 0.59 higher) on a 0-10 NRS.*</p> <p>*Difference on a 0-10 NRS calculated using the SD of 2.1 for the COPD group in Abernethy 2010 for individual participant data.</p>	<p>AMSTAR- I Score: 9/11</p> <p>y-n-y-y-y-y-y-y-n</p>



Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006429.pub3/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006429.pub3/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>eingeschlossene Studien:</b> n=33 eingeschlossene RCTs für Metaanalyse (n=901 eingeschlossene Patient*innen)</li> </ul>	<p><u>Adverse events</u> were insufficiently and inconsistently reported; therefore, meta-analysis was not possible.</p> <p>&gt;&gt; We found that oxygen can modestly reduce breathlessness. To be effective, oxygen has to be given during exercise. Most studies evaluated oxygen given during exercise testing in the laboratory. Oxygen therapy during daily life had uncertain effects on breathlessness and did not clearly change patient quality of life.</p>	
<p>Menadue C. Non-invasive ventilation during exercise training for people with chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2014;(5).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007714.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD007714.pub2/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To determine whether NIV during exercise training (as part of pulmonary rehabilitation) affects exercise capacity, HRQL and physical activity in people with COPD compared with exercise training alone or exercise training with sham NIV.</li> <li>• <b>Suchzeitraum:</b> 1/1987 and 11/ 2013</li> <li>• <b>Population:</b> Patient*innen mit stabiler COPD</li> <li>• <b>Einschlusskriterien:</b> no history of an exacerbation was reported over the past month</li> <li>• <b>Ausschlusskriterien:</b> participants with non-COPD respiratory disease or participants with concomitant neuromuscular disease, a restrictive thoracic disorder, significant cardiac failure or cardiac disease if data from participants with COPD could not be analysed separately.</li> <li>• <b>Interventionen:</b> application of NIV (including bilevel, inspiratory pressure support and proportional assist ventilation) delivered via a mask or mouthpiece during all supervised exercise training sessions</li> <li>• <b>Vergleich:</b> exercise training with or without sham NIV during all supervised exercise training sessions</li> <li>• <b>eingeschlossene Studien:</b> n=6 eingeschlossene RCTs oder Randomised cross-over trials für Metaanalyse (n=126 eingeschlossene Patient*innen)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- mean age: ranged from 63 to 71 years</li> <li>- men= n = 93 of 108 (für 5/6 Studien berichtet)</li> <li>- mean FEV1: 26% to 41%predicted</li> </ul> </li> </ul> <p><u>Exercise capacity: percentage change in peak work rate</u> Incremental cycle or incremental treadmill test, I<sup>2</sup>: 0%, n=60 (3 RCTs), <b>GRADE: Low</b></p> <ul style="list-style-type: none"> <li>- Exercise training alone or exercise training with sham non-invasive ventilation: ranged from a mean of 9% to 38%</li> <li>- Non-invasive ventilation during exercise training: in intervention groups was <b>17% higher</b> (7% to 27% higher)</li> </ul> <p><u>Exercise capacity: percentage change constant work rate</u> endurance time Constant work rate cycle endurance test, I<sup>2</sup>: 0%, n=48 (2 RCTs), <b>GRADE: Low</b></p> <ul style="list-style-type: none"> <li>- Exercise training alone or exercise training with sham non-invasive ventilation: ranged from a mean of 74% to 88%</li> <li>- Non-invasive ventilation during exercise training: in the intervention groups was <b>59% higher</b> (4% to 114% higher)</li> </ul> <p><u>Health-related quality of life</u>, Change in total score (SGRQ), I<sup>2</sup>: 0%, n= 48 (2 RCTs), <b>GRADE: Moderate</b></p> <ul style="list-style-type: none"> <li>- Non-invasive ventilation during exercise training: Mean health-related quality of life in the intervention groups was <b>2.45 points higher</b> (2.3 lower to 7.2 higher)</li> <li>- Physical activity: outcome was not reported in any of the included studies</li> <li>- No information regarding adverse events or cost was reported.</li> </ul>	<p>AMSTAR- I Score: 11/11</p> <p>y-y-y-y-y-y-y-y-y</p>
<p>Struik FM. Nocturnal non-invasive positive</p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To assess the effects of nocturnal-NIPPV at home via nasal mask or face mask in people with COPD by using a meta-analysis based on individual patient data (IPD).</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- mean age: 67; men= 77%; mean FEV1: 0.73 L, mean PaCO2: 53 mmHg</li> </ul> </li> <li>• NIPPV during the night for 3 and 12 months in people with COPD who had raised levels</li> </ul>	<p>AMSTAR- I Score: 9/11</p> <p>y-y-y-y-n-y-y-ca-y-y</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>pressure ventilation for stable chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2013;(6).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002878.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002878.pub2/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Suchzeitraum:</b> up to 8/2012</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Interventionen:</b> nocturnal-NIPPV (applied through a nasal or facemask) at home for at least five hours per night, for at least three consecutive weeks plus standard therapy</li> <li>• <b>Vergleich:</b> standard therapy alone</li> <li>• <b>eingeschlossene Studien:</b> n=7 eingeschlossene RCTs für Metaanalyse ( n=245 eingeschlossene Patient*innen)</li> </ul>	<p>of carbon dioxide had no clinically or statistically significant effect on gas exchange, six-minute walking distance, health-related quality of life, lung function, respiratory muscle strength and sleep efficiency. This means we found little or no difference in the outcomes.</p> <p><b>Nocturnal non-invasive positive pressure ventilation compared with standard treatment</b></p> <p><b>6MWD after 3 months,</b> n=40 (3 RCTs), <b>GRADE: Low</b>                  Standard treatment: The mean 6MWD in the control group was 324 m                  Nocturnal-NIPPV: The mean 6MWD in the intervention group was <b>27,7 higher</b> (95% KI -11,0; 66,3)</p> <p><b>Quality of life: SGQR after 12 months,</b> n=103 (2 RCTs), <b>GRADE: Low</b>                  Standard treatment: The mean SGRQ in the control group was 60,15                  Nocturnal-NIPPV: The mean SGRQ Total score in the intervention group was <b>0,90 higher</b> (95% KI -19,21; 21,01)</p>	
<p>Kopsaftis Z, Carson-Chahhoud KV, Austin MA, et al. Oxygen therapy in the pre-hospital setting for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2020; 1:CD005534.</p> <p><a href="http://www.ncbi.nlm.nih.gov/pubmed/31934729">http://www.ncbi.nlm.nih.gov/pubmed/31934729</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To determine the effect of different inspired oxygen concentrations ("high flow" compared to "controlled") in the pre-hospital setting (prior to casualty/emergency department) on outcomes for people with acute exacerbations of COPD (AECOPD).</li> <li>• <b>Suchzeitraum:</b> 16 September 2019</li> <li>• <b>Population:</b> people with acute exacerbations of COPD (AECOPD)</li> <li>• Ein- und Ausschlusskriterien</li> <li>• <b>Intervention:</b> titrated oxygen therapy</li> <li>• <b>Vergleich:</b> high-flow oxygen therapy</li> <li>• <b>eingeschlossene Studien:</b> 1 RCT, n=214 participants</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika:</b> mean age 68 years</li> <li>• <b>mortality (respiratory- related and allcause)</b> <ul style="list-style-type: none"> <li>- reduction in pre/in-hospital mortality: in favour of the titrated oxygen group (two deaths in the titrated oxygen group compared to 11 deaths in the high-flow control arm)</li> <li>- RR 0,22 (95% KI 0,05; 0,97); 1 RCT, n=214; <b>GRADE: low</b></li> <li>- absolute effect of 94/1000 (high-flow oxygen) vs 21/1000 (titrated oxygen)</li> <li>- number needed to treat for an additional beneficial outcome (NNTB): 14 (95% KI 12; 355) with titrated oxygen therapy</li> </ul> </li> <li>• <b>Arterial blood gas (pH);</b> 1 RCT, n=214; <b>GRADE: low</b> <ul style="list-style-type: none"> <li>- titrated oxygen therapy: MD <b>0.06 pH higher</b> (0.04 lower to 0.16 higher)</li> <li>- high-flow oxygen therapy: mean arterial blood gas (pH) was 7.29</li> </ul> </li> <li>• <b>Ventilation of any type</b> <ul style="list-style-type: none"> <li>- titrated oxygen therapy: 96 per 1000 (41 to 221)</li> <li>- high-flow oxygen therapy: 143 per 1000</li> <li>- RR 0.67 (95% KI 0,29; 1,55); 1 RCT, n=189, <b>GRADE: low</b></li> </ul> </li> <li>• <b>Length of hospital stay;</b> 1 RCT, n=214; <b>GRADE: low</b> <ul style="list-style-type: none"> <li>- titrated oxygen therapy: MD <b>0.88 days lower</b> (2.25 lower to 0.49 higher)</li> <li>- high-flow oxygen therapy: mean length of hospital stay was 6.3 days</li> </ul> </li> </ul> <p>&gt;&gt; The one included study found a reduction in pre/in-hospital mortality for the titrated oxygen arm compared to the high-flow control arm. However, the paucity of evidence</p>	<p>AMSTAR- II                  Qualität des Reviews: hoch</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
		somewhat limits the reliability of these findings and generalisability to other settings. There is a need for robust, well-designed RCTs to further investigate the effect of oxygen therapies in the pre-hospital setting for people with AECOPD.	

### Anhang 7.3 Ganzkörpervibration

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Zhou J. Whole-body vibration training - better care for COPD patients: A systematic review and meta-analysis. Int J Chron Obstruct Pulmon Dis 2018; 13:3243–54.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pub-med/30349230">https://www.ncbi.nlm.nih.gov/pub-med/30349230</a>.</p>	<ul style="list-style-type: none"> <li>• Metaanalyse, nur RCT</li> <li>• Herkunft: China</li> <li>• Suchzeitraum: 04/2018</li> <li>• Population: Patient*innen mit COPD</li> <li>• Interventionen: WBVT vs. conventional training</li> </ul> <p>• <b>Einschlusskriterien:</b></p> <ol style="list-style-type: none"> <li>1) patients with COPD;</li> <li>2) compare the effects difference between WBVT and conventional training;</li> <li>3) be RCTs;</li> <li>4) written in English</li> </ol> <p>• <b>Ausschlusskriterien:</b></p> <ol style="list-style-type: none"> <li>1) were reviews, letters, conference abstracts, book chapters, animal experiments, and case reports;</li> <li>2) essential information was incomplete;</li> <li>3) WBVT was not conducted for the purpose of improving patient's condition.</li> </ol> <ul style="list-style-type: none"> <li>• Endpunkte: functional exercise capacity, pulmonary function, and quality of life in COPD</li> <li>• Anzahl eingeschlossener Studien n=8 RCTs (eingeschlossene Patient*innen: n=365):             <ul style="list-style-type: none"> <li>- Glocckl 2012</li> <li>- Pleguezuelos 2013</li> <li>- Greulich 2014</li> <li>- Braz Júnior 2015</li> <li>- Salhi 2015</li> <li>- Spielmanns 2017 (1)</li> <li>- Glocckl 2017</li> <li>- Spielmanns 2017 (2)</li> </ul> </li> </ul>	<p><b>Baseline-Charakteristika</b></p> <ul style="list-style-type: none"> <li>• mainly elderly (average age: 58 to 75 years), community dwelling, and functionally independent</li> <li>• 1 study included people with exacerbated COPD (Greulich 2014)</li> <li>• other trials studied individuals with stable COPD</li> <li>• Generally, no special intervention was performed in a control group, but three trials performed physiotherapy (Greulich 2014), calisthenics training ( Spielmanns 2017), and conventional resistance training (Salhi 2015)</li> </ul> <ul style="list-style-type: none"> <li>• <u>WBVT increased</u> <ul style="list-style-type: none"> <li>- 6-minute walking distance (6-MWD) (WMD: 62.14 m; 95% CI: 48.12–76.16; P,0.001),</li> <li>- the change of 6-MWD (<math>\Delta</math>6-MWD) (WMD: 42.33 m; 95% CI: 15.21–69.45; P=0.002),</li> <li>- the change of the time to finish five repeated sit-to-stand tests (WMD: -2.07 seconds; 95% CI: -4.00 to -0.05; P=0.04),</li> </ul> </li> <li>• <u>WBVT decreased</u> <ul style="list-style-type: none"> <li>- the change of St George's Respiratory Questionnaire score (WMD: -6.65 points; 95% CI: -10.52 to -2.78; P,0.001).</li> </ul> </li> <li>• <u>no significant difference</u> was found between the two groups regarding             <ul style="list-style-type: none"> <li>- sit-to-stand test, 6-MWD (% predicated),</li> <li>- change of 6-MWD (% predicated),</li> <li>- St George's Respiratory Questionnaire score,</li> <li>- COPD Assessment Test score,</li> <li>- and change of COPD Assessment Test score.</li> </ul> </li> </ul> <ul style="list-style-type: none"> <li>• Subgruppenanalyse: <u>Side-alternating vibration</u> was applied in five trials in</li> </ul>	<p><b>AMSTAR-II:</b> Critically Low</p>	<ul style="list-style-type: none"> <li>• Bemerkungen zur Heterogenität der in den Review eingeschlossenen Studien:             <ul style="list-style-type: none"> <li>- differierende Interventionen in den Kontrollgruppen; unterschiedliche Trainingsprotokolle --&gt; ggf. Einfluss auf Vergleichbarkeit der Ergebnisse</li> </ul> </li> <li>• Verbesserung von             <ul style="list-style-type: none"> <li>- Mobilität/Funktionalität</li> </ul> </li> <li>• Keine Verbesserung der             <ul style="list-style-type: none"> <li>- COPD-Symptomatik</li> <li>- Lebensqualität</li> </ul> </li> <li>• der "type of WBVT" scheint Einfluss auf die Trainingseffekte zu haben (siehe Ergebnisse der Subgruppen-Analyse)</li> </ul>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
		<p>which 6-MWD did not show significant differences between two groups (WMD: 38.91, 95% CI: -1.11 to 78.92, P=0.11), but the change of 6-MWD (WMD: 43.73, 95% CI: 14.84–72.62, P=0.003) increased above the minimal clinically important difference (MCID) of 35 m.</p> <p><u>Vertical vibration</u> was applied in the remaining three trials, but patients enrolled in these trials did not show any improvement in their 6-MWD (WMD: 38.66, 95% CI: -47.22 to 125.54, P=0.38) and change of 6-MWD (WMD: 40.51, 95% CI: -40.49 to 121.52, P=0.33) significantly.</p> <p><u>Conclusion:</u> WBVT has beneficial effects on functional exercise capacity for COPD patients.</p>		
<p>Gloeckl R. Whole body vibration training in patients with COPD: A systematic review. Chron Respir Dis 2015; 12(3):212–21.  <a href="https://www.ncbi.nlm.nih.gov/pub-med/25904085">https://www.ncbi.nlm.nih.gov/pub-med/25904085</a>.</p>	<ul style="list-style-type: none"> <li>• Systematische Übersichtsarbeit; keine Metaanalyse, Einschluss RCT und NRSI</li> <li>• Suchzeitraum: 09/2014 (updated 02/2015)</li> <li>• Population: Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- were full papers published as original articles</li> <li>- were written in English</li> </ul> </li> <li>• <b>Ausschlusskriterien:</b> <ul style="list-style-type: none"> <li>- any kind of chest wall vibration for the purpose of mucus clearance</li> <li>- Book chapters, letters to the editor, unpublished work, and study protocols</li> </ul> </li> <li>• <b>Interventionen:</b> Trials studied either the effects of WBVT - versus an inactive control group,                             <ul style="list-style-type: none"> <li>- versus sham WBVT</li> <li>- during an acute COPD exacerbation or</li> <li>- as a modality on top of conventional endurance and strength training.</li> </ul> </li> <li>• Endpunkte: functional exercise capacity</li> <li>• Anzahl eingeschlossener Studien: n=4 RCTs, n=2 NRSIs (Non-randomized intervention with crossover to sham)                             <ul style="list-style-type: none"> <li>- Gloeckl 2012 (RCT)</li> <li>- Furness 2013 (NRSI)</li> <li>- Pleguezuelos 2013 (RCT)</li> </ul> </li> </ul>	<p>All randomized trials reported a significantly superior benefit on exercise capacity (6-minute walking distance) in favor of the WBVT group. Although there are only few studies available, there is some preliminary evidence that WBVT may be an effective exercise modality to improve functional exercise capacity in patients with COPD.                      (Details siehe Tabelle 2; <b>alle 4 RCTs: Studienqualität HIGH nach GRADE</b>)</p>	<p><b>AMSTAR-II:</b> Critically Low</p>	<p>Keine Metaanalyse durchgeführt, da zu große Heterogenitäten zwischen den einzelnen Studien (Methodik, Studienziele, WBVT-Protokolle) --&gt; dafür qualitative Auswertung vorhanden                      (Up to now, a meta-analysis and reliable comparison of these studies is not possible due to inhomogeneous study protocols and settings (study period, WBV device, WBV parameters, exercises performed on the WBV platform, disease severity, etc.))</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<ul style="list-style-type: none"> <li>- Furness 2014 (NRSI)</li> <li>- Greulich 2014 (RCT)</li> <li>- Braz Júnior 2015 (RCT)</li> </ul>			

### Anhang 7.4 Häusliche Trainingstherapie

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität (AMSTAR)
<p>Ashworth NL. Home versus center based physical activity programs in older adults. Cochrane Database of Systematic Reviews 2005;(1).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004017.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004017.pub2/abstract</a></p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004017.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD004017.pub2/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n= 2 (für COPD-Subgruppe, mit 68 eingeschlossenen Patient*innen)</li> <li>• <b>Suchzeitraum:</b> until 09/2002</li> <li>• <b>Population:</b> older adults (50 years or older); eine Subgruppe mit COPD</li> <li>• <b>Einschlusskriterien für COPD-Subgruppe:</b> Existing Chronic Obstructive Pulmonary Disease (COPD) and allied conditions plus pneumoconiosis and other lung diseases due to external agents</li> <li>• <b>Interventionen:</b> 'home based' vs. 'center based' exercise program</li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Measures of functional activity (ADLs, walking ability etc)</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Long-term maintenance of physical activity (e.g. activity log book, Community healthy activities model program for seniors-CHAMPS, etc)</li> <li>- Measures of Quality of Life (SF36, Sickness impact pro le, etc)</li> <li>- Cost</li> <li>- Health Service utilization</li> </ul> </li> <li>• <b>Sekundäre Endpunkte COPD related:</b> <ul style="list-style-type: none"> <li>- Mortality</li> <li>- Lung function tests</li> <li>- Exercise capacity</li> </ul> </li> </ul>	<p><u>Physiological measures:</u> Two trials looked at older adults with COPD. In patients with COPD the evidence is conflicting. One study showed similar changes in various physiological measures at 3 months that persisted in the home based group up to 18 months but not in the center based group. The other study showed significantly better improvements in physiological measures in the center based group after 8 weeks but again the possibility of a training effect is high.</p> <p><u>Quality of life:</u> n=1 Studie: Compared with controls, significantly more participants in the exercise groups experienced 'better' general well-being at 3 months (80% for center, 73% for home versus 47% for control) and 18 months (62% for center, 64% for home versus 50% for control). There was no significant difference between home and center groups however.</p> <p>= Strijbos 1996: the home based program consisted of frequent and <u>direct supervision</u> by a qualified physiotherapist, home-care nurse and general practitioner and was scored at 10. Baseline: n=30 participants Outcome: Quality of Life (General well-being) after 18 month Home-based vs. center-based: 8/13 vs. 9/14 better well-being OR [95%CI]: 0.89 [ 0.19, 4.24 ]</p> <p><u>Methodische Qualität:</u> Allocation concealment was 'unclear' in all the studies. None of the participants in the included studies were blinded to the interventions (for obvious reasons). None of the investigators/assessors appeared to be blinded either however. Dropouts were well described and reached a maximum of approximately 16%. Both studies were 'medium' quality.</p>	n-n-y-y-y-y-n-y-y-n
McCarthy B. Pulmonary rehabilitation	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n= 65 eingeschlossene RCTs für Metaanalyse ( n= 3822 eingeschlossene Patient*innen)</li> </ul>	>> This review highlights that pulmonary rehabilitation improves the health-related quality of life of people with COPD. Results	y-y-y-y-y-y-y-y-n

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität (AMSTAR)
<p>for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2015;(2).</p> <p><a href="http://online.library.wiley.com/doi/10.1002/14651858.CD003793.pub3/abstract">http://online.library.wiley.com/doi/10.1002/14651858.CD003793.pub3/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Suchzeitraum:</b> current as of 04/2014</li> <li>• <b>Population:</b></li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- participants had COPD</li> <li>- any or all participants were on continuous oxygen</li> </ul> </li> <li>• <b>Ausschlusskriterien:</b> <ul style="list-style-type: none"> <li>- who were mechanically ventilated; or</li> <li>- who had an acute exacerbation within four weeks before commencement of the intervention</li> </ul> </li> <li>• <b>Interventionen:</b> <ul style="list-style-type: none"> <li>• <b>Pulmonary rehabilitation</b> (Any in-patient, out-patient, community-based or home-based rehabilitation programme of at least four weeks' duration that included exercise therapy with or without any form of education and/or psychological support delivered to patients with exercise limitation attributable to COPD. We included any exercise therapy that included physical activity considered to be aerobically demanding.)</li> <li>vs. <b>Usual Care</b> (without education or additional interventions)</li> </ul> </li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li><u>Disease-specific health-related quality of life (HRQoL)</u></li> <li>- Chronic Respiratory Disease Questionnaire (CRQ)</li> <li>- St. George's Respiratory Questionnaire (SGRQ)</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Functional exercise capacity assessments</li> <li>- ◦ Six-minute walk test/distance (6MWT/6MWD)                             <ul style="list-style-type: none"> <li>◦ Incremental shuttle walk test (ISWT)</li> <li>◦ Endurance shuttle walk test (ESWT)</li> </ul> </li> <li>- Maximal exercise tests                             <ul style="list-style-type: none"> <li>◦ Incremental cycle ergometry</li> </ul> </li> </ul> </li> </ul>	<p>strongly support inclusion of pulmonary rehabilitation as part of the management and treatment of patients with COPD.</p> <p><u>QoL - Change in CRQ (dyspnoea)</u> CRQ Questionnaire.(Higher is better and 0.5 unit is an important difference), n=1283 (19 RCTs), <b>GRADE: Moderate</b> Usual care: Median change = 0 units Rehabilitation versus usual care: Mean QoL - change in CRQ (Dyspnoea) in the intervention groups was <b>0.79 units higher</b> (0.56 to 1.03 higher) MD 0.79, 95%CI 0.56 to 1.03; I<sup>2</sup>= 63%</p> <p><u>QoL - Change in CRQ (fatigue)</u> MD 0.68 (95%CI 0.45, 0.92), I<sup>2</sup>= 64%, 19 RCT, n = 1291, <b>GRADE:low</b></p> <p><u>QoL - Change in CRQ (Emotional funtion)</u> MD 0.56 (95%CI 0.34, 0.78), I<sup>2</sup>=58% , 19 RCT, n = 1291, <b>GRADE: nicht angegeben</b></p> <p><u>QoL - Change in CRQ (Mastery)</u> MD 0.71 (95%CI 0.47, 0.95), I<sup>2</sup>=63%,19 RCT, n = 1212, <b>GRADE:low</b></p> <p><u>QoL - Change in SGRQ (total)</u> (Lower is better and 4 units is an important difference), I<sup>2</sup>=59%, n=1146 (19 RCTs), <b>GRADE: Moderate</b> Usual care: Median change = 0.42 units Rehabilitation versus usual care: Mean QOL - change in SGRQ (total) in the intervention groups was <b>6.89 units lower</b> (-6.89 (95%CI -9.26; -4.52)</p> <p><u>Change in maximal exercise</u> (Incremental Shuttle walk test (ISWT)), n=694 (8 RCTs); <b>GRADE: Moderate</b> Usual care: Median change = 1 metre Rehabilitation versus usual care: Mean maximal exercise (incremental shuttle walk test) in the intervention groups was <b>39.77 metres higher</b> (22.38 to 57.15 higher)</p> <p><u>Change in functional exercise capacity</u> (6MWT)), n=1879 (38 RCTs), <b>GRADE: Very low</b> Usual care: Median change = 3.4 metres Rehabilitation versus usual care: Mean functional exercise capacity (6MWT) in the intervention groups was <b>43.93 metres higher</b> (32.64 to 55.21 higher)</p> <p><u>Aussagen des Reviews zu Home-based Rehabilitation:</u></p>	

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität (AMSTAR)
		<ul style="list-style-type: none"> <li>• Only six studies reported patient-based programmes, three of which were combined with a home-based follow-up component. Thirty-seven studies were hospital out-patient based; eight of these included a home-based element. In all, 21 programmes were community based, 11 of which were entirely home based, and one programme combined community- and home-based components.</li> </ul> <p><u>Rehabilitation versus usual care (subgroup analysis hospital versus community-based pulmonary rehabilitation)</u></p> <ul style="list-style-type: none"> <li>• In total, 39 included studies were considered to have a hospitalbased PR intervention delivered on an in-patient or out-patient basis. A total of 25 studies focused on programmes that were delivered in the community at community centres or in individuals' homes. One study had both a community-based and an out-patient- based intervention group, so it was excluded from the subgroup analysis (Mendes De Oliveira 2010).</li> <li>• In the subgroup analysis for the CRQ domain outcomes, the 'community' subgroup included nine studies and the 'hospital group' included 10 studies. For SGRQ outcomes, the community subgroup included nine studies and the hospital subgroup included 10 studies.</li> <li>• Evidence suggested a significant difference in treatment effect between subgroups for all domains of the CRQ, with higher mean values, on average, in the PR group in hospital than in the community- based group (Analysis 2.1; Analysis 2.2; Analysis 2.3; Analysis 2.4). No subgroup differences were reported for any of the SGRQ domains (Analysis 2.5; Analysis 2.6; Analysis 2.7; Analysis 2.8).</li> </ul> <p>&gt;&gt; hier: homebased &amp; community-based Therapien zusammen betrachtet; kein direkter Vergleich.</p>	

## Anhang 7.5 Atemtechniken

### Active chest physiotherapy

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
Basri R. Short-term effects of chest physiotherapy in acute exacerbation of chronic obstructive pulmonary disease. Journal of	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> To find out the short-term effects of chest physiotherapy in acute exacerbation of COPD</li> <li>• <b>Studiendesign:</b> double blinded RCT</li> <li>• <b>Population:</b> patients with AECOPD;</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> leichte Differenzen bezüglich Alter und Exazerbations-Historie</li> <li>- The Mean age of the subjects in group A was 53±3.7 years while in group B Mean age was 55±3.8 years.</li> <li>- baseline Means of VAS, SaO2 and PEFR of both the groups indicates that the patients were similar on baseline.</li> </ul>	<p><b>Selection bias</b>                      Randomisierung: <b>gering</b>                      Allocation concealment: <b>gering</b>                      Verblindung von Teilnehmern und Personal: <b>gering</b></p> <p><b>Detection bias</b>                      Verblindung der Ergebnisevaluation: <b>gering</b></p> <p><b>Attrition bias</b></p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>medical sciences (peshawar) 2017; 25(3):323–7. <a href="http://www.jmedsci.com/index.php/Jmedsci/article/view/31">www.jmedsci.com/index.php/Jmedsci/article/view/31</a></p> <p>• Nicht zitiert.</p>	<p>n=60</p> <ul style="list-style-type: none"> <li>• <b>Intervention:</b> 2 weeks - active chest physiotherapy techniques along with medical treatment &gt; included Breathing control exercise; Thoracic expansion exercises (incl. pursed lips), Forced expiration technique)</li> <li>• <b>Vergleich:</b> - only medical treatment</li> <li>• Pakistan</li> <li>• Messmethoden: visual analogue scale (VAS) for breathlessness</li> </ul>	<p>- experimental group showed more improvement on</p> <ul style="list-style-type: none"> <li>- Peak Expiratory Flow Rates (PEFR) (P&lt;0.05),</li> <li>- SaO2 (P&gt;0.05)</li> <li>- VAS for breathlessness (P&lt;0.05).</li> </ul> <p><b>Control group:</b> Reported Mean difference (paired t-test) for</p> <ul style="list-style-type: none"> <li>- VAS was 0.40±0.63 with P=0.03</li> <li>- PEFR 2.00±25.89 with P=0.76</li> <li>- SaO2 -3.7±3.10 with P=0.00 using 95% CI.</li> </ul> <p><b>Experimental group:</b> Reported Mean difference (paired t-test) for</p> <ul style="list-style-type: none"> <li>- VAS for breathlessness was 4.78±1.12 with P=0.03</li> <li>- PEFR -5.35±5.35 with P=0.02</li> <li>- SaO2 -3.64±3.20 with P=0.01 with 95% CI.</li> </ul> <p>- Mean difference (independent t-test) for VAS, SaO2 and for PEFR between groups (group A and B) using the 95% CI was 1.53, -6.7 and -25.65 respectively with statistically significant value (p&lt;0.05).</p>	<p>Verlust von Studienteilnehmern/ fehlende Daten: <b>unklar</b></p> <p>ITT-Analyse: nicht durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>unklar</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: <b>unklar</b> Interessenkonflikte/ Sponsoring: angegeben</p>

**Manual Chest Physiotherapy**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Cross JL. Evaluation of the effectiveness of manual chest physiotherapy techniques on quality of life at six months post exacerbation of COPD (MATREX): A randomised controlled equivalence trial. BMC Pulm Med 2012; 12:33. <a href="https://www.ncbi.nlm.nih.gov/pubmed/22748085">https://www.ncbi.nlm.nih.gov/pubmed/22748085</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> Manual chest physiotherapy: assessed its effectiveness on disease-specific quality of life.</li> <li>• <b>Studiendesign:</b> randomised controlled equivalence trial</li> <li>• <b>Population:</b> patients hospitalised with AECOPD; n=526</li> <li>• <b>Intervention:</b> Manual chest physiotherapy(MCP) + advice on airway clearance</li> <li>• <b>Vergleich:</b> advice on chest clearance alone</li> </ul> <p>&gt;active cycle of breathing techniques (ACBT) was used in both arms</p> <ul style="list-style-type: none"> <li>• <b>Follow-up:</b> 6 months</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, Geschlecht; Rauchstatus; SGRQ Baseline weitestgehend ausgeglichen</li> <li>- All patients were included in the analyses, of which 372 (71%) provided evaluable data for the primary outcome.</li> <li>- effect size of 0.3 standard deviations in SGRQ score was specified as the threshold for superiority</li> <li>- ITT analyses indicated no significant difference at 6 months post randomisation in             <ul style="list-style-type: none"> <li>-- <u>total SGRQ score</u> [adjusted effect size (no MCP - MCP) 0.03 (95% confidence interval, CI -0.14 to 0.19)],</li> <li>-- <u>SGRQ symptom score</u> [adjusted effect size 0.04 (95% CI -0.15 to 0.23)],</li> <li>-- <u>SGRQ activity score</u> [adjusted effect size -0.02 (95% CI -0.20 to 0.16)] or</li> <li>-- <u>SGRQ impact score</u> [adjusted effect size 0.02 (95% CI -0.15 to 0.18)].</li> </ul> </li> </ul>	<p><b>Selection bias</b> Randomisierung: <b>gering</b> Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>hoch</b> Kommentar:</p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>unklar</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>gering</b> ITT-Analyse: durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>unklar</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: gering Interessenkonflikte/ Sponsoring: angegeben</p>



Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<ul style="list-style-type: none"> <li>• Studienzeitraum: November 21, 2005, and April 30, 2008</li> <li>• UK; multicentre</li> <li>• Messmethoden: SGRQ</li> </ul>	<ul style="list-style-type: none"> <li>• <b>authors conclusion:</b> These data do not lend support to the routine use of MCP in the management of acute exacerbation of COPD. However, this does not mean that MCP is of no therapeutic value to COPD patients in specific circumstances.</li> </ul>	
<p>Rocha T. The Manual Diaphragm Release Technique improves diaphragmatic mobility, inspiratory capacity and exercise capacity in people with chronic obstructive pulmonary disease: A randomised trial. <i>Journal of physiotherapy</i> 2015; 61(4):182–9. <a href="https://www.ncbi.nlm.nih.gov/pubmed/26386894">https://www.ncbi.nlm.nih.gov/pubmed/26386894</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> Manual Diaphragm Release Technique: Does the technique also improve exercise capacity, maximal respiratory pressures, and kinematics of the chest wall and abdomen?</li> <li>• <b>Studiendesign:</b> RCT; Single-centre</li> <li>• <b>Population:</b> clinically stable COPD; n=20</li> <li>• <b>Intervention:</b> six treatments with the <u>Manual Diaphragm Release Technique</u> on non-consecutive days within a 2-week period</li> <li>• <b>Vergleich:</b> sham treatments</li> <li>• Italien</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> weitestgehend ausgeglichen (Alter, Gewicht; Geschlecht)</li> <li>- The Manual DiaphragmRelease Technique significantly improved diaphragmatic mobility over the course of treatments, with a between-group difference in cumulative improvement of 18 mm (95% CI 8 to 28).</li> <li>- The technique also significantly improved the 6- minute walk distance over the treatment course, with a between group difference in improvement of 22 m (95% CI 11 to 32).</li> </ul>	<p><b>Selection bias</b> Randomisierung: unklar Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>gering</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>unklar</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>gering</b> ITT-Analyse: durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>gering</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: <b>gering</b> Interessenkonflikte/ Sponsoring: angegeben</p>
<p>Engel RM. Medium term effects of including manual therapy in a pulmonary rehabilitation program for chronic obstructive pulmonary disease (COPD): A randomized controlled pilot trial. <i>J Man Manip Ther</i> 2016; 24(2):80–9.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> To investigate the effect of including manual therapy (MT) in a pulmonary rehabilitation program for patients with COPD.</li> <li>• Studiendesign: RCT</li> <li>• <b>Population:</b> Patient*innen mit COPD; n=33</li> <li>• <b>Interventionen:</b> MT intervention:2/week for 8 weeks</li> </ul>	<ul style="list-style-type: none"> <li>• Baseline-Patientencharakteristika: hinsichtlich Alter und RR weitestgehend ausgeglichen, leichte Unterschiede im Baseline SGRQ und 6MWD</li> <li>- p=0.02 Unterschied bezüglich Geschlecht (Baseline)</li> <li>- aged between 55 and 70 years (mean =65.5±4 years)</li> <li>• <b>Ergebnisse primärer Endpunkt:</b> significant difference in FVC between the three groups at 24 weeks (P=0.04). For the ST+SM+PR group versus PR only the increase was 0.40 l (CI:</li> </ul>	<p><b>Selection bias</b> Randomisierung: <b>gering</b> Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>gering</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>gering</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>unklar</b> ITT-Analyse: durchgeführt</p> <p><b>Reporting bias</b></p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<a href="https://www.ncbi.nlm.nih.gov/pubmed/27559277">https://www.ncbi.nlm.nih.gov/pubmed/27559277</a>	<p>- <u>soft tissue therapy (ST) + PR</u> &gt;&gt; ST: gentle Effleurage, friction, and crossfiber friction massage applied to the muscles of the posterior chest wall</p> <p>- <u>spinal manipulative therapy (SM) + ST + PR</u> &gt;&gt; SM: high velocity low amplitude (HVLA) joint manipulation to the thoracic inter-vertebral, costo-vertebral, and costo-transverse joints</p> <p>• <b>Vergleich:</b> <u>pulmonary rehabilitation (PR) only</u> (24-week program)</p> <p>• Australien</p> <p>• Messmethoden: 6-minute walking test (6MWT), St. George's respiratory questionnaire (SGRQ), and the hospital anxiety and depression (HAD)</p>	<p>0.02, 0.79; P=0.03).</p> <p>• <u>weitere Ergebnisse</u></p> <p>- ST+SM+PR group compared to PR only: difference between groups for <i>distance walked</i> (6MWT) at 16 (P=0.01) and 24 weeks (P=0.03).</p> <p>- <i>changes in 6MWT</i> for the ST+PR and ST+SM+PR groups individually compared to PR only were not significant at either 16 or 24 weeks (P=1.0 and 0.2; P=0.8 and 0.4 respectively).</p> <p>- There were no differences between groups for the SGRQ or HAD.</p> <p>• <b>Sicherheit:</b> No major or moderate adverse events (AE) were reported following the administration of 131 ST and 272 SM interventions.</p>	<p>selektive Ergebnisdarstellung: unklar</p> <p><b>Andere Biasursachen</b></p> <p>Baseline imbalance: unklar</p> <p>Interessenkonflikte/ Sponsoring: angegeben</p>

**Intrapulmonary percussive ventilation**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Reychler G. Intrapulmonary Percussive Ventilation as an Airway Clearance Technique in Subjects With Chronic Obstructive Airway Diseases. <i>Respir Care</i> 2018; 63(5):620–31.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/29692351">https://www.ncbi.nlm.nih.gov/pubmed/29692351</a>.</p>	<p>• <b>Fragestellung:</b> to summarize the physiological and clinical effects related to the use of IPV as an airway clearance technique in chronic obstructive airway diseases</p> <p>• <b>Suchzeitraum:</b> to May 2017</p> <p>• <b>Population:</b> Subjects &gt; 5 y old with obstructive disease (cystic fibrosis, asthma, <b>COPD</b>, bronchiectasis), stable or exacerbated</p> <p>• <b>Interventionen:</b> Use of intrapulmonary percussive ventilation as airway</p>	<p>• systematischer Review ohne Meta-Analyse</p> <p>• Baseline-Charakteristika COPD-Studien:</p> <p>- 3 studies were performed in ICUs during an exacerbation, - 2 studies were performed in stable out-patients.</p> <p><b>Cardiorespiratory Parameters, Lung Function, and Lung Mechanics in COPD</b></p> <p>- In subjects with COPD in stable conditions and during exacerbation, all cardio-respiratory parameters, lung function, and lung mechanics decreased with IPV. (n=3 studies) [...]</p> <p>- After 1 d of treatment in stable subjects, 1 study showed an improvement in inspiratory and expiratory muscle strength.</p>	<p>AMSTAR-II:</p> <p>- critically low</p>	<p>Only one of the included studies had a sample size &gt; 50 subjects.</p> <p>Subgruppe für COPD: 6 Studien</p> <p>- Antonaglia (RCT)</p> <p>- Ides (Observational)</p> <p>- Nava (RCT)</p> <p>- Testa (controlled)</p> <p>- Vargas RCT</p> <p>- Vargas (Observational)</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<p>clearance technique</p> <ul style="list-style-type: none"> <li>• <b>Vergleich:</b> No airway clearance technique used, placebo or other airway clearance techniques</li> <li>• <b>eingeschlossene Studien:</b> n=12 studies; n= 278 participants                             <ul style="list-style-type: none"> <li>- für COPD: n=6 studies (RCTs, controlled, observational); n=178 participants</li> </ul> </li> </ul>	<p><b>Length of Hospital Stay and Other Clinical Outcomes in COPD</b></p> <ul style="list-style-type: none"> <li>- The length of hospital stay was reduced by IPV compared to other airway clearance techniques or to a classical medical treatment alone in 2 studies in subjects with COPD during exacerbation.</li> <li>- In 1 study, a decrease in the need for mechanical ventilation was observed.</li> </ul> <p><b>Adverse Effects and Drop-Outs in COPD.</b> In subjects with COPD,</p> <ul style="list-style-type: none"> <li>- 2 studies revealed complications or discomfort.</li> <li>- Even though some subjects were intubated after inclusion in 1 study, it was not related to IPV.</li> <li>- In another study, 2 subjects did not tolerate settings with a higher frequency of percussions (1.220 cm H<sub>2</sub>O-350 c/min and 1.840 cm H<sub>2</sub>O-350 c/min).</li> </ul> <p>The main findings showed that IPV improves gas exchange during exacerbation and could reduce the hospital length of stay for patients with COPD.</p> <p>&gt;&gt; CONCLUSIONS: The systematic use of IPV as an airway clearance technique in chronic obstructive airway diseases is not supported by sufficiently strong evidence to recommend routine use in this patient population. However, IPV could offer some benefits in patients with COPD during exacerbation by improving gas exchange and by possibly reducing the length of hospital stay.</p>		

**Chest wall oscillation**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Goktalay T. Does high-frequency chest wall oscillation therapy have any impact on the infective exacerbations of chronic obstructive pulmonary disease? A randomized controlled single-blind study. Clin Rehabil 2013; 27(8):710–8. <a href="https://www.ncbi.nlm.nih.gov/pubmed/23503735">https://www.ncbi.nlm.nih.gov/pubmed/23503735</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> To investigate the impact of high-frequency chest wall oscillation in chronic obstructive pulmonary disease patients with infective exacerbation.</li> <li>• <b>Studiendesign:</b> randomized controlled single-blind study</li> <li>• <b>Population:</b> Stage III-IV COPD patients hospitalized with acute infective exacerbation; n=50 patients randomised</li> <li>• <b>Intervention:</b> group 2: usual exacerbation</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> bezüglich Alter, Gewicht; BODE Index baseline, 6MWD weitestgehend ausgeglichen</li> <li>- Mean (SD) age of the 50 participants (one (2%) female and 49 (98%) male) was 65.06 years (7.39) (range 45–80).</li> <li>- 50 (100%) patients (25 in Group I and 25 in Group II) were followed up for five days.</li> <li>- Application of high-frequency chest wall oscillation therapy resulted in no significant advantage in all outcomes (p &gt; 0.05).</li> <li>- Mean (SD) baseline <b>BODE index</b> value in Group I was 7.72</li> </ul>	<p><b>Selection bias</b> Randomisierung: <b>unklar</b> Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>unklar</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>unklar</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>unklar</b></p> <p>ITT-Analyse: nicht durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>unklar</b></p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<p>protocol + received additional high-frequency chest wall oscillation therapy (20 minutes three times a day for 5 days)</p> <ul style="list-style-type: none"> <li>• <b>Vergleich:</b> group 1: usual exacerbation protocol</li> </ul> <p>&gt;&gt; All patients have been treated with bronchodilators, antibiotics, if necessary oxygen and patient education, as part of acute chronic obstructive pulmonary disease exacerbation protocol.</p> <ul style="list-style-type: none"> <li>• <b>Follow-up:</b> five-days</li> <li>• Studienzeitraum: April 2009 to July 2011</li> <li>• Türkei</li> <li>• BODE; SGRQ</li> </ul>	<p>(1.76), in Group II (Intervention) was 7.72(1.89) (p = 0.55).                      - On the fifth-day assessment, mean (SD) <b>BODE index</b> value in Group I (usual protocol) was 7.24 (1.83), in group II was 6.44 (2.46) (p = 0.18).</p> <ul style="list-style-type: none"> <li>• "authors conclusion ": The application of high-frequency chest wall oscillation therapy offers no additional advantages on infective exacerbations in chronic obstructive pulmonary disease.</li> </ul>	<p><b>Andere Biasursachen</b>                      Baseline imbalance: <b>gering</b>                      Interessenkonflikte/ Sponsoring: angegeben</p>
<p>Nicolini A. Safety and effectiveness of the high-frequency chest wall oscillation vs intrapulmonary percussive ventilation in patients with severe COPD. Int J Chron Obstruct Pulmon Dis 2018; 13:617–25.  <a href="https://www.ncbi.nlm.nih.gov/pubmed/29497290">https://www.ncbi.nlm.nih.gov/pubmed/29497290</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> adding IPV or HFCWO to the best pharmacological therapy (PT) may provide additional clinical benefit over chest physiotherapy in patients with severe COPD.</li> <li>• <b>Studiendesign:</b> 4-week parallel randomized controlled study</li> <li>• <b>Population:</b> patients with severe COPD; bronchial hypersecretion, and effective cough</li> <li>• <b>Intervention:</b> treatment for 2 weeks                      - IPV-group: IPV group (treated with PT and IPV; percussive ventilator = IPV Impulsator, Percussionaire); n=20                      - HFCWO-group: PT group with (treated with PT and HFCWO; using a percussive vest; 20 minutes and was performed twice a day) n=20</li> <li>• Vergleich: control group (treated with PT alone) n=20</li> <li>• Follow-up</li> <li>• ggf. Informationen zu Aufhebung der Verblindung und Cross-over</li> <li>• relevante Ein- und Ausschlusskriterien</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, Geschlecht, Gewicht; Exazerbations-Historie weitestgehend ausgeglichen</li> <li>- Patients in both the IPV group and the HFCWO group showed a significant improvement in the tests of dyspnea and daily life and health status assessment (mMRC, BCSS, and CAT) compared to those in the control group.</li> <li>- Moreover, IPV patients showed an improvement in BCSS (p,0.001) and CAT (p,0.02) scores in comparison with HFCWO.</li> <li>- authors conclusion: The two techniques improved daily life activities and lung function in patients with severe COPD. IPV demonstrated a significantly greater effectiveness in improving some pulmonary function tests linked to the small bronchial airways obstruction and respiratory muscle strength and scores on health status assessment scales (BCSS and CAT) as well as a reduction of sputum inflammatory cells compared with HFCWO.</li> </ul>	<p><b>Selection bias</b>                      Randomisierung: <b>gering</b>                      Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b>                      Verblindung von Teilnehmern und Personal: <b>unklar</b></p> <p><b>Detection bias</b>                      Verblindung der Ergebnisevaluation: <b>gering</b></p> <p><b>Attrition bias</b>                      Verlust von Studienteilnehmern/ fehlende Daten: <b>unklar</b>                      ITT-Analyse: nicht durchgeführt</p> <p><b>Reporting bias</b>                      selektive Ergebnisdarstellung: unklar</p> <p><b>Andere Biasursachen</b>                      Baseline imbalance: gering                      Interessenkonflikte/ Sponsoring: angegeben</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<ul style="list-style-type: none"> <li>• Studienzeitraum</li> <li>• Italien</li> <li>• Messmethoden: CAT; BCSS; mMRC</li> </ul>		

**Positive expiratory pressure (PEP)**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Venturelli E. Efficacy of temporary positive expiratory pressure (TPEP) in patients with lung diseases and chronic mucus hypersecretion. The UNIKO(R) project: A multicentre randomized controlled trial. Clin Rehabil 2013; 27(4):336–46. <a href="https://www.ncbi.nlm.nih.gov/pubmed/22967853">https://www.ncbi.nlm.nih.gov/pubmed/22967853</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> To evaluate whether temporary positive expiratory pressure provides benefit in patients with lung diseases and chronic hypersecretion.</li> <li>• <b>Studiendesign:</b> Single blind multi-centre randomized trial</li> <li>• <b>Population:</b> patients with COPD and/or chronic bronchitis (n=78), or bronchiectasis (n=20), with a peak cough expiratory flow &gt;150 l/min and sputum production &gt;30 ml/day</li> <li>• <b>Intervention:</b> 10 consecutive days: - twice a day 20-minute cycles of manually assisted breathing techniques in sequence with the <u>addition of 15 minutes of temporary positive expiratory pressure</u></li> <li>• <b>Vergleich:</b> manually assisted breathing techniques alone.</li> <li>• Studienzeitraum: July 2008 to December 2010</li> <li>• Five Italian rehabilitation centres; in-patient</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> signifikant (p=0,017) mehr Frauen in der Interventionsgruppe; hinsichtlich Alter, Gewicht; Verteilung der Erkrankungen weitestgehend ausgeglichen</li> <li>- TPEP device (UNIKO)</li> <li>- No significant changes were recorded for the oxygenation index, while dynamic lung volumes and respiratory muscle strength significantly (P &lt;0.05) improved in the active group.</li> <li>- The group comparison analysis of the pre-to-post change showed that inspiratory capacity was significantly higher in the active than in the control group (+19.5% and +2.2%, P=0.044) at day 10.</li> <li>- A greater improvement in Δ-visual analog scale was recorded in the active group at day 3 and 8.</li> </ul>	<p><b>Selection bias</b> Randomisierung: <b>gering</b> Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>unklar</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: unklar</p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>hoch</b> ITT-Analyse: angewendet</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>gering</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: ggf. Gender-Imbalance</p> <p>Interessenkonflikte/ Sponsoring: Col der Autoren nicht angegeben</p>	<p>Endpunkte klinisch relevant?</p>
<p>Nicolini A. Use of positive expiratory pressure during six minute walk test: Results in patients with moderate to severe chronic ob-</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> investigate if the use of a positive expiratory pressure device could improve the distance walked by patients with moderate to severe COPD</li> <li>• <b>Studiendesign:</b> prospective RCT</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, Geschlecht, Lungenfunktionsparameter weitestgehend ausgeglichen</li> <li>- The average age of the participants was 71.9 ± 4.0 in the PEP group and 72.1 ± 4.1 in control group.</li> </ul>	<p><b>Selection bias</b> Randomisierung: <b>gering</b> Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>unklar</b></p>	

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>structive pulmonary disease. Multidiscip Respir Med 2013; 8(1):19.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/23497658">https://www.ncbi.nlm.nih.gov/pubmed/23497658</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Population:</b> patients with moderate to severe COPD (in and out- patients): n=100</li> <li>• <b>Intervention:</b> <ul style="list-style-type: none"> <li>- 6 MWT with PEP</li> <li>- PEP device consisted of a PEP valve 5 cmH2O connected to 1-meter tube and a mouthpiece</li> </ul> </li> <li>• <b>Vergleich:</b> 6 MWT without PEP</li> <li>• <b>Studienzeitraum:</b> April 2012 to September 2012</li> <li>• Italien</li> </ul>	<p><u>Functional capacity</u> assessed by the distance covered during 6MWT improved in the PEP group more than in the control group.</p> <ul style="list-style-type: none"> <li>- PEP group showed an increase in meters walked (61.66 ± 4.28) versus Control group (3.23 ± 0.59).</li> <li>- The difference was statistically significant (p &lt; 0.001).</li> </ul> <p><u>Oxygen saturation</u> improved to a statistically significant level during 6MWT (p &lt; 0.01). Heart rate was also reduced (p &lt; 0.03).</p>	<p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>gering</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>gering</b> ITT-Analyse: nicht durchgeführt/nicht notwendig</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>unklar</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: <b>gering</b> Interessenkonflikte/ Sponsoring: angegeben</p>	
<p>Osadnik CR. The effect of positive expiratory pressure (PEP) therapy on symptoms, quality of life and incidence of re-exacerbation in patients with acute exacerbations of chronic obstructive pulmonary disease: A multicentre, randomised controlled trial. Thorax 2014; 69(2):137–43.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pubmed/24005444">https://www.ncbi.nlm.nih.gov/pubmed/24005444</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> This study sought to determine the effect of PEP therapy on symptoms, quality of life and future exacerbations in patients with AECOPD</li> <li>• <b>Studiendesign:</b> multicentre RCT</li> <li>• <b>Population:</b> patients with AECOPD and sputum expectoration or a history of chronic sputum production</li> <li>• <b>Intervention:</b> <u>PEP therapy</u> (ia a mask (Astra Tech AB, Molndal, Sweden) in an upright position with elbows resting on a table.) <u>+ usual care</u> (including physical exercise)</li> <li>• <b>Vergleich:</b> <u>usual care</u> (including physical exercise):</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, Geschlecht, Gewicht; Sputumproduktion; Baseline SGRQ weitestgehend ausgeglichen</li> <li>- 90 inpatients (58 men; mean age 68.6 years, FEV1 40.8% predicted)</li> </ul> <p>There were no significant between-group differences over time for</p> <ul style="list-style-type: none"> <li>- <u>BCSS</u> score [mean (SE) at discharge 5.2 (0.4) vs 5.0 (0.4) for PEP and control group, respectively; p=0.978] or</li> <li>- <u>SGRQ</u> total score [41.6 (2.6) vs 40.8 (2.8) at 8 weeks, p=0.872].</li> <li>- <u>Dyspnoea</u> improved more rapidly in the PEP group over the first 8 weeks ( p=0.006), however these benefits were not observed at 6 months.</li> <li>- Exacerbations (p=0.986) and hospitalisations (p=0.359) did not differ between groups.</li> </ul> <p><b>Subgroup analyses</b> The nature (infective or non-infective) of the initial AECOPD</p>	<p><b>Selection bias</b> Randomisierung: <b>gering</b> Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>unklar</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>gering</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>gering</b> ITT-Analyse: nicht durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>gering</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: <b>gering</b> Interessenkonflikte/ Sponsoring: angegeben</p>	

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<p>- medical therapy including bronchodilators, corticosteroids, antibiotics, supplemental oxygen, non-invasive ventilation (NIV) if indicated, prescribed according to hospital protocols;</p> <p>- Physiotherapists: standardised physical exercise training regime that commenced as early as possible with the aim of achieving 30 min/day of walking or equivalent lower limb exercise.</p> <p>• <b>Follow-up:</b> 6 Monate</p> <p>• Studienzeitraum: August 2010 - January 2013</p> <p>• Australien</p> <p>• Messmethoden: SGRQ; BODE; BCSS</p>	<p>(p=0.180) and the need for ventilatory assistance (p=0.342) did not significantly influence the severity of symptoms over time.</p>		
<p>Nicolini A. Comparison of intermittent positive pressure breathing and temporary positive expiratory pressure in patients with severe chronic obstructive pulmonary disease. Arch Bronconeumol 2014; 50(1):18–24. <a href="https://www.ncbi.nlm.nih.gov/pubmed/24321380">https://www.ncbi.nlm.nih.gov/pubmed/24321380</a>.</p>	<p>• <b>Ziel:</b> hypothesis that adding TPEP or IPPB to standard pharmacological therapy may provide additional clinical benefit over, pharmacological therapy only in patients with severe COPD</p> <p>• <b>Studiendesign:</b> single-blind randomised trial</p> <p>• <b>Population:</b> patients with severe COPD</p> <p>• <b>Interventionen:</b></p> <p>- Gruppe 1: Intermittent positive pressure breathing (IPPB) --&gt; 30-minute session twice a day; n=15 participants</p> <p>- Gruppe 2: temporary positive expiratory pressure device (TPEP) --&gt;30-minute session twice a day;</p>	<p>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, Geschlecht, BCSS, CAT und mMRC at Baseline weitestgehend ausgeglichen</p> <p>- average age was 73±6 years in the TPEP group, 70±9 years in the IPPB group and 70±6 years in the control group</p> <p>Both patients in the IPPB group and in the TPEP group showed a significant, improvement in two of three tests (MRC,CAT) compared to the control, group. However,in the group comparison analysis for, the same variables between IPPB group and TPEP group we observed a, significant improvement in the IPPB group (P&lt;/.05 for MRC and P&lt;/.01 for, CAT).</p> <p>&gt;&gt; The two techniques (IPPB and TPEP) improves significantly dyspnea; quality of; life tools and lung function in patients with severe COPD. IPPB demonstrated a greater effectiveness to improve dyspnea and quality of life tools (MRC, CAT) than</p>	<p><b>Selection bias</b> Randomisierung: <b>gering</b> Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>unklar</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>gering</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>gering</b> ITT-Analyse: nicht durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>unklar</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: <b>gering</b></p> <p>Interessenkonflikte/ Sponsoring: angegeben</p>	

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<p>n=15 participants</p> <ul style="list-style-type: none"> <li>• <b>Vergleich:</b> pharmacological therapy alone; n=15 participants</li> <li>• Studienzeitraum: between June 2012 and November 2012.</li> <li>• Italien</li> </ul>	TPEP.		
<p>Nicolini A. Comparison of effectiveness of temporary positive expiratory pressure versus oscillatory positive expiratory pressure in severe COPD patients. Clin Respir J 2018; 12(3):1274–82. <a href="https://www.ncbi.nlm.nih.gov/pubmed/28665556">https://www.ncbi.nlm.nih.gov/pubmed/28665556</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> to compare the effectiveness of 2 devices Temporary PEP (T-PEP) and Oscillatory PEP (O-PEP) [...] in reducing COPD exacerbations and improving respiratory and health status assessment parameters.</li> <li>• <b>Studiendesign:</b> RCT</li> <li>• <b>Population:</b> severe to very severe COPD</li> <li>• <b>Interventionen:</b> ; 12 days long; 30 minutes per session; 2x/day; 2 devices</li> <li>- Temporary PEP (T-PEP) (n=40) and</li> <li>- Oscillatory PEP (O-PEP) (n=40)</li> <li>&gt;&gt; which use PEP applied at a low expiratory pressure of 1 cm H2 O which creates oscillations that decrease bronchial obstruction</li> <li>• <b>Vergleich:</b> control (n=40)</li> <li>• Follow Up: 6 Monate</li> <li>• Studienzeitraum: January 2014 - June 2015</li> <li>• Italien</li> <li>• Messmethoden (CAT, mMRC; BCSS)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, Geschlecht, BCSS, CAT und mMRC at Baseline weitestgehend ausgeglichen</li> <li>- T-PEP statistically reduced the exacerbations after 1 and 3 months compared to the control group.</li> <li>- Both the 2 devices improved dyspnea scale (MMRC), lung function parameters, and health status assessment (CAT) tests compared to the control group.</li> <li>- Both interventions were well-tolerated by our patients.</li> </ul> <p>CONCLUSIONS: O-PEP and T-PEP are useful for COPD treatment but only T-PEP reduces exacerbations. Adding tools for airway clearance to medical therapy can help the management of COPD.</p>	<p><b>Selection bias</b> Randomisierung: <b>gering</b> Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>unklar</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>gering</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>unklar</b></p> <p>ITT-Analyse: nicht durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>unklar</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: <b>gering</b> Interessenkonflikte/ Sponsoring: angegeben</p>	



**Controlled Breathing**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>van Gestel AJ. The effects of controlled breathing during pulmonary rehabilitation in patients with COPD. <i>Respiration</i> 2012; 83(2):115–24.  <a href="https://www.ncbi.nlm.nih.gov/pubmed/21474911">https://www.ncbi.nlm.nih.gov/pubmed/21474911</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> To compare the effects of a conventional 4-week pulmonary rehabilitation program with those of rehabilitation plus controlled breathing interventions.</li> <li>• <b>Studiendesign:</b> RCT; 4 weeks</li> <li>• <b>Population:</b> Patient*innen mit COPD; clinical stable; n=40</li> <li>• <b>Intervention:</b> rehabilitation plus controlled breathing (10 supplemental 30-min sessions of controlled breathing using techniques of respiratory biofeedback training)</li> <li>• <b>Vergleich:</b> rehabilitation (Cardiopulmonary Exercise Training; outpatient clinic 3 times per week (1.5-hour sessions) for 3–4 weeks performing 10 sessions of physical training)</li> <li>• Studienzeitraum: November 2008 and July 2009</li> <li>• Deutschland; Schweiz</li> <li>• Messmethoden: 6-min walking distance (6MWD), health related quality of life (chronic respiratory questionnaire, CRQ) and cardiac autonomic function (rMSSD)</li> <li>• to <u>train effortless diaphragmatic breathing techniques</u> the biofeedback loop starts at the sensor that measures the patient's breathing rhythm at both umbilical and abdominal level</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich ALTER, Größe, Gewicht; Geschlecht; Lungenfunktionsparameter weitestgehend ausgeglichen</li> <li>- Forty COPD patients (23 females) with a mean (SD) age of 66.0 (6.3) years and a FEV1 of 47.1 (18.9) % predicted</li> <li>no statistically significant differences between the two groups regarding</li> <li>-change in FEV 1 (MD -0.8% predicted, 95% CI -4.4 to 2.9% predicted, p = 0.33),</li> <li>- 6MWD (MD 12.2 m, 95% CI -37.4 to 12.2 m, p = 0.16),</li> <li>- CRQ (MD in total score 0.2, 95% CI -0.1 to 0.4, p = 0.11) and</li> <li>- rMSSD (MD 2.2 ms, 95% CI -20.8 to 25.1 ms, p = 0.51).</li> <li>• authors conclusion: In patients with COPD undergoing a pulmonary rehabilitation program, controlled breathing using respiratory biofeedback has no effect on exercise capacity, pulmonary function, quality of life or cardiac autonomic function.</li> </ul>	<p><b>Selection bias</b> Randomisierung: <b>unklar</b> Allocation concealment: <b>unklar</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>unklar</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>unklar</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>gering</b></p> <p>ITT-Analyse: nicht durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>gering</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: <b>gering</b> Interessenkonflikte/ Sponsoring: angegeben</p>
<p>Valenza MC. Effectiveness of controlled breathing techniques on anxiety and depression in hospitalized patients with COPD: A randomized clinical Trial. <i>Respir Care</i> 2014; 59(2):209–15.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> efficacy of controlled breathing techniques in improving dyspnea, sleep disturbance, anxiety, depression, and quality of life</li> <li>• <b>Studiendesign:</b> RCT</li> <li>• <b>Population:</b> Patients hospitalized with acute COPD exacerbation (non-infectious)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter; Rauchstatus; Hospitalisationen/Jahr weitestgehend ausgeglichen; Unterschiede im Baseline SGRQ: Interventionsgruppe annähernd 5 Punkte weniger im Total-Score</li> <li>- 46 male subjects, 67– 86 years old</li> <li><b>mMRC</b></li> <li>-dyspnea scores significantly improved in the intervention group (P =0.004), whereas the control</li> </ul>	<p><b>Selection bias</b> Randomisierung: <b>gering</b> Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>unklar</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>unklar</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>gering</b></p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p><a href="https://www.ncbi.nlm.nih.gov/pubmed/23882107">https://www.ncbi.nlm.nih.gov/pubmed/23882107</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Intervention:</b> 10-day controlled breathing program; 2x/ day; 30 minutes - included: relaxation exercises, pursed-lips breathing, and active expiration</li> <li>• <b>Vergleich:</b> standard medical treatment</li> <li>• Spanien</li> <li>• Messmethoden: Hospital Anxiety and Depression Scale; SGRQ, mMRC; European Quality of Life Questionnaire (EQ-5D)</li> </ul>	<p>group's dyspnea score increased between baseline and discharge.</p> <p>- difference between baseline and discharge: 2,917 ±3,21 (95% CI -1,228 to 0,280)</p> <p><b>Hospital Anxiety and Depression scale</b> - anxiety and depression subscores showed better improvement after the controlled breathing intervention.</p> <p>- <u>Depression:</u> Higher mean change values were found in the depression score (10.56 ± 0.465; 95% CI -9.79 to 1.05 ).</p> <p>- <u>Anxiety:</u> Difference between Baseline and Discharge: 6.314 ± 0.712 (95%CI -18.36 to 2.014)</p> <p><b>European Quality of Life</b> - All subscales showed better improvement at discharge in the intervention group, with greater improvements in the mobility score (difference between baseline and discharge: 0.881 ± 0.789 (95%CI -0.738 to 0.168) and the anxiety/depression score.</p> <p>• authors conclusion: In hospitalized patients with chronic lung disease, controlled breathing techniques improved mobility and reduced dyspnea, anxiety, and depression scores.</p>	<p>ITT-Analyse: durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>unklar</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: <b>unklar</b> Interessenkonflikte/ Sponsoring: no Col</p>
<p>Liu F. Effects of an animated diagram and video-based online breathing program for dyspnea in patients with stable COPD. Patient Prefer Adherence 2013; 7:905–13. <a href="https://www.ncbi.nlm.nih.gov/pubmed/24049441">https://www.ncbi.nlm.nih.gov/pubmed/24049441</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> to evaluate the effectiveness of an online breathing program which included an animated diagram and video-guided instruction on pulmonary function, exercise capacity, and health-related quality of life in patients with COPD.</li> <li>• <b>Studiendesign:</b> RCT</li> <li>• <b>Population:</b> patients with stable COPD; n=60</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, Geschlecht; Gewicht; Rauchstatus weitestgehend ausgeglichen</li> </ul> <p><b>6MWD</b> - increased by 74.6 m in the dyspnea breathing group and decreased by 5.8 m in the control group; this difference was statistically significant (P , 0.05).</p> <p><b>SGRQ</b> - two groups were comparable at baseline on the measures</p>	<p><b>Selection bias</b> Randomisierung: <b>unklar</b> Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>unklar</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>unklar</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>gering</b></p> <p>ITT-Analyse: nicht durchgeführt; Poweranalyse vorhanden</p> <p><b>Reporting bias</b></p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<ul style="list-style-type: none"> <li>• <b>Intervention:</b> web-based home breathing programs; trained for 4 months using an online program which included an animated diagram and video-guided instruction</li> <li>- included: pursed lips breathing, Deep inspiration-slow blowing, Deep inhale-holding-slow exhale, Global exercise</li> <li>• <b>Vergleich:</b> conventional patient education on discharge from hospital</li> <li>• China</li> </ul>	<p>of this questionnaire, ie, impact, activity, symptoms, and total score.</p> <ul style="list-style-type: none"> <li>- statistically significant change in these measures in the dyspnea breathing program group (SGRQ total after 4 month: - 18,6; P &lt; 0.05) and no change in the control group (P &gt; 0.05).</li> </ul>	<p>selektive Ergebnisdarstellung: <b>unklar</b></p> <p><b>Andere Biasursachen</b></p> <p>Baseline imbalance: <b>gering</b></p> <p>Interessenkonflikte/ Sponsoring: no Col</p>
<p>Borge CR. Effects of guided deep breathing on breathlessness and the breathing pattern in chronic obstructive pulmonary disease: A double-blind randomized control study. Patient Educ Couns 2015; 98(2):182–90.  <a href="https://www.ncbi.nlm.nih.gov/pubmed/25468399">https://www.ncbi.nlm.nih.gov/pubmed/25468399</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> to investigate whether guided deep breathing using a device improves breathlessness, quality of life, and breathing pattern in moderate and severe stage of COPD</li> <li>• <b>Studiendesign:</b> double-blind RCT; parallel group</li> <li>• <b>Population:</b> moderate/severe COPD</li> <li>• <b>Interventionen:</b> 4 weeks; all listened to the same music</li> <li>- <u>guided deep breathing group</u> (GDBG); (RespeRate Device)</li> <li>&gt; first time at the hospital for 15 min used and later at home, twice a day (i.e. morning and evening) for four weeks</li> <li>- <u>music listening group</u> (MLG)</li> <li>&gt; were not given any instructions to breathe slowly</li> <li>- <u>sitting still group</u> (SSG)</li> <li>&gt; sit down and listen to the same music for 1-2 min, but without any instructions about breathing or music during the at the rest of the session</li> <li>• Follow-up: 4 months</li> <li>• Studienzeitraum: between July 2011 and September 2013</li> <li>• Norwegen; muticentre</li> </ul>	<ul style="list-style-type: none"> <li>• Baseline-Patientencharakteristika:</li> <li>- Predicted lung function is significantly higher in the SSG compared to GDBG and MLG (p &lt; 0.05)</li> <li>- number of comorbidities was significantly lower in the MLG compared to GDBG and SSG at TI (p &lt; 0,05)</li> <li>- n=150 Teilnehmer</li> </ul> <p><b>GRC Scale</b></p> <p>Positive effects of the GDBG were detected in GRC scale in breathlessness at four weeks (p=0.03) with remaining effect compared to MLG (p=0.04), but not to SSG at four months follow-up.</p> <p>GDBG showed positive effect for respiratory rate (p&lt;0.001) at four weeks follow-up, n=49,</p> <ul style="list-style-type: none"> <li>-Respiratory rate (RR) am Anfang der Session: baseline 16 (SD 5,1); nach 4 Wochen: 13,4 (5,6) = -2,6</li> <li>- Respiratory rate (RR) am Ende der Übung: baseline: 11,8 (5,1); RR nach 4 Wochen: 9 (5) = -2,8</li> </ul> <p><b>SGRQ</b></p> <p>A positive significant change (p&lt;0.05-0.01) was found in all groups of SGRQ symptom score.</p>	<p><b>Selection bias</b></p> <p>Randomisierung: <b>gering</b></p> <p>Allocation concealment: <b>gering</b></p> <p><b>Performance bias</b></p> <p>Verblindung von Teilnehmern und Personal: <b>gering</b></p> <p><b>Detection bias</b></p> <p>Verblindung der Ergebnisevaluation: <b>gering</b></p> <p><b>Attrition bias</b></p> <p>Verlust von Studienteilnehmern/ fehlende Daten: <b>gering</b></p> <p>ITT-Analyse: durchgeführt</p> <p><b>Reporting bias</b></p> <p>selektive Ergebnisdarstellung: <b>unklar</b></p> <p><b>Andere Biasursachen</b></p> <p>Baseline imbalance: <b>hoch</b></p> <p>Interessenkonflikte/ Sponsoring: angegeben</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<ul style="list-style-type: none"> <li>Messmethoden: SGRQ; Global Rating Change scale (GRC)</li> </ul>	<p><b>authors conclusion:</b> GDBG had a beneficial effect on respiratory pattern and breathlessness. MLG and SSG also yielded significant improvements.</p>	
<p>Torres-Sanchez I. Effects of different physical therapy programs on perceived health status in acute exacerbation of chronic obstructive pulmonary disease patients: A randomized clinical trial. <i>Disabil Rehabil</i> 2018; 40(17):2025–31. <a href="https://www.ncbi.nlm.nih.gov/pubmed/28478693">https://www.ncbi.nlm.nih.gov/pubmed/28478693</a>.</p>	<ul style="list-style-type: none"> <li><b>Ziel:</b> To evaluate the repercussion of different physical therapy interventions on the perceived health status of chronic obstructive pulmonary disease (COPD) patients during acute exacerbation</li> <li><b>Studiendesign:</b> RCT</li> <li><b>Population:</b> patients hospitalized due to AECOPD; n=90</li> <li><b>Interventionen:</b> <ul style="list-style-type: none"> <li>controlled breathing (relaxation exercises, pursed lips breathing and active expiration) + range of motion exercises group + standard medical treatment ; daily during 30–40 min or</li> <li>Resistance exercises group (included daily lower limb) + standard medical treatment</li> </ul> </li> <li><b>Vergleich:</b> Control group = standard medical treatment</li> <li>Studienzeitraum: September 2015 to June 2016</li> <li>Spanien</li> <li>Messmethoden: EuroQol-5D (EQ-5D) questionnaire</li> </ul>	<ul style="list-style-type: none"> <li><b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter und Gewicht; Lungenfunktionsparameter weitestgehend ausgeglichen</li> <li>Baseline Dyspnea shows differences between control and controlled breathing+range of motion exercises group (p&lt;0.05).</li> <li>Mean age of the patients was 71.70 ± 9.79 years</li> <li>Perceived health status improved significantly in all groups.</li> <li>Significant differences in: mobility, self-care and usual activities subscales of EQ-5D and Visual Analogue Scale between control and controlled breathing + range of motion exercises group. (favorisiert Intervention)</li> <li>Significant differences were found in all variables except pain between control group and Resistance exercises group. (favorisiert Intervention)</li> <li>usual care and anxiety/depression subscales of EQ-5D showed significant differences between controlled breathing + range of motion exercises group and Resistance exercises group, the improvements being greater in Resistance exercises group.</li> <li>Dyspnea improved in higher measure in Resistance exercises GROUP when compared with control and controlled breathing + range of motion exercises GROUP (mean change 4.09 vs. 2.73 and 2.09 for dyspnea, respectively, and 7.21 vs. 4.79 and 7.27 for FEV1, respectively).</li> </ul> <p>&gt;&gt; In conclusion, short duration physical therapy programs in addition to the standard care appear to be helpful in the management of acute exacerbated COPD patients.</p> <p><b>Tabelle 3</b></p>	<ul style="list-style-type: none"> <li><b>Selection bias</b></li> <li>Randomisierung: <b>gering</b></li> <li>Allocation concealment: <b>gering</b></li> <li><b>Performance bias</b></li> <li>Verblindung von Teilnehmern und Personal: <b>unklar</b></li> <li><b>Detection bias</b></li> <li>Verblindung der Ergebnisevaluation: <b>unklar</b></li> <li><b>Attrition bias</b></li> <li>Verlust von Studienteilnehmern/ fehlende Daten: <b>unklar</b></li> <li>ITT-Analyse: nicht durchgeführt; Poweranalyse erfolgt</li> <li><b>Reporting bias</b></li> <li>selektive Ergebnisdarstellung: <b>gering</b></li> <li><b>Andere Biasursachen</b></li> <li>Baseline imbalance: <b>hoch</b></li> <li>Interessenkonflikte/ Sponsoring: angegeben</li> </ul>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
		Die erste Interventionsgruppe konnte im Vergleich zur Kontrollgruppe signifikante Veränderungen in den Subskalen des EuroQol-5D unter anderem hinsichtlich Mobilität (MD 0,67 (95% KI 0,40; 0,93) vs. MD Kontrollgruppe 0,28 (95%KI 0,10; 0,47)) und alltäglicher Aktivitäten (MD 0,53 (95%KI 0,06; 1,01) vs. MD Kontrollgruppe 0,28 (95%KI 0,05; 0,51)) erreichen. Auch die Krafttrainings-Gruppe konnte in fast allen Bereichen des Testes (Ausnahme Schmerzskala) signifikante Verbesserungen erzielen. Sowohl die Atemnot (Borg-Skala: MD Krafttraining 4,09 (95%KI 2,50; 5,68); MD Atemintervention 2,09 (95%KI 0,63; 3,55); MD Kontrollgruppe 2,73 (95%KI 1,99;3,47), als auch die Einschätzung von Angst und Depression(MD 1,65 (95% KI 1,04; 1,75) vs. MD 0,04 (95%KI 0,06; 0,32) vs. MD 0,04 (95%KI 0,06; 0,32)) verbesserte sich in höherem Maße in der Krafttrainings-Gruppe, es konnten jedoch auch Verbesserungen in den anderen beiden Gruppen aufgezeigt werden.	

**Yoga, Tai Chi, Singing**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
Ngai SP. Tai Chi for chronic obstructive pulmonary disease (COPD). Cochrane Database Syst Rev 2016; 6(6):CD009953. <a href="https://www.ncbi.nlm.nih.gov/pubmed/27272131">https://www.ncbi.nlm.nih.gov/pubmed/27272131</a> .	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=12 eingeschlossene RCTs für Metaanalyse ( n=811 eingeschlossene Patient*innen)</li> <li>• <b>Suchzeitraum:</b> from inception to 9/2015</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b> No exclusions were based on age, gender, disease severity or smoking history.</li> <li>• <b>Interventionen:</b> Tai Chi alone or Tai Chi in addition to an-other intervention vs.usual care or another intervention identical to that used in the Tai Chi group</li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Level of dyspnoea: All measures related to dyspnoea were considered (e.g. Borg Scale, Modified Medical Research Council (MMRC) Dyspnoea Scale, Dyspnoea Visual Analogue Scale (DVAS)).</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- mean age: ranged from 61 to 74 years</li> <li>- Programmes lasted for six weeks to one year</li> </ul> </li> <li>• <b>Tai Chi versus usual care</b> <ul style="list-style-type: none"> <li>Level of dyspnoea Assessed with Modified Borg Scale, n=137 (1 RCT); GRADE: Low                             <ul style="list-style-type: none"> <li>- Usual care: 2.1 units</li> <li>- Tai Chi: 0.2 unit lower (95%CI -0.67 to 0.27 unit)</li> </ul> </li> <li><b>Functional capacity</b> Assessed with 6-minute walk test (metre), n=318 (6 RCTs), GRADE: Very low                             <ul style="list-style-type: none"> <li>- Usual care: Mean 317.38 metres</li> <li>- Tai Chi: 29.64 metres farther (95% CI 10.52 to 48.77 metres)</li> </ul> </li> <li><b>Functional capacity</b> Assessed with endurance shuttle walk test (second), n=38 (1 RCT), GRADE: Low                             <ul style="list-style-type: none"> <li>- Usual care: Mean 430 seconds</li> <li>- Tai Chi: 373 seconds longer (95%CI 135.42 to 610.58 seconds)</li> </ul> </li> <li><b>Quality of life (SGRQ)</b>, n=233 (3 RCTs), GRADE: Very low</li> </ul> </li></ul>	AMSTAR-Score: 9/11  y-n-y-y-y-y-y-y-y-n-y

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<ul style="list-style-type: none"> <li>- Functional capacity or aerobic capacity</li> <li>• Sekundäre Endpunkte:               <ul style="list-style-type: none"> <li>- Pulmonary function</li> <li>- Quality of life status                   <ul style="list-style-type: none"> <li>◦ Generic health-related quality of life</li> <li>◦ Disease-specific health-related quality of life</li> </ul> </li> <li>- Quadriceps or other muscle strength</li> <li>- Balance</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>- Usual care: Mean 48. 93 units</li> <li>- Tai Chi: 7.85 units lower (95%CI -16.53 to 0.83 unit)</li> <li><u>Quality of life (CRQ)</u>, n=?48 (2 RCTs), GRADE: Low</li> <li>- Usual care: Mean 4. 75 units</li> <li>- Tai Chi: 0.41 unit higher (95%CI -0.54 to 1.35 units)</li> <li>&gt;&gt; No adverse events were reported, implying that Tai Chi is safe to practise in people with COPD.</li> </ul>	
<p>McNamara RJ. Singing for adults with chronic obstructive pulmonary disease (COPD). Cochrane Database Syst Rev 2017; 12(12):CD012296. <a href="https://www.ncbi.nlm.nih.gov/pubmed/29253921">https://www.ncbi.nlm.nih.gov/pubmed/29253921</a>.</p> <ul style="list-style-type: none"> <li>• Nicht zitiert.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=3 eingeschlossene RCTs für Metaanalyse ( n=112 eingeschlossene Patient*innen)</li> <li>• <b>Suchzeitraum:</b> inception - 08/2017</li> <li>• <b>Population:</b> Patient*innen mit stabiler COPD</li> <li>• <b>Einschlusskriterien:</b> adults with COPD of any age or disease severity. The COPD was required to be stable. We included participants with COPD who used sup-plemental oxygen.</li> <li>• <b>Interventionen:</b> <ol style="list-style-type: none"> <li>1. singing versus no intervention (usual care) or another control intervention</li> <li>2. singing plus pulmonary rehabilitation versus pulmonary rehabilitation alone</li> </ol> </li> <li>• Primäre Endpunkte:               <ul style="list-style-type: none"> <li>- Health-related quality of life</li> <li>- Dyspnoea</li> </ul> </li> <li>• Sekundäre Endpunkte:               <ul style="list-style-type: none"> <li>- Respiratory muscle strength</li> <li>- Pulmonary function</li> <li>- Psychological status</li> <li>- Functional exercise capacity</li> <li>- Peak exercise capacity</li> <li>- Healthcare utilisation</li> <li>- Physical activity level</li> <li>- Adverse events/side effects</li> </ul> </li> </ul>	<p><b>Baseline-Charakteristika</b></p> <ul style="list-style-type: none"> <li>- mean age: range 67 to 72 years</li> <li>- mean FEV1: range from 37% to 64% of predicted values</li> <li>- frequency of the singing intervention: ranged from 1 to 2 times a week over a 6 to 24 week period.</li> <li>- duration of the singing sessions: 60 minutes (conducted in groups led by a singing teacher)</li> <li>• <u>Health- related quality of life</u> (respiratory specific) SGRQ, n=58 (2 RCTs), GRADE: Low</li> <li>Control: The mean change in SGRQ (total score) ranged across control groups from -5.0 to -0.4</li> <li>Singing: The mean change in SGRQ (total score) in the intervention groups was 0.8 units higher (3. 0 units lower to 4.7 units higher)</li> <li>• <u>Health- related quality of life</u> (generic) SF-36 (Physical Component Summary (PCS) score), n=52 (2 RCTs), GRADE: Low</li> <li>Control: The mean change in SF-36 (PCS score) ranged across control groups from -3.8 to -2.5</li> <li>Singing: The mean change in SF-36 (PCS score) in the intervention groups was 12.6 units higher (5.5 units higher to 19.8 units higher)</li> <li>• <u>Health- related quality of life</u> (generic) SF-36 (Mental Component Summary (MCS) score), n=52 (2 RCTs), GRADE: Low</li> <li>Control: The mean change in SF-36 (MCS score) ranged across control groups from -3.2 to 4.3</li> <li>Singing: The mean change in SF-36 (MCS score) in the intervention groups was 5.4 units higher (3.9 units lower to 14.7 units higher)</li> <li>• <u>Dyspnoea Basal Dyspnea Index</u> (BDI) (score),n=30 (1 RCT), GRADE: Very low</li> <li>Control:The mean change in BDI (score) was 0.3</li> <li>Singing: The mean change in BDI (score) in the intervention groups was 0.4 units</li> </ul>	<p>AMSTAR-Score: 11/11</p> <p>y-y-y-y-y-y-y-y-y-y-y-y-y</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
		<p>higher (0.7 units lower to 1.5 units higher)</p> <ul style="list-style-type: none"> <li>• <u>Psychological status</u>, n= 52 (2 RCT) There was no statistically significant improvement in the HADS anxiety score (MD -1.09, 95% CI - 3.02 to 0.83, n = 52) or HADS depression score (MD -0.87, 95% CI -2.16 to 0.42, n = 52).</li> <li>• <u>Physical activity level</u>: n=24, (1 RCT) There were no statistically significant differences between the singing group and control group for sedentary time (minutes per day), but the confidence interval is wide (MD -8.60, 95%CI -88.33 to 71.13). There were statistically significant differences in the remaining measures of physical activity favouring the control group (steps (steps per day) MD -1774.00, 95% CI -2847.73 to -700.27; physical activity duration (minutes per day) MD -142.20, 95% CI -262.56 to - 21.84; active energy expenditure (kJ per day) MD -373.00, 95% CI -625.28 to -120.72).</li> </ul> <p>No <u>adverse events/side effects</u> were reported by any of included studies</p>	
<p>Cramer 2019. The risks and benefits of yoga for patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis</p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>• Deutschland; UK; Australien</li> <li>• <b>Fragstellung:</b> To determine the effectiveness and safety of yoga interventions on disease symptoms, quality of life and function in patients diagnosed with chronic obstructive pulmonary disease (COPD).</li> <li>• <b>Suchzeitraum:</b> through 6 June 2019</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Interventionen:</b> <ol style="list-style-type: none"> <li>1. Interventions including yoga breathing only (based on yoga theory and/or traditional yoga practices), without physical postures, meditation, or lifestyle advice.</li> <li>2. Complex yoga interventions including yoga breathing and at least 1 of the following: physical postures, meditation, and/or lifestyle advice (based on yoga theory and/or practices).</li> </ol> </li> <li>• <b>Vergleich:</b> no treatment, sham yoga, or any active control intervention</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika:</b> <ul style="list-style-type: none"> <li>- median age of included patients: 57.6 years; the studies included a median of 16.7% female patients.</li> <li>- median duration of yoga interventions: 12 weeks, with a median frequency of five yoga sessions per week.</li> </ul> </li> <li>• <b>effects of yoga compared to no treatment on</b> <ul style="list-style-type: none"> <li>- <u>quality of life</u> on the COPD Assessment Test (MD = 3.81; 95% CI = 0.97 to 6.65; P = 0.009, I2 = 70%; n=3 studies; n=115 participants)</li> <li>- <u>exercise capacity</u> assessed by the 6-minute walk test (MD = 25.53 m; 95% CI = 12.16 m to 38.90 m; P = 0.001, I2 = 0%; n=7 studies; n=288 participants),</li> <li>- <u>pulmonary function</u> assessed by FEV1 predicted (MD = 3.95%; 95% CI = 2.74% to 5.17%; P &lt; 0.001, I2 = 0%; n=3 studies; n=118 participants).</li> </ul> </li> <li>• <b>Subgruppe:</b> <p>In subgroup analyses, when limiting the analysis to studies using breathing-based yoga interventions, we found positive effects compared to no treatment on</p> <ul style="list-style-type: none"> <li>- <u>dyspnea</u> (standardized MD= -0.43 (95% CI -0.81, -0.05; p=0.03; I<sup>2</sup>=0%; n=2 studies; n=11 participants)</li> <li>- <u>exercise capacity</u> (MD= 22.74 m (7.01 m, 38.48 m); p=0.003; I<sup>2</sup>=0%; n=4 studies; n= 146 participants)</li> <li>- <u>predicted forced expiratory volume in one second</u> (MD 3.97% (2.79%, 5.15%); p&lt; 0,001; I<sup>2</sup>=0%; n=3 studies; n=138 participants)</li> </ul> </li> </ul>	<p>AMSTAR-II: - critically low</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<ul style="list-style-type: none"> <li>• <b>eingeschlossene Studien:</b> n=11 RCTs (n=586 participants)</li> </ul>	<p>When limiting the analysis to complex yoga interventions, we only found effects on exercise capacity.</p> <ul style="list-style-type: none"> <li>• <b>Sicherheit:</b> <ul style="list-style-type: none"> <li>- 2/ 11 studies reported safety-related outcomes. (a case of cancer; hospitalizations - no reasons reported)</li> <li>- None of these studies reported whether the adverse events were intervention-related or not.</li> </ul> </li> </ul> <p>&gt;&gt; Effects were only present in breathing-focused yoga interventions but not in interventions including yoga postures.                  &gt;&gt; Yoga may be an effective option for improving physical capacity and breathing parameters in chronic obstructive pulmonary disease rehabilitation.                  &gt;&gt; The safety of yoga in chronic obstructive pulmonary disease is inconclusive due to insufficient safety reporting in clinical trials to date.</p>	

**Diaphragmatic breathing**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Yamaguti WP. Diaphragmatic breathing training program improves abdominal motion during natural breathing in patients with chronic obstructive pulmonary disease: A randomized controlled trial. Arch Phys Med Rehabil 2012; 93(4):571–7. <a href="https://www.ncbi.nlm.nih.gov/pubmed/22464088">https://www.ncbi.nlm.nih.gov/pubmed/22464088</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> To investigate the effects of a diaphragmatic breathing training program (DBTP) on thoracoabdominal motion and functional capacity in patients with chronic obstructive pulmonary disease.</li> <li>• <b>Studiendesign:</b> prospective RCT</li> <li>• <b>Population:</b> patients with COPD ((N 30; FEV 1, 42% ± 13% predicted)</li> <li>• <b>Intervention:</b> Subjects in the Training group (TG) completed a 4-week supervised Diaphragmatic breathing training</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, Gewicht, Geschlecht, Schwere der Erkrankung, 6MWD, SGRQ, Bode-Index weitestgehend ausgeglichen</li> <li>- TG showed a greater abdominal motion during natural breathing quantified by a reduction in the RC/ABD ratio when compared with the CG (F=8.66; P&lt;.001).</li> <li>- Abdominal motion during voluntary diaphragmatic breathing after the intervention was also greater in the TG than in the CG (F=4.11; P&lt;.05).</li> <li>- The TG showed greater diaphragmatic mobility after the 4-week DBTP than did the CG (F=15.08; P&lt;.001).</li> <li>- An improvement in the 6-minute walk test and in health-related quality of life was also observed in the TG.</li> </ul> <p><b>Conclusions:</b> DBTP for patients with chronic obstructive pulmonary disease induced increased diaphragm participation</p>	<p><b>Selection bias</b>                      Randomisierung: <b>gering</b>                      Allocation concealment: <b>unklar</b></p> <p><b>Performance bias</b>                      Verblindung von Teilnehmern und Personal: <b>gering</b></p> <p><b>Detection bias</b>                      Verblindung der Ergebnisevaluation: <b>unklar</b></p> <p><b>Attrition bias</b>                      Verlust von Studienteilnehmern/ fehlende Daten: <b>gering</b></p> <p>ITT-Analyse: durchgeführt</p> <p><b>Reporting bias</b>                      selektive Ergebnisdarstellung: <b>unklar</b></p> <p><b>Andere Biasursachen</b>                      Baseline imbalance: gering                      Interessenkonflikte/ Sponsoring: Col nicht beschrieben</p>	<p>Endpunkte klinisch relevant?                      n= 30 Teilnehmer</p> <p>keine Langzeitwirkung untersucht</p>



Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<p>program (DBTP;3 individualized weekly sessions)</p> <ul style="list-style-type: none"> <li>• <b>Vergleich:</b> Controlgroup (CG) received usual care</li> <li>• Brasilien</li> <li>• <b>Endpunkte:</b> <ul style="list-style-type: none"> <li>-rib cage to abdominal motion ratio (RC/ABD ratio) (primary outcome)</li> <li>- diaphragmatic mobility (secondary outcome)</li> </ul> </li> </ul>	during natural breathing, resulting in an improvement in functional capacity.		

**Pursed lips breathing (PLB)**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
Mayer AF, Karloh M, Dos Santos K, de Araujo CLP, Gulart AA. Effects of acute use of pursed-lips breathing during exercise in patients with COPD: a systematic review and meta-analysis. Physiotherapy. 2018 Mar;104(1):9-17	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To investigate the effects of acute use of PLB in exercise performance, dyspnoea, ventilatory parameters and oxygen saturation during exercise in patients with COPD.</li> <li>• <b>Suchzeitraum:</b> up to May 2016.</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- &gt;40 years of age; clinical diagnosed COPD confirmed with spirometry; absence of: pulmonary diseases other than COPD, heart disease and/or neuromuscular disease.</li> </ul> </li> <li>• <b>Interventionen:</b> PLB as a ventilatory strategy during exercise conditions</li> <li>• <b>Vergleich:</b> non-exposed to the PLB group</li> <li>• <b>eingeschlossene Studien:</b> n=8 ; 197 patients (cross-over studies)</li> </ul>	<ul style="list-style-type: none"> <li>• Meta-analysis of PLB acute effect on exercise performance (six minute walk test) Mean Difference (MD): 6.14 (95% CI -35.03, 47.30), n= 2 Studies; 78 participants; I<sup>2</sup>=33%</li> <li>• Meta-analysis of PLB acute effect on dyspnoea evaluated by: <ul style="list-style-type: none"> <li>(A) <u>Visual Analogue Scale</u> MD: -0.11 (95% CI -1.05-0.83); n=2 studies; 44 participants; I<sup>2</sup>=0%</li> <li>(B) <u>BORG dyspnea scale</u> MD: -0.15 (95% CI -0.45-0.15); n= 5 studies; 372 participants; I<sup>2</sup>=0%</li> </ul> </li> <li>&gt;&gt; PLB is effective in reducing minute ventilation and respiratory rate during exercise in patients with COPD. It is still unclear who responds to PLB and how these responders benefit from its use. Further studies with better methodological quality are necessary to understand the implications of its acute use on the functional capacity and symptoms of patients with COPD.</li> </ul>	AMSTAR-II: critically low
Sakhaei S. The Impact of Pursed-lips Breath-	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> to evaluate the effect of PLB on cardiac, pulmonary and oxygenation level in patients with Chronic Obstructive Pulmonary Disease (COPD).</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Gewicht und Größe ausgeglichen; Unterschied hinsichtlich Alter (p= 0.001)</li> <li>- PLB intervention group: patients with mild to moderate disease</li> </ul>	<b>Selection bias</b> Randomisierung: <b>niedrig</b> Allocation concealment: <b>niedrig</b>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>ing Maneuver on Cardiac, Respiratory, and Oxygenation Parameters in COPD Patients. Open Access Maced J Med Sci 2018; 6(10):1851–6. <a href="https://www.ncbi.nlm.nih.gov/pub-med/30455761">https://www.ncbi.nlm.nih.gov/pub-med/30455761</a>.</p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>• <b>Studiendesign:</b> three-group clinical RCT</li> <li>• <b>Population:</b> Patient*innen mit COPD (n=40) + n=20 healthy subjects</li> <li>• <b>Intervention:</b> patients were trained to perform the PLB                             <ul style="list-style-type: none"> <li>- Gruppe 1: n=20 Patienten mit COPD</li> <li>- Gruppe 2: n=20 gesunde Teilnehmer</li> </ul> </li> <li>• <b>Vergleich:</b> received just routine cares and drug treatments.                             <ul style="list-style-type: none"> <li>- Kontrollgruppe: n=20 Patienten mit COPD</li> </ul> </li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- age over 40, diagnosis of COPD, stability in clinical condition, unused rehabilitation programs other than PLB, the absence of underlying chronic illnesses (hypertension, cardiomyopathy, or diabetes) and the patient's willingness to participate in the study.</li> </ul> </li> <li>• Studienzeitraum: 2017</li> <li>• Iran</li> </ul>	<p>were selected</p> <p>On evaluation within the COPD patient intervention group in Saturation of Peripheral Oxygen (SPO2) index with the mean difference of 2.05 percent, Respiratory Rate(RR)-0.65 minute and Pulse Rate(PR)-1.6 bpm was significant (<math>p \leq 0.05</math>), and systolic blood pressure index in healthy subjects was increased (3.35 mmHg).</p>	<p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>unklar</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>unklar</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>hoch</b></p> <p>ITT-Analyse: nicht durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>unklar</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: <b>unklar</b></p> <p><b>Interessenkonflikte/ Sponsoring:</b> Angabe: keine</p>
<p>Collins EG. The Effect of Breathing Retraining Using Metronome-Based Acoustic Feedback on Exercise Endurance in COPD: A Randomized Trial. Lung 2019. <a href="https://www.ncbi.nlm.nih.gov/pub-med/30739217">https://www.ncbi.nlm.nih.gov/pub-med/30739217</a>.</p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>• <b>Ziel:</b> to assess the impact of exercise-training plus breathing-retraining using a metronome-based acoustic feedback on exercise duration, dynamic hyperinflation, and quality of life in patients with moderate-to-severe COPD.</li> <li>• <b>Studiendesign:</b> prospective RCT</li> <li>• <b>Population:</b> Patient*innen mit COPD; n=119</li> <li>• <b>Intervention:</b> exercise training (training on the treadmill for 25 min and progressed as tolerated up to 45 min of exercise) plus breathing-retraining using acoustic feedback (n= 58) &gt;&gt;patients were instructed to inhale through the nose and exhale through the mouth with <u>their lips pursed</u></li> <li>• <b>Vergleich:</b> or exercise-training alone (n= 61)</li> <li>• USA</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika (relevante):</b> hinsichtlich Alter, Gewicht, Lungenfunktionsparameter weitestgehend ausgeglichen</li> <li>- exercised on a treadmill thrice-weekly for 12 weeks</li> </ul> <p>At completion of training, improvements in <b>exercise duration</b> in the breathing-retraining plus exercise-training and exercise-training alone groups <u>were similar</u> (<math>p = 0.35</math>). At isotime, inspiratory capacity increased (less exercise-induced dynamic hyperinflation) by 3% (<math>p = 0.001</math>) in the breathing-retraining plus exercise-training group and remained unchanged in the exercise-alone group. The between-group change in inspiratory capacity, however, was not significant (<math>p = 0.08</math>).</p> <p><b>QoL</b> At the conclusion of training, dyspnea during activities of daily living, fatigue, emotional function and mastery improved in both groups of patients. Improvements in mastery were greater in the breathing-retraining group than in the exercise-alone group (<math>p = 0.042</math>).</p>	<p><b>Selection bias</b> Randomisierung: <b>unklar</b></p> <p>Allocation concealment: <b>unklar</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: Verblindung aufgrund Studienaufbau nicht möglich</p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>unklar</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>niedrig</b></p> <p>ITT-Analyse: nicht durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>unklar</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: <b>niedrig</b></p> <p><b>Interessenkonflikte/ Sponsoring:</b> angegeben</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
		<p>• <b>authors conclusion:</b> In patients with COPD, breathing-retraining using a metronome-based acoustic feedback did not result in improved exercise endurance or decreased dynamic hyperinflation when compared to exercise-training alone.</p>	
<p>Ubolsakka-Jones C. Positive expiratory pressure breathing speeds recovery of postexercise dyspnea in chronic obstructive pulmonary disease. <i>Physiother Res Int</i> 2019; 24(1):e1750.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pub-med/30251299">https://www.ncbi.nlm.nih.gov/pub-med/30251299</a>.</p>	<p><b>Studiendesign:</b> prospective randomized cross-over trial</p> <p><b>Population:</b> n=13 male COPD patients (GOLD II &amp; III)</p> <p><b>Intervention:</b> at the end of exercise (marching): six breaths against a 5-cm H<sub>2</sub>O expiratory load (positive expiratory pressure [PEP]) , with 3-hr rest between interventions</p> <p><b>Vergleich:</b> at the end of exercise: six breaths against no load (Sham)</p> <p>-Recovery was followed for the next 10 min.</p> <p><b>Einschlusskriterien</b></p> <ul style="list-style-type: none"> <li>- clinically stable and free of exacerbations</li> </ul> <p><b>Ausschlusskriterien</b></p> <ul style="list-style-type: none"> <li>- age over 70 years, cardiovascular disease, any musculoskeletal problems that limited exercise, neurological or cognitive impairment, or psychiatric illness</li> </ul> <p><b>Thailand</b></p>	<p>- None of the patients used supplemental oxygen or reported dyspnea at rest.</p> <p>- Dyspnea recovered significantly faster after the PEP intervention in all patients, taking 2.8 ± 0.4 min to return to baseline compared with 5.1 ± 0.6 min for Sham (p &lt; 0.01).</p> <p>- PEP was equally effective in reducing dyspnea in all patients irrespective of the degree of dynamic hyperinflation</p> <p>- Changes in oxygen saturation, end-tidal CO<sub>2</sub>, heart rate, and breathing frequency were similar in PEP and Sham.</p>	<p><b>Selection bias</b></p> <p>Randomisierung: unklar Allocation concealment: unklar</p> <p><b>Performance bias</b></p> <p>Verblindung von Teilnehmern und Personal: hoch</p> <p><b>Detection bias</b></p> <p>Verblindung der Ergebnisevaluation: hoch</p> <p><b>Attrition bias</b></p> <p>Verlust von Studienteilnehmern/ fehlende Daten: unklar ITT-Analyse: nein</p> <p><b>Reporting bias</b></p> <p>selektive Ergebnisdarstellung: unklar</p> <p><b>Andere Biasursachen</b></p> <p>Baseline imbalance: unklar</p> <p><b>Interessenkonflikte/ Sponsoring:</b> Dr Ubolsakka-Jones is academic advisor to the company distributing BreatheMAX (= eingesetztes PEP-Gerät)</p>

**Physiotherapien (verschiedene)**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Zhang C. Effectiveness of physiotherapy techniques for rehabilitation after acute chronic obstructive pulmonary disease exacerbation: A meta-analysis. <i>Int J Clin Exp Med</i> 2018; 11(8):7572–82.</p>	<p>• <b>Fragestellung:</b> to investigate the effect of all potential physiotherapy techniques on motor function in COPD exacerbation patients.</p> <p>• <b>Suchzeitraum:</b> until August 30, 2017,</p> <p>• <b>Population:</b> Patients with severe COPD/after exacerbation</p>	<p><b>ELTGOL</b> is a bronchial de-obstruction technique.</p> <ul style="list-style-type: none"> <li>- no different effect between ELTGOL and the control group in exercise distance (WMD -2.74, 95% CI=-9.76 to 4.29, subgroup I<sup>2</sup>=0%, P=0.44; n=5 studies; 162 participants)</li> <li>- or endurance time (SMD -3.15, 95% CI=-9.58 to 4.05, subgroup I<sup>2</sup>=0%; P=0.83; n=3 studies; 118 Participants)</li> <li>- Thus, the test of overall effect of ELTGOL is undoubtedly insignificant (overall I<sup>2</sup>=0%; P=0.43).</li> </ul>	<p>AMSTAR-II:</p> <ul style="list-style-type: none"> <li>- critically low</li> </ul>	<ul style="list-style-type: none"> <li>- keine verlässliche Metaanalyse: Pooling trotz sehr hoher Heterogenitäten und Verwendung eines fixed effects models</li> <li>- keine methodische Bewertung der eingeschlossenen Studien</li> <li>- keine Aussage zu excluded studies</li> </ul>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>pdfs.semanticscholar.org/2884/726f7d57818c6e9103a926364a2372c48cc7.pdf.</p> <p>• Nicht zitiert.</p>	<p>• <b>Interventionen:</b> verschiedene Physiotherapie-Verfahren</p> <ul style="list-style-type: none"> <li>- High frequency Chest wall oscillation</li> <li>- ELTGOL</li> <li>- TENS</li> </ul> <p>• eingeschlossene Studien: n=13 RCTs</p>	<p><b>HFCWO</b></p> <p>-&gt; studies containing application of HFCWO in COPD exacerbation:</p> <ul style="list-style-type: none"> <li>- increased exercise distance (WMD 23.14, 95% CI=10.93 to 35.36, subgroup I2=50%; P=0.0002; n=4 studies; 143 participants))</li> <li>- and relatively long motor tolerance duration (SMD 60.85, 95% CI=32.81 to 88.89, subgroup I2=35%; P&lt;0.00001; n=4 studies; 175 participants)</li> <li>- Motor function improvement of HFCWO in COPD exacerbation was significantly higher than that in control group (P&lt;0.00001).</li> </ul>		
<p>Ubolnuar N. Effects of Breathing Exercises in Patients With Chronic Obstructive Pulmonary Disease: Systematic Review and Meta-Analysis. Ann Rehabil Med 2019;43(4):509-523</p> <p>• Nicht zitiert.</p>	<p>• <b>Fragestellung:</b> evidence on the effects of breathing exercises (BEs) on ventilation, exercise capacity, dyspnea, and quality of life (QoL) in COPD patients</p> <p>• <b>Suchzeitraum:</b> through May 2018</p> <p>• <b>Population:</b> Patient*innen mit COPD (any stage)</p> <p>• <b>Ausschlusskriterien (Auswahl)</b></p> <ul style="list-style-type: none"> <li>- unstable COPD, on ventilator, or with other diseases, not English, BE was less than 50% of total treatment in the experimental group</li> </ul> <p>• <b>Interventionen:</b> breathing exercises (BE):</p> <ul style="list-style-type: none"> <li>- PLB (pursed-lip breathing),</li> <li>- VF (ventilatory feedback) training,</li> <li>- VF plus exercise,</li> <li>- singing,</li> <li>- DBE (diaphragmatic breathing),</li> <li>- and combined BEs (combination of DBE with other BEs)</li> </ul> <p>• <b>Vergleich:</b> any, except BE</p> <p>• eingeschlossene Studien: n=19 RCTs teilweise cross-over; n=745</p>	<p><b>Pursed-lip breathing</b></p> <p>There was no significant between-group difference [...], dyspnea (p=0.15), and 6MWD (p=0.85).</p> <p><b>Ventilatory feedback training alone</b></p> <p>No significant differences in [...], dyspnea (p=0.15)</p> <p><b>Ventilatory feedback training plus exercise</b></p> <p>There was no significant between-group difference in [...], dyspnea (p=0.83), exercise capacity (p=0.68–0.90), and QoL (p=0.97).</p> <p><b>Singing exercise</b></p> <p>There was moderate quality evidence of significant difference in the physical component summary of SF-36, between the singing group and the control group (MD 12.64 (95% CI 5.50 ; 19.77, n=2 studies; p=0.0005) However, there was no statistically significant difference in other QoL related measures (p=0.07–0.52) or exercise capacity (p=0.44)</p> <p><b>Diaphragmatic breathing</b></p> <p>There was no statistically significant difference in dyspnea (p=0.47) and SGRQ score (p=0.58), between the DBE group and the control group.</p>	<p>AMSTAR-II: critically low</p>	<p>ventilatory related outcomes nicht extrahiert; da bisher nicht in PICO-Frage formuliert</p> <p>nach Recherche veröffentlicht</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	participants • Quality of evidence: low to moderate.			

### Anhang 7.6 Patientenschulung

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
Wittmann M. Patient education in COPD during inpatient rehabilitation improves quality of life and morbidity. <i>Pneumologie</i> 2007; 61(10):636–42. <a href="https://www.ncbi.nlm.nih.gov/pub-med/17886195">https://www.ncbi.nlm.nih.gov/pub-med/17886195</a> .	<ul style="list-style-type: none"> <li>• <b>Studiendesign:</b> prospektiv, randomisiert</li> <li>• <b>Follow-up /Assessments:</b> während der Rehabilitation; nach 12 Monaten</li> <li>• <b>Population:</b> Patient*innen mit COPD (n=212 )</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- Patient*innen mit der Rehabilitations- Indikation chronisch obstruktive Bronchitis</li> <li>- manifeste Obstruktion (FEV1/VC &lt; 70%)</li> <li>- Alter: 18- 70 Jahre</li> </ul> </li> <li>• <b>Ausschlusskriterien:</b> <ul style="list-style-type: none"> <li>- Asthma bronchiale/Allergie der Atemwege, ΔFEV1 nach Bronchospasmyse &gt; 15 %, Notwendigkeit einer intermittierenden Selbstbeatmung, dekompensiertes Cor pulmonale, FEV1/VC &lt; 0,25, maligner Tumor, Herzerkrankung NYHA III -IV, andere schwere Organerkrankungen</li> <li>- unzureichende deutsche Sprachkenntnisse, Schulung über Atemwegserkrankheiten in den letzten 2 Jahren, mangelnde Kooperationsfähigkeit.</li> </ul> </li> <li>• <b>Endpunkte:</b> <ul style="list-style-type: none"> <li>- Sozialmedizinische Parameter</li> <li>- Lebensqualität (SGRQ)</li> </ul> </li> <li>• <b>Studienzeitraum:</b> 06/1999 - 03/2001</li> <li>• Deutschland</li> <li>Schulung + Aktionsplan + multidisziplinäre, stationäre Rehabilitation</li> <li>vs.</li> </ul>	<ul style="list-style-type: none"> <li>• Baseline-Patientencharakteristika: hinsichtlich ALter, Geschlecht, Rauchstatus; Lungenfunktionsparameter weitestgehend ausgeglichen</li> <li>- Kontrollgruppe (KG): n=90, Alter 54,4 ± 6,1 Jahre, FEV1 1,83 ± 0,61</li> <li>- Schulungsgruppe (SG): n=94, Alter 53,5 ± 7,6 Jahre, FEV1 1,81 ± 0,61</li> <li>- Rücklaufquote der Fragebogen nach 1 Jahr: 98%</li> <li>- Drop-Out: n= 28 mit Angabe von Gründen</li> <li><b>Resultate 1 Jahr nach der Rehabilitation:</b>  <u>In beiden Gruppen</u> reduzierte sich im Jahr nach der Rehabilitation                             <ul style="list-style-type: none"> <li>- die Zahl der Krankenhausaufnahmen (KG: 24,7% auf 11,5%, p=0,02; SG: 30,8% auf 9,9%, p = 0,001)</li> <li>- Der Anteil der Raucher*innen in beiden Gruppen war gering unterschiedlich, er blieb bis ein Jahr nach der Rehabilitation unverändert: Kontrollgruppe (n = 88) 41 % Raucher*innen, Schulungsgruppe (n=92) 48%.</li> </ul> </li> <li><u>nur in der SG</u> reduzierte sich:                             <ul style="list-style-type: none"> <li>- die Zahl der Intensivbehandlungstage (11,8 auf 2,2 p = 0,02)</li> <li>- die Inanspruchnahme ärztlicher Notdienste (18,3 auf 5,5 %, p = 0,01)</li> <li>- die Zahl der Notfalleinweisungen (19,6% auf 8,7%, p=0,03)</li> </ul> </li> <li>relevante Besserung der Lebensqualität:                             <ul style="list-style-type: none"> <li>- SG: OR = 2,5; CI 1,07 -5,84; p = 0,03</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li><b>Selection bias</b> Randomisierung: gering Allocation concealment: unklar</li> <li><b>Performance bias</b> Verblindung von Teilnehmern und Personal: nicht möglich</li> <li><b>Detection bias</b> Verblindung der Ergebnisevaluation: unklar</li> <li><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: gering ITT-Analyse: nicht durchgeführt</li> <li><b>Reporting bias</b> selektive Ergebnisdarstellung: unklar</li> <li><b>Andere Biasursachen</b> Baseline imbalance: gering Interessenkonflikte/ Sponsoring: Projekt B4 des Rehabilitationswissenschaftlichen Forschungsverbundes Bayern[...] gefördert von VdR und BMBF. Keine Angaben zu Col der Autoren</li> </ul>	<ul style="list-style-type: none"> <li>• methodische Qualität, keine Angaben zu Interessenkonflikten</li> </ul>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<p>multidisziplinäre, stationäre Rehabilitation</p> <ul style="list-style-type: none"> <li>• <b>Rehabilitation inkludiert:</b> Fachärztliche Optimierung der medikamentösen Therapie, Erlernen der korrekten Inhalationstechniken, körperliches Training, Atemphysiotherapie mit dem Erlernen von Selbstkontroll- und Selbsthilfetechniken, im Bedarfsfall Hilfen zur Tabakentwöhnung, psychologische Unterstützung, Sozialberatung und Ernährungsberatung.</li> <li>• <b>Schulung:</b> <ol style="list-style-type: none"> <li>1. Doppelstunde: <ul style="list-style-type: none"> <li>• Aufbau und Funktion der Atemwege</li> <li>• Chronische Bronchitis und Lungenemphysem: Ursachen, Entstehung, Verlauf</li> <li>• Möglichkeiten der Tertiärprävention</li> </ul> </li> <li>2. Doppelstunde: <ul style="list-style-type: none"> <li>• Grundlagen der Inhalation</li> <li>• Die Medikamente anhand des Stufenplans</li> </ul> </li> <li>3. Doppelstunde: <ul style="list-style-type: none"> <li>• Bedeutung der nichtmedikamentösen Therapiemaßnahmen: <ul style="list-style-type: none"> <li>Physiotherapie, Bronchusdrainage, körperliches Training</li> <li>• Vermeiden von Verschlechterungen, Infektophylaxe</li> <li>• Frühzeitiges Erkennen von Verschlechterungen und richtiges Reagieren</li> </ul> </li> </ul> </li> <li>4. Doppelstunde: <ul style="list-style-type: none"> <li>• Wiederholung und Übung des Erlernten</li> <li>• Steigerung von Krankheitsakzeptanz und Bewältigung im psychosozialen Umfeld</li> </ul> </li> <li>5. Nachbesprechung in der Kleingruppe: <ul style="list-style-type: none"> <li>• Aushändigung des Aktionsplans</li> </ul> </li> </ol> </li> </ul>	<p>- Die geschulten Patient*innen absolvierten nach 1 Jahr vermehrt körperliches Training (Wochentrainingszeit mehr als 1 Stunde: SG n = 58, KG n = 34, p&lt; 0,01).</p>		
<p>Bosch D. COPD outpatient education programme (ATEM) and BODE index. Pneumologie 2007; 61(10):629–35.</p>	<ul style="list-style-type: none"> <li>• <b>Studiendesign:</b> prospektiv, randomisiert</li> <li>• <b>Follow up/ Assessments:</b> bei Eintritt in die Studie; nach 12 Monaten</li> <li>• <b>Population:</b> Patient*innen mit leichter bis sehr schwerer COPD (n=50 eingeschlossen)</li> <li>• <b>Einschlusskriterien:</b></li> </ul>	<ul style="list-style-type: none"> <li>• Baseline-Patientencharakteristika: hinsichtlich Alter, Gewicht, BODE-Index weitestgehend ausgeglichen</li> <li>- aktiver Rauchstatus Intervention: 13%; Kontrollgruppe: 27% --&gt; statistisch nicht signifikant</li> <li>&gt; deutlich mehr Teilnehmer in der Interventionsgruppe (30/38), als in der Kontrollgruppe (11/12)</li> </ul>	<p><b>Selection bias</b> Randomisierung: unklar</p> <p>Allocation concealment: unklar</p> <p><b>Performance bias</b></p>	<ul style="list-style-type: none"> <li>• methodische Qualität, keine Angaben zu Interessenkonflikten</li> <li>• Inbalance in Verteilung der Studienteilnehmer zu den Gruppen (30 vs. 11)</li> </ul>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p><a href="https://www.ncbi.nlm.nih.gov/pub-med/17661240">https://www.ncbi.nlm.nih.gov/pub-med/17661240</a>.</p>	<p>- Diagnose einer COPD; spirometrisch gesicherte Obstruktion; FEV1/VC max &lt;70%</p> <p>• <b>Ausschlusskriterien:</b></p> <p>- Komorbidität mit maßgeblicher Beeinflussung von Lungenfunktion, Symptomatik oder Leistungsfähigkeit (symptomatische kardiopulmonale Zweiterkrankung)</p> <p>• <b>Endpunkte</b> (keine Unterteilung in primär und sekundär)</p> <p>- BODE-Index (BMI, FEV1; mMRC; 6MWD)</p> <p>- Morbiditätsmarker (Hospitalisationsrate; Antibiotikabedarf)</p> <p>• <b>Studienzeitraum:</b> 01/2005 - 01/2006</p> <p>• Deutschland, multicenter study</p> <p>• statistische Auswertung: deskriptiv</p> <p>Schulungsprogramm (ATEM) vs. Standardtherapie (mit späterer Möglichkeit der Schulung)</p> <p>ATEM</p> <p>- ambulantes, strukturiertes, zielgruppenspezifisches Patientenschulungsprogramm</p> <p>- Anleitung zur Lebensstilmodifikation</p> <p>- Kleingruppen; 3 Schulungstermine á 120 min; 1 Nachschulungstermin 6 Wochen später (á 120 min)</p> <p>- Schulung von ausgebildeten Krankenschwestern durchgeführt + fachärztliche Supervision</p>	<p>• <b>Drop Out n=9</b> (ohne Angabe von Gründen) Intervention n=8 (21%) Kontrolle: n=1 (8%)</p> <p>• <b>Interventionsgruppe (I) (n=30); Kontrollgruppe (K) (n=11)</b> (Mittelwert ± SD):</p> <p><u>BODE-Index gesamt</u></p> <p>- <b>I:</b> Start: 3,0 ± 2,0 --&gt; nach 12 Monaten: 2,5 ± 1,6; p=0,047 =&gt; statistisch signifikanter Abfall; Verbesserung von 16,7%</p> <p>- <b>K:</b> Start: 2,6 ± 1,6 --&gt; nach 12 Monaten: 3,6 ± 1,8; p=0,012 =&gt; stat. signifikanter Anstieg</p> <p><u>mMRC</u></p> <p>- <b>I:</b> Start: 1,6 ± 0,9 --&gt; nach 12 Mon.: 1,1 ± 0,8; p=0,005 =&gt; sig. Verbesserung</p> <p>- <b>K:</b> Start: 1,6 ± 0,8 --&gt; nach 12 Mon.: 2,4 ± 0,7; p=0,02 =&gt; sig. Verschlechterung</p> <p><u>6-MWD</u></p> <p>- <b>I:</b> Start: 406 ± 92 --&gt; nach 12 Mon.: 436 ± 94; p=0,001 =&gt; sig. Verbesserung (7,4%)</p> <p>- <b>K:</b> Start: 396 ± 79 --&gt; nach 12 Mon.: 386 ± 99; p=0,3 =&gt; nicht signifikante Verringerung</p> <p><u>sportliche Betätigung (Befragung)</u></p> <p>- <b>I:</b> Start: 27% --&gt; nach 12 Mon.: 60%</p> <p>- <b>K:</b> Start: 27% --&gt; nach 12 Mon.: 45%</p> <p><u>Beeinträchtigung der Lebensführung (Befragung)</u></p> <p>- <b>I:</b> Start: 84% --&gt; nach 12 Mon.: 60%</p> <p>- <b>K:</b> Start: 63% --&gt; nach 12 Mon.: 82%</p> <p><u>COPD-bedingte Krankenhausbehandlungen in den letzten 12 Monaten (Befragung)</u></p> <p>- <b>I:</b> Start: 1,1 ± 1,0 --&gt; nach 12 Mon.: 0,3 ± 0,6; p&lt;0,0001</p> <p>- <b>K:</b> Start + ebenso nach 12 Mon.: 0,6 ± 0,7</p> <p><u>Wissenszuwachs</u> (Ursache der COPD; atemphysikalischer Möglichkeiten; Ernährungszustand, körperliches training; Notfallmedikation)</p> <p><b>I:</b> Start: 2,3 ± 1,1 --&gt; nach 12 Mon.: 4,2 ± 1,1 (p&lt;0,001)</p> <p><b>K:</b> Start: 2,1 ± 1,5 --&gt; nach 12 Mon.: 2,4 ± 1,4 (p=0,4)</p>	<p>Verblindung von Teilnehmern und Personal: nicht anwendbar</p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: unklar</p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: hoch</p> <p>ITT-Analyse: keine ITT-Analyse durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: unklar</p> <p><b>Andere Biasursachen</b> Baseline imbalance: unklar</p> <p>Interessenkonflikte/ Sponsoring: keine Angaben</p>	

Anhang 7.7 Ernährung

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Ferreira IM. Nutritional supplementation for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2012; 12:CD000998. <a href="https://www.ncbi.nlm.nih.gov/pub-med/23235577">https://www.ncbi.nlm.nih.gov/pub-med/23235577</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=17 eingeschlossene RCTs für Metaanalyse ( n= 632 eingeschlossene Patient*innen)</li> <li>• <b>Suchzeitraum:</b> current to 04/2012</li> <li>• <b>Population:</b> Patient*innen mit stabiler COPD</li> <li>• <b>Einschlusskriterien:</b> stable patients with COPD, among whom at least 75% of participants had a forced expired volume in one second (FEV1) less than 70% predicted, and less than 12% reversibility after use of a bronchodilator</li> <li>• <b>Interventionen:</b> <ul style="list-style-type: none"> <li>- subjects received oral, enteral or parenteral nutritional support vs. (i) placebo (ii) their usual diet or (iii) other treatment regimens such as anabolic substances</li> </ul> </li> <li>• <b>Primäre Endpunkte:</b> <ol style="list-style-type: none"> <li>1. Anthropometric measures (body weight, fat-free mass index, lean body mass, mid-arm muscle circumference (MAMC), skinfold measures).</li> <li>2. Functional exercise (timed walk test).</li> </ol> </li> <li>• <b>Sekundäre Endpunkte:</b> <ol style="list-style-type: none"> <li>1. Pulmonary mechanics (lung volumes, respiratory muscle function).</li> <li>2. Peripheral muscle function.</li> </ol> </li> </ul>	<p><u>Anthropometric measures (Illustrative comparative risks* (95% CI)</u></p> <p><b>Weight</b> (mixed population) kg (Follow-up: 2 to 24 weeks; n=512 participants; 14 RCTs; <b>GRADE: moderate</b>)</p> <ul style="list-style-type: none"> <li>- The mean weight (mixed population) in the control groups was 56.43 kg</li> <li>- The mean weight (mixed population) in the intervention groups was 0.69 higher (0.86 lower to 2.24 higher)</li> </ul> <p><b>Weight</b> (undernourished) kg (Follow-up: 2 to 24 weeks; n=325 participants; 11 RCTs; <b>GRADE: moderate</b>)</p> <ul style="list-style-type: none"> <li>- The mean weight (undernourished) in the control groups was 60.34 kg</li> <li>- The mean weight (undernourished) in the intervention groups was 1.65 higher (0.14 to 3.16 higher)</li> </ul> <p><b>Fat-free mass index</b> (mixed population) kg/m<sup>2</sup> (Follow-up: 3 to 4 months; n=93 participants; 3 RCTs; <b>GRADE: low</b>)</p> <ul style="list-style-type: none"> <li>- The mean fat-free mass index (mixed population) in the control groups was 14.8 kg/m<sup>2</sup></li> <li>- The mean fat-free mass index (mixed population) in the intervention groups was 0.08 higher (0.51 lower to 0.66 higher)</li> </ul> <p><b>Fat-free mass index</b> (undernourished patients) kg/m<sup>2</sup> (Follow-up: 3 to 4 months; n=62 participants; 2 RCTs; <b>GRADE: low</b>)</p> <ul style="list-style-type: none"> <li>- The mean fat-free mass index (undernourished patients) in the control groups was 14.5 kg/m<sup>2</sup></li> <li>- The mean fat-free mass index (undernourished patients) in the intervention groups was 0.31 higher (0.32 lower to 0.95 higher)</li> </ul> <p><u>Functional exercise</u></p> <p>There was low-quality evidence (five RCTs, 142 participants) of no significant difference between groups in the six-minute walk distance (MD 14.05 m; 95% CI -24.75 to 52.84), 12-minute walk distance or in shuttle walking. However, the pooled change from baseline for the six-minute walk distance was significant (MD 39.96 m; 95% CI 22.66 to 57.26).</p> <p><u>Health-related quality of life</u></p> <p>There was low-quality evidence (4 RCTs, 130 participants) of no significant difference in HRQoL total score (SMD -0.36; 95% CI -0.77 to 0.06) when pooling results from both the St George's Respiratory Questionnaire (SGRQ) and the Chronic Respiratory Questionnaire (CRQ).</p> <p>Two trials (n=67) used the SGRQ to measure individual domains of activity, impact and symptoms. At the end of treatment, the pooled total SGRQ score was both statistically and clinically significant (MD 6.55; 95% CI -11.7 to -1.41). The 3 RCTs (n=123) that used the CRQ to measure the change in individual domains (dyspnoea, fatigue, emotion, mastery), found no significant difference between groups.</p>	<p>AMSTAR: y-y-y-y-y-y-y-y-n-n</p> <p>Score: 9/11</p>



Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	3. HRQoL derived from validated scales (e.g. St. George's Respiratory Questionnaire (SGRQ), Chronic Respiratory Questionnaire (CRQ), Short-Form-36 (SF-36)).	>> This review of 17 studies (632 participants) that provided nutritional supplementation for patients with COPD for more than two weeks found growing evidence that nutritional supplementation improved body weight, respiratory muscle strength, walking and quality of life.	

### Anhang 7.8 Selektiv eingebrachte Literatur

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
Wiles L, Cafarella P, Williams MT. Exercise training combined with psychological interventions for people with chronic obstructive pulmonary disease. <i>Respirology</i> (Carlton, Vic.) 2015; 20(1):46–55. DOI: 10.1111/resp.12419. <a href="http://www.ncbi.nlm.nih.gov/pubmed/25339508">http://www.ncbi.nlm.nih.gov/pubmed/25339508</a> .	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> to examine the effect of interventions which combine exercise training and psychological interventions for a range of health outcomes in people with COPD</li> <li>• <b>Suchzeitraum:</b> 08/2013</li> <li>• <b>Population:</b> Patient*innen mit COPD oder COPD/ Asthma overlap</li> <li>• <b>Interventionen:</b> All forms of psychological interventions delivered to individuals or groups in conjunction with exercise training or standard comprehensive pulmonary rehabilitation (CPR), of greater than 2 weeks duration in any setting</li> <li>• <b>Vergleich:</b> All comparators which did not include a combination of exercise training and psychological intervention</li> </ul>	<p>keine Metaanalyse aufgrund Heterogenität durchgeführt: Range der SMD beschrieben</p> <p>Compared with control conditions (e.g. wait listing list for active intervention, usual care), SMD consistently favoured interventions which included both exercise + psychological components;  <b>SMD range:</b>                      - dyspnoea -1.63 to -0.25;                      - anxiety -0.50 to -0.20;                      - depression -0.46 to -0.18;                      - QOL 0.09 to 1.16;                      - functional exercise capacity 0.22 to 1.23 ) (siehe Fig. 2a,b).</p> <p>When compared with active comparators (e.g. education/lecture series, exercise/ psychotherapy alone), SMD consistently favoured interventions that included exercise training and a psychological component for                      - dyspnoea (SMD range -0.35 to -0.97),                      - anxiety (SMD range -0.13 to -1.00) and                      - exercise capacity (SMD range 0.64 to 0.71),                      - but were inconsistent for depression (-0.11 to 1.27) and QOL (0.02 to -2.00) (siehe Fig 3a,b)</p>	AMSTAR-II: critically low	selektiv eingebrachte Literatur

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<ul style="list-style-type: none"> <li>eingeschlossene Studien: 12 RCT</li> </ul>			

## Anhang 8 Evidenztabellen Medikamentöse Therapie

### Anhang 8.1 Cochrane Reviews Medikamentöse Therapie

#### SAMA or SAMA/SABA vs. SABA

Zitat	Studiencharakteristika	Population	Methodische Qualität
<p>Appleton S. Ipratropium bromide versus short acting beta-2 agonists for stable chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2006;(2).</p>	<p><b>Suchzeitraum:</b> 07/2008  <b>Fragestellung:</b> relative efficacy and safety of regular long term use (at least four weeks) of ipratropium bromide and short- acting beta- 2 agonist therapy in patients with stable COPD  <b>Setting:</b> outpatient</p> <p><b>Interventionen und Vergleiche:</b> at least 4 weeks of treatment with                      1) <u>Ipratropium bromide vs. SABA</u> (metaproterenol, fenoterol or salbutamol (albuterol)); delivered via nebuliser or MDI (metered dose inhaler)                      2) <u>Ipratropium bromide + SABA versus SABA alone</u> (salbutamol or metaproterenol); delivered via nebuliser or MDI</p> <p><b>Studientyp:</b> RCT  <b>Eingeschlossene Studien:</b> 11 (n=3912 Studienteilnehmer)</p>	<p><b>Population:</b> Non-asthmatic adults with stable COPD</p> <ul style="list-style-type: none"> <li>'Stable' was defined as no recent infections, exacerbations, hospitalisation in the past month + no severe, concurrent other diseases (including cardiac, liver and renal disease)</li> <li><u>COPD definition (BTS 1997):</u> tobacco smoking related, chronic, slowly progressive disorder characterised by airways obstruction (FEV1 &lt;80% predicted and FEV1/FVC ratio &lt;70%) which does not change markedly over several months</li> <li>mean age 64 y. (group 1); mean age 65 y. (group 2)</li> </ul>	<p>y-n-y-y-y-y-n-ca-y-n</p> <p>Score: 7</p>
<b>Studienergebnisse</b>			
<p><b>Ipratropium bromide vs. SABA (n=8 studies)</b>                      1) Health status [health related quality of life scores (HRQL)]                      • Meta-analysis of "between treatment group" differences showed small, statistically significant differences in CRQ domain scores between treatments. These favoured IpB treatment and were found in all four domains of the CRQ (n=1529; studies=5, RoB in 5/5 studies: low):                      - Dyspnoea: MD: 0.16 units (95% CI: 0.09, 0.23), I<sup>2</sup> = 49%;                      - Fatigue: MD: 0.13 units (95% CI: 0.02, 0.23), I<sup>2</sup> = 38%;                      - Emotion: MD: 0.17 units (95% CI: 0.04, 0.29), I<sup>2</sup> = 50%;                      - Mastery: MD: 0.18 units (95% CI: 0.06, 0.30), I<sup>2</sup> = 30%.</p>			

Zitat	Studiencharakteristika	Population	Methodische Qualität
	<p><u>2) Dyspnoea scores ( measured directly, at rest or during exercise, or indirectly by self-report in symptom diaries)</u></p> <ul style="list-style-type: none"> <li>• Symptoms scores did not change significantly over time within any treatment group (studies=3) and metaanalysis showed no statistically significant differences between treatments (n=1533, studies=5) for:                             <ul style="list-style-type: none"> <li>- Wheezing: MD: -0.04 (95% CI: -0.13, 0.04);</li> <li>- Shortness of Breath: MD: 0.00 (95% CI: -0.09, 0.09);</li> <li>- Tightness of Chest: MD: 0.01 (95% CI: -0.06, 0.09).</li> </ul> </li> </ul> <p>SABA treatment however, was associated with a small reduction in the scores for Coughing: MD: -0.08 (95% CI: -0.13, -0.03).</p> <p><u>3) Exercise capacity - six minute walk distance (6MWD), shuttle walk test</u></p> <p>&gt;&gt; keine eindeutige Aussage möglich:</p> <ul style="list-style-type: none"> <li>• n=1 study (small unblinded) found that ipratropium treatment was associated with a significant increase from baseline in the distance walked in the six minute walk test. Another study reported no significant difference in the distance walked in a six minute walk test between the IpB and salbutamol treated groups during the parallel phase (day 43-84) of the trial (n=423; studies=2: MD 62.60 [-15.65, 140.85]), I<sup>2</sup> = not applicable, RoB 1 study: low; 1 study unclear</li> </ul> <p><u>4) Adverse and haemodynamic effects - blood pressure and pulse rate effects from the medication</u></p> <ul style="list-style-type: none"> <li>• regardless of delivery method (MDI, nebulised), fewer subjects receiving IpB experienced medication-related adverse events compared with subjects receiving SABA, either salbutamol or metaproterenol (n=1858; studies=6; Peto OR = 0.71, 95% CI: 0.53, 0.97; I<sup>2</sup> =63% with either fixed or random effects models, RoB 5/6 studies low; 1/6 study unclear)</li> <li>• Subgroup analysis based on type of beta-2 agonist showed that there was no benefit of IpB treatment, when compared with salbutamol, delivered via MDI or nebuliser (Peto OR: 0.94, 95% CI: 0.64, 1.39). However, IpB treatment was associated with significantly less adverse events compared to metaproterenol (Peto OR: 0.47, 95% CI: 0.29, 0.76; I<sup>2</sup> =72%), however the I<sup>2</sup> was high.</li> </ul> <p><b>Kommentar:</b></p> <ul style="list-style-type: none"> <li>• Review von 2006 &gt;&gt; 4 July 2008: New search has been performed: no new studies found</li> <li>• Applikationen siehe S. 5 Review</li> <li>• Differente Angaben bezüglich Anzahl eingeschlossener Studien verschiedener Analysen im Text vs. zusammenfassende Auswertetabellen</li> <li>• teilweise hohe Heterogenität der verglichenen Studien</li> </ul>		

**LAMA vs. SAMA**

Zitat	Studiencharakteristika	Population	Methodische Qualität
<p>Cheyne L. Tiotropium versus ipratropium bromide for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2015;(9).</p>	<p><b>Suchzeitraum:</b> 08/2015</p> <p><b>Fragestellung:</b> relative effects of tiotropium to ipratropium bromide on markers of quality of life, exacerbations, symptoms, lung function and serious adverse events in patients with COPD</p> <p><b>Interventionen und Vergleiche:</b> tiotropium vs. ipratropium</p> <p><b>Studientyp:</b> RCT</p> <p><b>Eingeschlossene Studien:</b> 2 (n=1073)</p>	<p><b>Population:</b> stable (moderate to severe) COPD in adults &gt;&gt; a diagnosis of COPD as defined by an external set of diagnostic criteria (eg. from GOLD, ATS, BTS and TSANZ. - mean age: 65 y.</p> <p><u>Vincken 2002:</u> clinical diagnosis of COPD according to ATS guidance</p> <p><u>Voshaar 2008:</u> spirometric criteria were specified</p>	<p>y-n-y-y-y-y-y-ca-n-y</p> <p>Score: 8</p>

Zitat	Studiencharakteristika	Population	Methodische Qualität
	<p>Theophylline, inhaled steroids and oral steroids (prednisolone) up to and including a dose of 10 mg (if the dose was stable for at least six weeks) were allowed in both studies.</p>		
<b>Studienergebnisse</b>			
<u>Primäre Endpunkte</u>			
<b>SAEs</b>			
<ul style="list-style-type: none"> <li>• fewer people experiencing one or more non-fatal SAEs on tiotropium compared to ipratropium (OR 0.5; 95% CI 0.34 to 0.73, high quality evidence; n=1073; studies=2)</li> </ul> <p>&gt;&gt; absolute reduction in risk from 176 to 97 per 1000 people over three to 12 months</p>			
<b>Disease specific adverse events</b>			
<ul style="list-style-type: none"> <li>• the tiotropium group were less likely to experience a COPD-related serious adverse event when compared to ipratropium bromide (OR 0.59; 95% CI 0.41 to 0.85, moderate quality evidence)</li> </ul>			
<u>Sekundäre Endpunkte</u>			
<b>Hospital admissions</b>			
<ul style="list-style-type: none"> <li>• fewer hospital admissions in the tiotropium group (OR 0.34; 95% CI 0.15 to 0.70, moderate quality evidence; n=538; study=1)</li> </ul>			
<b>patients experiencing one or more exacerbations leading to hospitalisation</b>			
<ul style="list-style-type: none"> <li>• fewer patients on tiotropium (OR 0.56; 95% CI 0.31 to 0.99, moderate quality evidence)</li> </ul>			
<b>Mortality</b>			
<ul style="list-style-type: none"> <li>• no significant difference between the treatments (OR 1.39; 95% CI 0.44 to 4.39, moderate quality evidence; n=1073; studies=2)</li> </ul>			
<b>SGRQ</b>			
<ul style="list-style-type: none"> <li>• the mean SGRQ score at 52 weeks was lower in the tiotropium group than the ipratropium group (lower on the scale is favourable) (MD -3.30; 95% CI -5.63 to -0.97, moderate quality evidence; n=535; study=1).</li> </ul>			
<b>Exazerbations</b>			
<ul style="list-style-type: none"> <li>• fewer participants suffering one of more exacerbations in the tiotropium arm (OR 0.71; 95% CI 0.52 to 0.95, high quality evidence; n=1073; studies=2) and there was also a reported difference in the mean number of exacerbations per person per year which reached statistical significance (MD -0.23; 95% CI -0.39 to -0.07, P = 0.006, moderate quality evidence)</li> </ul>			
<b>Withdrawals</b>			
<ul style="list-style-type: none"> <li>• significantly fewer withdrawals from the tiotropium group (OR 0.58; 95% CI 0.41 to 0.83, high quality evidence; n=1073; studies=2)</li> </ul>			
<b>Kommentar:</b>			
<p>One study used tiotropium via the HandiHaler (18 µg) for 12 months and the other via the RespiMat device (5 µg and 10 µg) for 12 weeks.</p>			

**SAMA or SAMA/LABA vs. LABA**

Zitat	Studiencharakteristika	Population	Methodische Qualität
Appleton S. Ipratropium bromide versus long-acting beta-2 agonists for stable chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2006;(3).	<p><b>Suchzeitraum:</b> 07/2008  <b>Fragestellung:</b> relative efficacy and safety of regular long term use (at least four weeks) of ipratropium bromide and LABA in patients with stable COPD  <b>Setting:</b> outpatient  <b>Interventionen und Vergleiche:</b>                      1) Ipratropium bromide vs. LABA.                      2) Ipratropium bromide + LABA vs. LABA alone  <b>Studientyp:</b> RCT  <b>Eingeschlossene Studien:</b> 7 (n= 2652)</p>	<p><b>Population:</b> Non-asthmatic adults with stable COPD as defined by BTS 1997</p> <p>'Stable' was defined as no recent infections, exacerbations, hospitalisation in the past month.                      - mean age: 63-65 y.</p>	<p>y-n-y-y-y-y-y-y-n-n</p> <p>Score: 8</p>
<p><b>Studienergebnisse</b></p> <p>1) <u>Ipratropium bromide vs. LABA (n=6 studies)</u></p> <ul style="list-style-type: none"> <li>• no significant differences in quality of life, exacerbations, or symptoms</li> <li>• Formoterol appeared to confer some benefits over ipratropium treatment in terms of morning peak flow</li> </ul> <p>2) <u>Ipratropium bromide + LABA vs. LABA alone (n=3 studies)</u></p> <ul style="list-style-type: none"> <li>• significant improvement in                             <ul style="list-style-type: none"> <li>- supplemental short-acting betaagonist use and</li> <li>- HRQL in favour of combination therapy compared with salmeterol alone</li> </ul> </li> </ul>			

**LAMA vs. LABA**

Zitat	Studiencharakteristika	Population	Methodische Qualität
Chong J. Tiotropium versus long-acting beta-agonists for stable chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2012;(9).	<p><b>Suchzeitraum:</b> 02/2012  <b>Fragestellung:</b> relative clinical effects of tiotropium bromide alone versus LABA alone, upon measures of quality of life, exacerbations, lung function and serious adverse events, in people with stable COPD  <b>Setting:</b> Community  <b>Interventionen und Vergleiche:</b>                      1) tiotropium (delivered by HandiHaler) alone vs. LABAs alone</p> <p><u>LABA:</u> salmeterol (four studies, 8936 participants), formoterol (one study, 431 participants) or indacaterol (two studies, 2856 participants)                      &gt;&gt; All participants were instructed to discontinue anticholinergic or LABAs</p>	<p><b>Population:</b> people with stable (moderate to severe) COPD (as judged by a set of criteria equivalent to e.g. GOLD, ATS, BTS, TSANZ)</p> <p><b>described COPD severity</b></p> <ul style="list-style-type: none"> <li>• severe (mean % predicted FEV1 between 35% to 40%; n=2 studies),</li> <li>• moderate to severe (mean % predicted FEV1 between 49% to 57%, n=4 studies),</li> <li>• not described in n=1 study</li> </ul> <p>• mean age of between 60 and 65 years and were predominately male</p>	<p>y-n-y-y-y-y-y-y-y-y</p> <p>Score: 10</p>

Zitat	Studiencharakteristika	Population	Methodische Qualität
	<p>during treatment, but could receive ICS at a stable dose.  <b>Studientyp:</b> RCT and full economic evaluations  <b>Eingeschlossene Studien:</b> 7 (n=12.223; extracted data for 11,223 participants)</p>		
<b>Studienergebnisse</b>			
<b><u>Primäre Endpunkte</u></b>			
<b>SGRQ</b>			
<ul style="list-style-type: none"> <li>• did not pool data because of a high level of heterogeneity</li> <li>• Subgroup analyses based on the type of LABA found statistically significant differences among effects on quality of life depending on whether tiotropium was compared with salmeterol, formoterol or indacaterol</li> </ul>			
<b>Exacerbations</b>			
<ul style="list-style-type: none"> <li>• Tiotropium reduced the number of participants experiencing one or more exacerbations compared with LABA (OR 0.86; 95%CI 0.79 to 0.93; n=12,123; studies=6; moderate quality evidence)</li> <li>• no difference seen among the different types of LABA</li> </ul>			
<b>Mortality</b>			
<ul style="list-style-type: none"> <li>• no statistical difference in mortality observed between the treatment groups (OR 0.82; 95% CI 0.60 to 1.13; n=12,123; studies=6; very low quality evidence)</li> </ul>			
<b><u>Sekundäre Endpunkte</u></b>			
<b>Exacerbations leading to hospitalisation</b>			
<ul style="list-style-type: none"> <li>• tiotropium was associated with a reduction compared with LABA treatment (OR 0.87; 95% 0.77 to 0.99)</li> </ul>			
<b>Hospitalisation all-cause</b>			
<ul style="list-style-type: none"> <li>• no difference</li> </ul>			
<b>Symptom score</b>			
<ul style="list-style-type: none"> <li>• no statistically significant difference</li> </ul>			
<b>Non-fatal SAEs</b>			
<ul style="list-style-type: none"> <li>• lower rate of recorded SAEs recorded with tiotropium compared with LABA (OR 0.88; 95% CI 0.78 to 0.99)</li> </ul>			
<b>Study withdrawals</b>			
<ul style="list-style-type: none"> <li>• lower rate in tiotropium group (OR 0.89; 95% CI 0.81 to 0.99).</li> </ul>			
<b>Kommentar:</b>			
<ul style="list-style-type: none"> <li>• älterer Review von 2012</li> <li>• hohe Dropout-Raten in den Studien</li> </ul>			

LAMA vs. Placebo or LABA or LAMA

Zitat	Studiencharakteristika	Population	Methodische Qualität
Ni H. Acclidinium bromide for stable chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2014;(9).	<p><b>Suchzeitraum:</b> 04/2014</p> <p><b>Fragestellung:</b> efficacy and safety of acclidinium bromide in stable COPD</p> <p><b>Setting:</b> Community</p> <p><b>Interventionen und Vergleiche:</b></p> <ol style="list-style-type: none"> <li>1. Acclidinium bromide vs. placebo</li> <li>2. Acclidinium bromide vs.long-acting beta2-agonist (LABA)</li> <li>3. Acclidinium bromide vs. long-acting muscarinic antagonist (LAMA)</li> </ol> <p><b>Studientyp:</b> RCT</p> <p><b>Eingeschlossene Studien:</b> 12 (n= 9547)</p>	<p><b>Population:</b> adults with stable COPD</p> <ul style="list-style-type: none"> <li>- mean age: 61,7 - 65,6 y.</li> <li>- moderate to severe symptoms at randomisation</li> </ul>	<p>y-y-y-y-y-y-y-y-y-y</p> <p>Score: 11</p>
<b>Studienergebnisse</b>			
<p><u>1. Acclidinium bromide vs. placebo</u></p> <p><b>All-cause mortality</b></p> <ul style="list-style-type: none"> <li>• no difference between acclidinium and placebo (OR 0.92; 95% CI 0.43 to 1.94; n=5252; studies=9; low quality)</li> </ul> <p><b>exacerbations</b></p> <ul style="list-style-type: none"> <li>• number of patients requiring a short course of oral steroids or antibiotics, or both: no difference (OR 0.88; 95% CI 0.74 to 1.04; n=5624; studies=10; moderate quality)</li> </ul> <p><b>SGRQ</b></p> <ul style="list-style-type: none"> <li>• Acclidinium improved: mean difference of -2.34 (95% CI -3.18 to -1.51; I<sup>2</sup> = 48%, 7 trials, 4442 participants)</li> <li>&gt;&gt; More patients on acclidinium achieved a clinically meaningful improvement of at least four units decrease in SGRQ total score (OR 1.49; 95% CI 1.31 to 1.70; I<sup>2</sup> = 34%; n= 4420; Studies=7; NNT = 10, 95% CI 8 to 15, high quality evidence) over 12 to 52 weeks than on placebo</li> </ul> <p><b>Exacerbations requiring hospitalisation</b></p> <ul style="list-style-type: none"> <li>• Acclidinium reduced the number of patients by 4 to 20 fewer per 1000 over 4 to 52 weeks (OR 0.64; 95% CI 0.46 to 0.88; I<sup>2</sup> = 0%, studies=10, n=5624; NNT = 77, 95% CI 51 to 233, high quality evidence) compared to placebo</li> </ul> <p><b>SAEs</b></p> <ul style="list-style-type: none"> <li>• no difference in non-fatal serious adverse events (OR 0.89; 95% CI 0.7 to 1.14; n=5651; studies=10; moderate quality evidence) between acclidinium and placebo.</li> </ul> <p><u>2. Acclidinium bromide vs.long-acting beta2-agonist (LABA)</u></p> <p>Inadequate data prevented the comparison of acclidinium to formoterol or other LABAs.</p> <p><u>3. Acclidinium bromide vs. long-acting muscarinic antagonist (LAMA)</u></p> <p>Compared to tiotropium, acclidinium did not demonstrate significant differences for</p> <ul style="list-style-type: none"> <li>• exacerbations requiring oral steroids or antibiotics, or both (OR 2.64; 95% CI 0.31 to 22.18; n=729; studies= 2; very low quality evidence),</li> <li>• exacerbation-related hospitalisations (OR 0.54; 95% CI 0.07 to 4.11; n=729; studies=2; very low quality evidence) and</li> <li>• non-fatal serious adverse events (OR 0.67, 95% CI 0.17 to 2.65; n=729; studies=2; very low quality evidence).</li> </ul> <p><b>Kommentar:</b> All studies were industry sponsored</p>			

LAMA/LABA vs. LAMA or LABA

Zitat	Studiencharakteristika	Population	Methodische Qualität
<p>Ni H. Combined acclidinium bromide and long-acting beta2-agonist for COPD. Cochrane Database of Systematic Reviews 2018</p>	<p><b>Suchzeitraum:</b> 10/2018  <b>Fragestellung:</b> efficacy and safety of combined acclidinium bromide and long-acting beta2-agonists in stable COPD</p> <p><b>Setting:</b> outpatient  <b>Interventionen und Vergleiche:</b>                      1) acclidinium/formoterol FDC (fixed-dose combination) vs. acclidinium                      2) acclidinium/formoterol FDC vs. formoterol                      3) acclidinium/formoterol FDC vs. placebo</p> <p>included the following cointerventions provided they are not part of the randomised treatment: salbutamol or albuterol as rescue medication, oral sustained-release theophylline, ICSs or systemic corticosteroids (oral or parenteral) at stable doses and oxygen therapy of less than 15 hours/day</p> <p><b>Studientyp:</b> RCT  <b>Eingeschlossene Studien:</b> 7 (n=5921 Studienteilnehmer*innen)</p>	<p><b>Population:</b> people with stable COPD</p> <ul style="list-style-type: none"> <li>• &gt;18 years of age</li> <li>• diagnosis of COPD (according to GOLD 2018, ATS/ERS 2011, TSANZ 2018, NICE 2010, or WHO).</li> <li>• diagnosed with stable moderate-to-severe airway obstruction according to GOLD criteria (postbronchodilator FEV1/FVC ratio less than 70% and FEV1 30% or greater but less than 80% of predicted normal value).</li> <li>• Participants had evidence of airway obstruction (postbronchodilator FEV1/ FVC ratio less than 70%) with symptoms of dyspnoea, chronic cough or sputum production with or without a history of smoking.</li> <li>• excluded studies that enrolled participants with bronchial asthma, bronchiectasis, cystic fibrosis or other chronic lung diseases.</li> <li>• mean postbronchodilator FEV1: between 50.5% and 61% of predicted normal and the baseline mean FEV1 of 1.23 L to 1.43 L</li> <li>• mean age ranged from 60.7 to 64.7 years</li> <li>• mostly men with a mean smoking pack-years of 46.4 to 61.3 of which 43.9% to 63.4% were current smokers</li> </ul>	<p>y-y-y-y-y-y-y-y-y-y</p> <p>Score: 11</p>
<p><b>Studienergebnisse</b></p> <p>Combination therapy significantly improved trough FEV1 compared to acclidinium, formoterol or placebo.</p> <p><b>FDC versus acclidinium</b>                      There was no evidence of a difference between FDC and acclidinium for</p> <ul style="list-style-type: none"> <li>• <u>exacerbations requiring steroids or antibiotics, or both</u> (OR 0.95, 95%CI 0.71 to 1.27; 2 trials, 2156 participants; moderate-certainty evidence);</li> <li>• <u>quality of life</u> measured by SGRQ total score (MD -0.92, 95% CI -2.15 to 0.30);</li> <li>• participants with significant <u>improvement in SGRQ score</u> (OR 1.17, 95% CI 0.97 to 1.41; 2 trials, 2002 participants; moderate-certainty evidence);</li> <li>• <u>non-fatal SAE</u> (OR 1.19, 95% CI 0.79 to 1.80; 3 trials, 2473 participants; moderate-certainty evidence);</li> <li>• <u>hospital admissions due to severe exacerbations</u> (OR 0.62, 95%CI 0.29 to 1.29; 2 trials, 2156 participants; moderate-certainty evidence) or</li> <li>• <u>adverse events</u> (OR 0.95, 95% CI 0.76 to 1.18; 3 trials, 2473 participants; moderate-certainty evidence).</li> </ul> <p>Compared with acclidinium, FDC</p> <ul style="list-style-type: none"> <li>• <u>improved symptoms TDI</u> focal score: MD 0.37, 95%CI 0.07 to 0.68; 2 trials, 2013 participants) with a higher chance of achieving a minimal clinically important difference (MCID) of at least one unit improvement (OR 1.34, 95% CI 1.11 to 1.62; high certainty evidence);</li> </ul> <p>&gt;&gt; the number needed to treat for an additional beneficial outcome (NNTB) being 14 (95% CI 9 to 39).</p>			



Zitat	Studiencharakteristika	Population	Methodische Qualität
	<p><b>FDC versus formoterol</b>                      compared to formoterol, combination therapy</p> <ul style="list-style-type: none"> <li>• <u>reduced exacerbations</u> requiring steroids or antibiotics, or both (OR 0.78, 95% CI 0.62 to 0.99; 3 trials, 2694 participants; high-certainty evidence);</li> <li>• <u>may decrease SGRQ</u> total score (MD -1.88, 95% CI -3.10 to -0.65; 2 trials, 2002 participants; low-certainty evidence; MCID for SGRQ is 4 units);</li> <li>• <u>increased TDI</u> focal score (MD 0.42, 95% CI 0.11 to 0.72; 2 trials, 2010 participants) with more participants attaining an MCID (OR 1.30, 95% CI 1.07 to 1.56; high-certainty evidence) and an NNTB of 16 (95% CI 10 to 60).</li> <li>• <u>lowered the risk of adverse events</u> compared to formoterol (OR 0.78, 95% CI 0.65 to 0.93; 5 trials, 3140 participants; high-certainty evidence; NNTB 22)</li> </ul> <p>• no difference between FDC and formoterol for <u>hospital admissions</u>, <u>all-cause mortality</u> and <u>non-fatal SAEs</u>.</p> <p><b>FDC versus placebo</b>                      Compared with placebo, FDC demonstrated <u>no evidence of a difference in</u></p> <ul style="list-style-type: none"> <li>• <u>exacerbations</u> requiring steroids or antibiotics, or both (OR 0.82, 95% CI 0.60 to 1.12; 2 trials, 1960 participants; moderate-certainty evidence) or</li> <li>• <u>hospital admissions</u> due to severe exacerbations (OR 0.55, 95% CI 0.25 to 1.18; 2 trials, 1960 participants; moderate-certainty evidence), although estimates were uncertain</li> </ul> <p>• <u>SGRQ total</u> score was significantly better with FDC compared to placebo (MD -2.91, 95% CI -4.33 to -1.50; 2 trials, 1823 participants) resulting in a corresponding increase in SGRQ responders who achieved at least four units decrease in SGRQ total score (OR 1.72, 95% CI 1.39 to 2.13; high-certainty evidence) with an NNTB of 7 (95% CI 5 to 12).</p> <p>• FDC also improved symptoms measured by <u>TDI</u> focal score (MD1.32, 95%CI 0.96 to 1.69; 2 studies, 1832 participants) with more participants attaining at least one unit improvement in TDI focal score (OR 2.51, 95% CI 2.02 to 3.11; high-certainty evidence; NNTB 4).</p> <p>• <u>no differences in non-fatal SAEs</u>, <u>adverse events</u> and <u>all-cause mortality</u> between FDC and placebo.</p> <p><b>Kommentar:</b>                      All studies were sponsored by Almirall (SA, Barcelona, Spain) and Forest Laboratories, Inc (New York, USA) or Menarini Group through its affiliate Berlin-Chemie and Astra-Zeneca.</p>		
Farne HA. Long-acting beta2-agonist in addition to tiotropium versus either tiotropium or long-acting beta2-agonist alone for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2015;(10).	<p><b>Suchzeitraum:</b> 07/2015</p> <p><b>Fragestellung:</b> relative effects on markers of quality of life, exacerbations, symptoms, lung function and serious adverse events in people with COPD randomised to LABA plus tiotropium versus tiotropium alone; or LABA plus tiotropium versus LABA alone</p> <p><b>Setting:</b> community</p> <p><b>Interventionen und Vergleiche:</b>                      1) LABA plus tiotropium vs. tiotropium alone                      2) LABA plus tiotropium vs. LABA alone</p> <p>LABA: n=4 studies olodaterol (1x/d); n=3 studies indacaterol (1x/d); n=2 studies formoterol (2x/d); n=1 study salmeterol (2x/d)</p>	<p><b>Population:</b> diagnosis of moderate or severe COPD (included studies that used an external set of criteria to screen participants for this condition (e.g. GOLD, ATS, BTS, TSANZ)</p> <ul style="list-style-type: none"> <li>• 4 studies included also participants with very severe COPD (FEV1 less than 30% predicted)</li> <li>• mean age: 63 to 73 years</li> <li>• gender distribution varied from 50% to 93% men</li> <li>• mean baseline FEV1 varied between 38% and 67% predicted</li> </ul>	<p>y-n-y-y-y-y-y-ca-n-y</p> <p>Score: 8</p>

Zitat	Studiencharakteristika	Population	Methodische Qualität
	<p><b>Studientyp:</b> RCT  <b>Eingeschlossene Studien:</b> 10 (n=10894)</p> <p><b>Co-Treatments erlaubt:</b></p> <ul style="list-style-type: none"> <li>• 10/10 studies: rescue medication, when necessary, to relieve symptoms (inhaled salbutamol/ albuterol)</li> <li>• 8/10 studies permitted continued use of regimens of ICS</li> <li>• 1/10 studies: respiratory medications such as oxygen, anti-leukotrienes, and methylxanthines were continued</li> <li>• 2/10 studies permitted temporary increases in the dose or addition of oral corticosteroids and methylxanthines</li> <li>• 1/10 studies: Participants were either newly diagnosed or discontinued the use of any COPD medications</li> </ul>		
<b>Studienergebnisse</b>			
<p><b>1) LABA + tiotropium vs. tiotropium alone</b>                      treatment with tiotropium plus LABA resulted in  <b>SGRQ</b></p> <ul style="list-style-type: none"> <li>• slightly larger improvement (MD -1.34, 95% CI -1.87 to - 0.80; n=6709 participants; 5 studies; moderate quality evidence). The MD was smaller than the four units that is considered clinically important, but a responder analysis indicated that 7% more participants receiving tiotropium plus LABA had a noticeable benefit (greater than four units) from treatment in comparison to tiotropium alone. (Most data from oldetarol-studies)</li> </ul> <p><b>Hospital admission</b></p> <ul style="list-style-type: none"> <li>• no significant differences</li> </ul> <p>&gt; all-cause OR 1.01; 95% CI 0.86 to 1.19, n=4856; studies=4; moderate quality evidence                      &gt;exacerbation OR 1.02; 95% CI 0.80 to 1.28; n=4856; studies=4, low quality evidence</p> <p><b>Mortality</b></p> <ul style="list-style-type: none"> <li>• no significant differences (all-cause OR 1.24; 95% CI 0.81 to 1.90; n=9633; studies=8)</li> </ul> <p><u>Sekundäre Endpunkte</u></p> <p><b>Exacerbations</b> (moderate heterogeneity; I<sup>2</sup> = 43%)</p> <ul style="list-style-type: none"> <li>• no statistically significant differences between the groups</li> </ul> <p><b>Symptom scores</b></p> <ul style="list-style-type: none"> <li>• no statistically significant differences between the group</li> </ul> <p><b>Serious adverse events</b></p> <ul style="list-style-type: none"> <li>• no statistically significant differences between the group</li> </ul> <p><b>Withdrawals</b> (moderate heterogeneity; I<sup>2</sup> = 54%)</p> <ul style="list-style-type: none"> <li>• no statistically significant differences between the group</li> </ul>			
<p><b>2) LABA plus tiotropium vs. LABA alone</b></p>			

Zitat	Studiencharakteristika	Population	Methodische Qualität
	<p><b>SGRQ</b></p> <ul style="list-style-type: none"> <li>• small but significant improvement (MD -1.25, 95% CI -2.14 to -0.37; n=3378 participants; 4 studies; most data from oldetarol-studies)</li> <li>&gt;&gt; difference was smaller than four units, this still represented an increase of 10 people with a clinically important improvement for 100 treated.</li> </ul> <p><b>Exazerbation rates</b></p> <ul style="list-style-type: none"> <li>• improvement (OR) 0.80, 95% CI 0.69 to 0.93; n=3514 participants; 3 studies).</li> </ul> <p><b>Hospital admission</b></p> <ul style="list-style-type: none"> <li>&gt; all-cause OR 0.93; 95% CI 0.76 to 1.14; n=3514; studies=3, moderate quality evidence</li> <li>&gt;exacerbation OR 0.90; 95%CI 0.66 to 1.22; n=3514; studies=3, low quality evidence</li> </ul> <p><b>Mortality</b></p> <ul style="list-style-type: none"> <li>• uncertainty to the true impact on mortality (all-cause OR 1.15; 95%CI 0.62 to 2.13; n=3514; studies=3; low quality evidence)</li> </ul> <p><b>Serious adverse events (non-fatal)</b></p> <ul style="list-style-type: none"> <li>• n=4 studies (3552 participants) reported the number of participants experiencing serious, but non-fatal, adverse events during the study period (n=1 study: none SAEs)</li> <li>• no statistically significant difference between the treatment groups (OR 0.94, 95% CI 0.77 to 1.14)</li> </ul> <p><b>Kommentar:</b> Appl. S. 15 des Reviews</p>		

**LAMA/LABA vs. LABA/ICS**

Zitat	Studiencharakteristika	Population	Methodische Qualität
<p>Horita N. Long-acting muscarinic antagonist (LAMA) plus long-acting beta-agonist (LABA) versus LABA plus inhaled corticosteroid (ICS) for stable chronic obstructive pulmonary disease (COPD). Cochrane Database of Systematic Reviews 2017;(2).</p>	<p><b>Suchzeitraum:</b> 06/2016 <b>Fragestellung:</b> benefits and harms of LAMA+LABA versus LABA+ICS for treatment of people with stable COPD</p> <p><b>Setting:</b> outpatient</p> <p><b>Interventionen und Vergleiche:</b> 1) LAMA+LABA vs. LABA+ICS</p> <p><u>LABA+ICS:</u></p> <ul style="list-style-type: none"> <li>• salmeterol/fluticasone propionate (10/11 studies combined; n=1 study uncombined)</li> </ul> <p><u>LAMA+LABA:</u></p> <ul style="list-style-type: none"> <li>• indacaterol/glycopyrronium (n=3 studies)</li> <li>• umeclidinium/vilanterol (n=3 studies)</li> <li>• tiotropium/olodaterol (n=1 study)</li> <li>• tiotropium/indacaterol (n=1 study)</li> <li>• tiotropium/salmeterol (n=1 study)</li> <li>• tiotropium/formoterol (n=1 study)</li> <li>• aclidinium/formoterol (n=1 study)</li> </ul>	<p><b>Population:</b> adults with a diagnosis of [stable] COPD according to GOLD 2016</p> <ul style="list-style-type: none"> <li>• most studies: people with moderate to severe COPD, without recent exacerbations.</li> <li>• 1 große Studie (37% der Studienteilnehmer) : included only people with recent exacerbations</li> <li>- mean age: 61 - 71 (median; 63 y.)</li> </ul> <p><u>Rekrutierung nach GOLD-Kategorien (A-D):</u></p> <ul style="list-style-type: none"> <li>• GOLD B: n=5 studies</li> <li>• GOLD D: n=1 study</li> <li>• GOLD A/B: n=2 studies</li> <li>• regardless of Category: n=3 studies</li> </ul>	<p>y-y-y-y-y-y-y-y-y-y</p> <p>Score: 11</p>

Zitat	Studiencharakteristika	Population	Methodische Qualität
	<p>(treatments administered via a single combined device or via two separate devices; duration ranged from 6 to 52 weeks)</p> <p><b>Studientyp:</b> RCT, teilweise parallel-group design und cross-over design <b>Eingeschlossene Studien:</b> 11 (n= 9839)</p>		
<b>Studienergebnisse</b>			
<p>Compared to the LABA+ICS arm, the results for the pooled <b>primary outcomes</b> for the LAMA+LABA arm were as follows:</p> <p><b>Exacerbations</b></p> <ul style="list-style-type: none"> <li>• significant decrease in the number of people experiencing one or more exacerbations with LAMA+LABA (OR 0.82, 95% CI 0.70 to 0.96; P = 0.01; I<sup>2</sup> = 17%; low quality evidence; n=8932; studies=9)</li> </ul> <p><u>Subgruppen:</u></p> <ul style="list-style-type: none"> <li>• treated with indacaterol/ glycopyrronium had fewer exacerbations (OR 0.72, 95% CI 0.63 to 0.83; P &lt; 0.001; I<sup>2</sup> = 0%) compared to participants treated with LABA+ICS. In contrast, LAMA+LABA was not related to reduced risk of exacerbation in umeclidinium/vilanterol and other LAMA+LABA subgroups.</li> </ul> <p><b>SAEs</b></p> <ul style="list-style-type: none"> <li>• non-significant decrease (OR 0.91, 95% CI 0.79 to 1.05, P = 0.18, I<sup>2</sup> = 0, moderate quality evidencen=9793; studies=10)</li> </ul> <p><b>SGRQ total score change from the baseline</b></p> <ul style="list-style-type: none"> <li>• non-significant decrease (MD -1.22; 95% CI -2.52 to 0.07, P = 0.06, I<sup>2</sup> = 71%, low quality evidence; n=5858; studies=6)</li> </ul> <p><u>Subgruppen:</u></p> <ul style="list-style-type: none"> <li>• significant decrease in scores in participants treated with indacaterol/ glycopyrronium and 'other LAMA/LABA inhalers' compared to participants treated with LABA+ICS (indacaterol/glycopyrronium: MD -1.29, 95% CI -2.08 to -0.50; P = 0.001; I<sup>2</sup> = 0%; other LAMA/ LABA inhalers: MD -5.00, 95% CI -7.35 to -2.65, P &lt; 0.0001).</li> </ul> <p><b>sekundäre Endpunkte</b></p> <p><b>Pneumonia</b></p> <ul style="list-style-type: none"> <li>• significant reduction in the number of participants experiencing one or more episodes of pneumonia with LAMA+LABA (OR 0.57; 95% CI 0.42 to 0.79, P = 0.0006, I<sup>2</sup> = 0%, low quality evidence; n=8540; studies=8)</li> </ul> <p><b>All-cause death</b></p> <ul style="list-style-type: none"> <li>• similar risk (OR 1.01; 95% CI 0.61 to 1.67, P = 0.88, I<sup>2</sup> = 0%, low quality evidence; n=8200; studies=8)</li> </ul> <p><b>SGRQ otal score change from the baseline (4 points or greater)</b></p> <ul style="list-style-type: none"> <li>• more frequent change (OR 1.25; 95% CI 1.09 to 1.44, P = 0.002, I<sup>2</sup> = 0%, moderate quality evidence; n=3192; studies=2)</li> </ul> <p><b>Kommentar:</b></p> <p>10/11 studies: sponsored by pharmaceutical companies --&gt; rated high risk of 'other bias'</p> <p>1/11 studies:unsponsored --&gt; rated at high risk of performance and detection bias, and possible selective reporting</p>			

LABA/ICS vs LAMA

Zitat	Studiencharakteristika	Population	Methodische Qualität
<p>Sliwka A. Once daily Long-acting beta2-agonists/Inhaled corticosteroids combined inhalers versus inhaled long-acting muscarinic antagonists for people with chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2018</p>	<p><b>Suchzeitraum:</b> 05/2018</p> <p><b>Fragestellung:</b> compare a once-daily combination of ICS/LABA versus inhaled LAMA alone for people with COPD</p> <p><b>Setting:</b> studies were conducted at 102 medical centres in 11 countries (Canada, Czech Republic, Germany, Poland, Romania, USA, Argentina, France, Italy, Norway, Russian Federation, Ukraine)</p> <p><b>Interventionen und Vergleiche:</b> 1) inhaled ICS/LABA (fluticasone furoate and vilanterol 100/25 mcg once daily; FF/VI) versus LAMA (18 mcg tiotropium; TIO).</p> <p><b>Studientyp:</b> RCT <b>Eingeschlossene Studien:</b> n=2 (880 participants)</p>	<ul style="list-style-type: none"> <li>included adults (over 21 years old) with a diagnosis of COPD confirmed by an external set of criteria for this condition, eg GOLD 2018, ATS, BTS, or TSANZ.</li> <li>Participants were men and women aged 40 or older who had COPD with various degrees of severity.</li> <li>studies enrolled participants with both <u>partially reversible and non-reversible</u> COPD and baseline mean %pred FEV1 of 43.4 to 49.6.</li> </ul>	<p>y-y-y-y-y-y-y-y-y-y-y-y</p> <p>Score: 11</p>
<b>Studienergebnisse</b>			
<p><b>FF/VI vs TIO (ICS/LABA vs LAMA):</b></p> <ul style="list-style-type: none"> <li><b>mortality:</b> OR 0.20, 95% CI 0.02 to 1.73, 880 participants (deaths reported only in the TIO arm), very low-quality evidence --&gt; risk with LAMA: 9 per 1000;</li> <li><b>COPD exacerbation</b> (requiring short-burst oral corticosteroids or antibiotics, or both): OR 0.72, 95% CI 0.35 to 1.50, 880 participants, very low-quality evidence --&gt; risk with LAMA: 41 per 1000; risk with LABA/ICS: 30 (15 to 60) per 1000;</li> <li><b>pneumonia:</b> reported in both studies only during treatment with FF/VI: OR 6.12, 95%CI 0.73 to 51.24, 880 participants, very low-quality evidence; and</li> <li><b>total serious adverse events:</b> OR 0.96, 95% CI 0.50 to 1.83, 880 participants, very low-quality evidence.</li> </ul> <p>&gt;&gt; no statistically significant difference for pooled secondary outcomes, including</p> <ul style="list-style-type: none"> <li>SGRQ mean total score change;</li> <li>hospital admissions (all-cause);</li> <li>disease-specific adverse events;</li> <li>mean weekly rescue medication use (results available from only one of the studies);</li> <li>mean weekly percentage of rescue-free days for FF/VI.</li> </ul> <p>&gt;&gt;no statistically significant differences between ICS/LABA and LAMA for improvement in symptoms measured by CAT score nor for FEV (change from baseline trough in 24-hour weighted mean on treatment day 84).</p> <p>Many pooled estimates lacked precision. Data for other endpoints such as exacerbations leading to intubation and physical activity measures were not available in included trials.</p>			
<b>Kommentar:</b>			

Zitat	Studiencharakteristika	Population	Methodische Qualität
	Fallzahlen ausreichend?  evidence presented in this review = of very low quality, review authors have very little confidence in the findings		
Welsh EJ. Combination inhaled steroid and long-acting beta2-agonist versus tiotropium for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2013;(5).	<p><b>Suchzeitraum:</b> 11/2012</p> <p><b>Fragestellung:</b> relative effects of inhaled combination therapy (LABA/ICS) and tiotropium on markers of exacerbations, symptoms, quality of life, lung function, pneumonia and serious adverse events in patients with COPD</p> <p><b>Interventionen und Vergleiche:</b> 1) ICS + LABA (such as fluticasone/salmeterol, budesonide/formoterol, beclomethasone/ formoterol) vs. inhaled tiotropium bromide.</p> <p><b>Studientyp:</b> RCT</p> <p><b>Eingeschlossene Studien:</b> 3 (n=1528)</p>	<p><b>Population:</b> Populations with a diagnosis of COPD; only included studies where an external set of criteria had been used to screen participants for this condition (e.g. GOLD, ATS, BTS, TSANZ). - mean age: n.a.</p> <p><b>INSPIRE:</b> <u>GOLD stage III (FEV1 30% to &lt;50% pred)</u> • n=540 on fluticasone/ salmeterol with a mean FEV1 of 1.09 • n=537 with a mean FEV1 of 1.11 L on tiotropium <u>GOLD stage IV (FEV1 &lt; 30% pred)</u> • n=100 patients on fluticasone/ salmeterol with a mean FEV1 of 0.73 L • n=101 patient with a mean FEV1 of 0.71 L on tiotropium •48% of participants in the fluticasone/ salmeterol arm and 51% in the tiotropium arm stopped taking ICS at baseline</p>	<p>y-y-y-y-y-y-y-y-n-n</p> <p>Score: 9</p>
<b>Studienergebnisse</b>			
<ul style="list-style-type: none"> <li>• The results from these trials were not pooled (because of disparity in the trial lengths and because the primary focus of the review was on long-term outcomes)</li> <li>• Größte der 3 Studien ist INSPIRE (n=1323)</li> <li>• INSPIRE had a high and unbalanced withdrawal rate. The proportion of missing outcome data compared to the observed outcome data is enough to induce a clinically relevant bias in the intervention effect. The relative efficacy and safety of combined inhalers and tiotropium remains uncertain.</li> </ul> <p><b>Kommentar:</b> pairwise metaanalysis zum Vergleich LABA/ICS vs. LAMA in neuerem Review (Oba-Network-meta-analysis 2018; Ref ID 27070) durchgeführt.</p>			

**LAMA/LABA vs. LABA/ICS vs. LABA vs. LAMA**

Zitat	Studiencharakteristika	Population	Methodische Qualität
Oba Y. Dual combination therapy versus long-acting bronchodilators alone for chronic obstructive	<p><b>Suchzeitraum:</b> 04/2018</p> <p><b>Fragestellung:</b> efficacy and safety of available formulations from four different groups of inhalers (i.e. LABA/LAMA combination, LABA/ICS combination, LAMA and LABA) in people with moderate to severe</p>	<p><b>Population:</b> people aged 35 years or older with a diagnosis of COPD and a baseline FEV1 of less than 80% of predicted</p> <ul style="list-style-type: none"> <li>• moderate to severe COPD</li> </ul>	<p>y-y-y-y-y-y-y-y-n-y</p> <p>Score: 10</p>

Zitat	Studiencharakteristika	Population	Methodische Qualität
pulmonary disease (COPD): a systematic review and network meta-analysis. Cochrane Database of Systematic Reviews 2018	<p>COPD</p> <p><b>Setting:</b> outpatient</p> <p><b>Interventionen und Vergleiche:</b> &gt;&gt; studies comparing at least two of the following therapies:</p> <ol style="list-style-type: none"> <li>1. LAMA monotherapy</li> <li>2. LABA monotherapy</li> <li>3. Fixed-dose or free combination of LABA/ICS</li> <li>4. Fixed-dose or free combination of LABA/LAMA</li> </ol> <p>&gt;&gt; allowed the use of a short-acting bronchodilator, such as salbutamol( also known as albuterol), and ipratropium as rescue treatment.</p> <p><b>Studientyp:</b> RCT</p> <p><b>Eingeschlossene Studien:</b> 99 (n=101.311 participants)</p> <ul style="list-style-type: none"> <li>• high-risk group: 26 studies (n=32.265 participants)</li> <li>• low-risk group: 73 studies (n=69,046 participants)</li> </ul>	<ul style="list-style-type: none"> <li>• in accordance with ATS/ERS 2004, GOLD 2018, or equivalent criteria</li> <li>• excluded studies that enrolled participants with a history of asthma or other respiratory disease</li> </ul> <p>• <u>high-risk group:</u> one or more exacerbations in the previous 12 months</p>	
<b>Studienergebnisse</b>			
<p><b>LABA/LAMA vs. LABA/ICS</b></p> <ul style="list-style-type: none"> <li>• <u>Moderate to severe exacerbation:</u> high-risk population OR 0.87; 95%CI 0.76 to 1.00 (n=3372; studies=1; moderate quality evidence)</li> <li>• <u>Moderate to severe exacerbation:</u> low-risk population OR 0.86; 95%CI 0.65 to 1.14 (n=4315; studies=6; moderate quality evidence)</li> <li>• <u>Severe exacerbations:</u> high-risk population OR 0.88; 95% CI 0.74 to 1.06 (n=3354; studies=s; moderate quality evidence)</li> <li>• <u>Severe exacerbations:</u> low-risk population OR 0.66; 95% CI 0.27 to 1.63 (n=2860; studies=4; moderate quality evidence)</li> <li>• <u>Pneumonia:</u> high-risk population OR 0.62; 95% CI 0.40 to 0.96 (n=3358; studies=1; moderate quality evidence)</li> <li>• <u>Pneumonia:</u> low-risk population OR 0.43; 95% CI 0.19 to 0.97 (n=5395; studies=7; moderate quality evidence)</li> </ul> <p><b>LABA/LAMA vs. LAMA</b></p> <ul style="list-style-type: none"> <li>• <u>Moderate to severe exacerbation:</u> high-risk population OR 1.06; 95%CI 0.89 to 1.27 (n=2206; studies 1; moderate quality evidence)</li> <li>• <u>Moderate to severe exacerbation:</u> low-risk population OR 0.93; 95% CI 0.66 to 1.30 (n=5192; studies=8; low quality evidence)</li> <li>• <u>Severe exacerbations:</u> high-risk population OR 0.73; 95% CI 0.45 to 1.16 (n=304; studies=1; moderate quality evidence)</li> </ul>			

Zitat	Studiencharakteristika	Population	Methodische Qualität
	<ul style="list-style-type: none"> <li>• <b>Severe exacerbations:</b> low-risk population OR 0.99; 95%CI 0.57 to 1.72 (n=4937; studies=7; moderate quality evidence)</li> <li>• <b>Pneumonia:</b> high-risk population OR 0.98; 95%CI 0.59 to 1.61 (n=2510; studies=2; moderate quality evidence)</li> <li>• <b>Pneumonia:</b> low-risk population OR 1.23; 95%CI 0.84 to 1.81 (n=18538; studies=22; moderate quality evidence)</li> </ul> <p><b>LABA/LAMA vs. LABA</b></p> <ul style="list-style-type: none"> <li>• <b>Moderate to severe exacerbation:</b> low-risk population OR 0.77; 95%CI 0.62 to 0.97 (n=2488; studies=5; moderate quality evidence)</li> <li>• <b>Severe exacerbations:</b> low-risk population OR 0.78; 95%CI 0.55 to 1.12 (n=2898; studies=6; moderate quality evidence)</li> <li>• <b>Pneumonia:</b> low-risk population OR 1.54; 95%CI 0.95 to 2.49 (n=8252; studies=10; moderate quality evidence)</li> </ul> <p><b>LABA/ICS vs. LAMA</b></p> <ul style="list-style-type: none"> <li>• <b>Moderate to severe exacerbation:</b> high-risk population OR 1.12; 95%CI 0.90 to 1.39 (n=1580; studies=2; moderate quality evidence)</li> <li>• <b>Moderate to severe exacerbation:</b> low-risk population OR 0.63; 95%CI 0.24 to 1.66 (n=623; studies=1; low quality evidence)</li> <li>• <b>Severe exacerbations:</b> high-risk population OR 1.28; 95%CI 0.95 to 1.73 (n=1580; studies=2; moderate quality evidence)</li> <li>• <b>Severe exacerbations:</b> low-risk population OR 3.05; 95%CI 0.32 to 29.47 (n=623; studies=1; low quality evidence)</li> <li>• <b>Pneumonia:</b> high-risk population OR 1.80; 95%CI 1.06 to 3.06 (n=1580; studies=2; moderate quality evidence)</li> <li>• <b>Pneumonia:</b> low-risk population OR 5.82; 95%CI 0.70 to 48.80 (n=885; studies=2; low quality evidence)</li> </ul> <p><b>LAMA vs. LABA</b></p> <ul style="list-style-type: none"> <li>• <b>Moderate to severe exacerbation:</b> high-risk population OR 0.84; 95%CI 0.76 to 0.92 (n=7376; studies=1; high quality evidence)</li> <li>• <b>Moderate to severe exacerbation:</b> low-risk population OR 0.92; 95%CI 0.79 to 1.07 (n=4567; studies=5; moderate quality evidence)</li> <li>• <b>Severe exacerbations:</b> high-risk population OR 0.88; 95%CI 0.78 to 1.01 (n=7376; studies=1; moderate quality evidence)</li> <li>• <b>Severe exacerbations:</b> low-risk population OR 0.64; 95%CI 0.36 to 1.13 (n=3320; studies=4; low quality evidence)</li> <li>• <b>Pneumonia:</b> high-risk population OR 0.83; 95%CI 0.61 to 1.13 (n=10815; studies=2; moderate quality evidence)</li> <li>• <b>Pneumonia:</b> low-risk population OR 1.01; 95%CI 0.61 to 1.69 (n=11338; studies=10; moderate quality evidence)</li> </ul>		



Zitat	Studiencharakteristika	Population	Methodische Qualität
<p><b>Kommentar:</b> Network-Metaanalyse &gt;&gt; es wurden nur die paarweisen direkten Metaanalysen in unsere Darstellung aufgenommen</p>			

**LAMA/LABA/ICS**

Zitat	Studiencharakteristika	Population	Methodische Qualität
Tan DJ. Inhaled corticosteroids with combination inhaled long-acting beta2-agonists and long-acting muscarinic antagonists for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2016;(11).	<p><b>Suchzeitraum:</b> 09/2016 (Cochrane Airways Group Specialised Register of Trials), 12/2015 (Cochrane Library + MEDLINE) 01/2016 (ClinicalTrials.gov + WHO trials portal + pharmaceutical company clinical trials' databases)</p> <p><b>Interventionen und Vergleiche:</b> 1) ICS + LABA/LAMA vs. LABA/LAMA alone</p> <p><b>Studientyp:</b> RCT</p> <p><b>Eingeschlossene Studien:</b> 0</p>	<b>Population:</b> stable COPD	keine AMSTAR -Bewertung möglich, da keine Studien eingeschlossen werden konnten
<p><b>Studienergebnisse</b></p> <p><b>Geplante Endpunkte</b></p> <p><b>Primary outcomes</b></p> <p>1) <u>Acute exacerbation of COPD (AECOPD)</u>: defined as needing treatment with oral steroids, antibiotics or hospital attendance for a COPD exacerbation, or a combination of these treatments. Exacerbation events based on standardised patientreported outcome tools for measuring changes in symptoms were also accepted.</p> <p>2) <u>Respiratory health-related quality of life (HRQoL)</u>: measured by the Chronic Respiratory Questionnaire (CRQ) or St. George's Respiratory Questionnaire (SGRQ).</p> <p>3) <u>Pneumonia and other serious adverse events</u>: defined as requiring treatment or hospital admission for pneumonia or other serious adverse events.</p> <p><b>Secondary outcomes</b></p> <p>4) <u>Symptom score</u>: measures of breathlessness, cough, wheeze and sputum production, preferably using validated scales.</p> <p>5) <u>Lung function</u>: pre-bronchodilator (BD) and post-BD measure including FEV and FVC.</p> <p>6) <u>Physical capacity</u>: measures including timed walking tests, endurance tests.</p> <p>7) <u>Mortality</u></p>			

**ICS Pneumonie**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
Kew KM. Inhaled steroids and risk of pneumonia for chronic obstructive	<p>• <b>Fragestellung:</b> To assess the risk of pneumonia associated with the use of fluticasone and budesonide for COPD.</p>	<p>• <b>Baseline-Charakteristika:</b> - often male with a mean age of around 63, mean pack-years smoked over 40 and mean predicted forced expiratory volume of one second (FEV1)</p>	AMSTAR: y-y-y-y-y-y-y-ca-y	• finding should be interpreted with caution because of possible differences in the assignment of pneumonia diagnosis, and because no

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
pulmonary disease. Cochrane Database of Systematic Reviews 2014;(3).	<ul style="list-style-type: none"> <li>• <b>Suchzeitraum:</b> September 2013</li> <li>• <b>Population:</b> people with COPD</li> <li>• <b>Ein- und Ausschlusskriterien:</b> <ul style="list-style-type: none"> <li>- RCTs of at least 12 weeks' duration</li> </ul> </li> <li>• <b>Vergleiche:</b> <ul style="list-style-type: none"> <li>- ICS (budesonide or fluticasone) vs. placebo</li> <li>or</li> <li>- ICS + LABA vs. the same LABA</li> </ul> </li> <li>• <b>eingeschlossene Studien:</b> <ul style="list-style-type: none"> <li>- fluticasone (26 studies; n = 21,247)</li> <li>- budesonide (17 studies; n = 10,150)</li> </ul> </li> <li>• RoB der eingeschlossenen Studien (wenn GRADE nicht durchgeführt wurde)</li> </ul>	<p>less than 50%</p> <ul style="list-style-type: none"> <li>• <u>Fluticasone</u> <ul style="list-style-type: none"> <li>- increased non-fatal serious adverse pneumonia events (requiring hospital admission) (43/1000 vs. 25/1000; OR 1.78, 95% CI 1.50 to 2.12; 18 more per 1000 treated over 18 months; I<sup>2</sup> = 0%, 17 RCT, n = 19504; <b>GRADE:</b> high quality)</li> <li>- no evidence suggested that this outcome was reduced by delivering it in combination with salmeterol or vilanterol (subgroup differences: I<sup>2</sup> = 0%, P = 0.51), or that different doses, trial duration or baseline severity significantly affected the estimate</li> </ul> </li> <li>• <u>Budesonide</u> <ul style="list-style-type: none"> <li>- also increased non-fatal serious adverse pneumonia events compared with placebo, but the effect was less precise and was based on shorter trials (15/1000 vs. 9/1000; OR 1.62, 95% CI 1.00 to 2.62; six more per 1000 treated over nine months; I<sup>2</sup> = 28%, 7 RCT, n = 6472, <b>GRADE:</b> moderate quality).</li> </ul> </li> <li>• <u>indirect comparison of budesonide versus fluticasone monotherapy</u> <ul style="list-style-type: none"> <li>- revealed no significant differences with respect to serious adverse events (pneumonia-related or all-cause) or mortality</li> <li>- risk of any pneumonia event (i.e. less serious cases treated in the community) was higher with fluticasone than with budesonide (OR 1.86, 95% CI 1.04 to 3.34); this was the only significant difference reported between the two drugs</li> </ul> </li> </ul>	Score: 10	trials directly compared the two drugs..

OCS

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
Walters-Julia AE. Oral corticosteroids for stable chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2005;(3).	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To assess the effects of oral corticosteroids on the health status of patients with stable COPD.</li> <li>• <b>Suchzeitraum:</b> December 2003 and 2004</li> <li>• <b>Population:</b> patients with stable COPD</li> <li>• <b>Ein- und Ausschlusskriterien:</b> RCT in adults with stable COPD, a history of smoking, excluding known asthmatics</li> </ul>	<p><u>FEV1</u></p> <ul style="list-style-type: none"> <li>- significant difference in FEV1 after two weeks treatment, WMD 53.30 ml; 95% CI 22.21 to 84.39 favouring oral steroid use compared to placebo (14 RCT, n=396, no significant heterogeneity).</li> <li>- significant increase in odds for individual patient FEV1 response greater than 20% from baseline with high dose oral steroid treatment compared to placebo, OR 2.71; 95% CI 1.84 to 4.01 (10 studies, n = 259; I<sup>2</sup> = 0%)</li> </ul> <p><u>QoL</u></p> <ul style="list-style-type: none"> <li>- All differences in health-related quality of life were less than the minimum clinically important</li> </ul>	AMSTAR: y-y-y-ca-y-y-n-ca-n-n Score: 6

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<ul style="list-style-type: none"> <li>• <b>Interventionen:</b> oral steroids</li> <li>• <b>Vergleich:</b> Placebo</li> <li>• <b>eingeschlossene Studien:</b> 24 RCT</li> </ul>	difference.  <u>Authors' conclusions</u> There is no evidence to support the long-term use of oral steroids at doses less than 10-15 mg prednisolone though some evidence that higher doses (30 mg prednisolone) improve lung function over a short period. Potentially harmful adverse effects e.g. diabetes, hypertension, osteoporosis would prevent recommending long-term use at these high doses in most patients.	

**Prophylaktische Antibiose**

Zitat	Studiencharakteristika	Population	Methodische Qualität
Herath SC. Prophylactic antibiotic therapy for chronic obstructive pulmonary disease (COPD). Cochrane Database of Systematic Reviews 2018	<p><b>Suchzeitraum:</b> 07/2018</p> <p><b>Fragestellung:</b> determine whether or not regular (continuous, intermittent or pulsed) treatment of COPD patients with prophylactic antibiotics reduces exacerbations or affects quality of life.</p> <p><b>Settings:</b> Outpatients presenting to hospital clinics</p> <p><b>Interventionen und Vergleiche:</b></p> <p>1) antibiotic vs placebo</p> <ul style="list-style-type: none"> <li>• included studies of oral antibiotics, including</li> <li>- penicillin (amoxicillin, amoxicillin, clavulanic acid),</li> <li>- tetracycline (doxycycline, tetracycline),</li> <li>- quinolones (ciprofloxacin, moxifloxacin),</li> <li>- macrolides (clarithromycin, erythromycin, roxithromycin, azithromycin) and</li> <li>- sulphonamides (co-trimoxazole),</li> </ul> <p>&gt;&gt;administered in appropriate doses for a period of at least three months</p> <p><b>Studientyp:</b> RCT</p> <p><b>eingeschlossene Studien:</b> n=16; für Analyse: n=14 (3932 Teilnehmer*innen)</p>	<p><b>Population:</b></p> <ul style="list-style-type: none"> <li>• adults (&gt; 18 years of age) with a diagnosis of COPD, as defined by ATS, ERS or GOLD, with airflow obstruction evident by spirometry (post-bronchodilator FEV1 of less than 80% of the predicted value and an FEV1/FVC of 0.7 or less)</li> <li>• included studies only if they confirmed diagnosis with lung function testing (spirometry).</li> <li>• excluded: participants with bronchiectasis, asthma, or genetic diseases, such as cystic fibrosis or primary ciliary dyskinesia</li> </ul>	<p>y-n-y-y-y-y-y-y-n-y</p> <p>Score: 9</p>
<b>Studienergebnisse</b>			
<p><u>Antibiotics versus placebo (data from pulsed and continuous courses of antibiotics)</u></p> <p><b>Number of people with one or more exacerbations</b></p> <ul style="list-style-type: none"> <li>• OR 0.57; 95%CI 0.42 to 0.78 (n=2716; studies=8; moderate quality evidence, I<sup>2</sup> = 42%)</li> <li>• Subgroup analysis of continuous versus intermittent versus pulsed antibiotics suggested that pulsed antibiotics were less effective at reducing exacerbations (P = 0.01 for subgroup difference; I<sup>2</sup> = 77.3%)</li> </ul>			

Zitat	Studiencharakteristika	Population	Methodische Qualität
	<p>• Definitions: continuous prophylactic antibiotics (every day), or antibiotics that were used intermittently (three times per week) or pulsed (e.g. for five days every eight weeks)</p> <p><b>Rate of exacerbation per patient/ year</b></p> <ul style="list-style-type: none"> <li>• Rate ratio 0.67; 95%CI 0.54 to 0.83 (n=1384; studies=5; moderate quality evidence, I<sup>2</sup> = 52%)</li> <li>• Test for subgroup difference between continuous and intermittent antibiotics not significant (P = 0.38; I<sup>2</sup> = 0%)</li> </ul> <p><b>HRQoL, SGRQ (total score)</b></p> <ul style="list-style-type: none"> <li>• The mean HRQoL (SGRQ total score) in the intervention group was 1.94 lower (3.13 lower to 0.75 lower); n=2237; studies=7; high quality evidence</li> <li>• Test for subgroup differences between continuous, intermittent and pulsed antibiotics not significant (P = 0.35; I<sup>2</sup> = 5.2%)</li> </ul> <p><b>All-cause mortality</b></p> <ul style="list-style-type: none"> <li>• OR 0.87; 95%CI 0.66 to 1.15; n=3309; studies=6; moderate quality evidence)</li> <li>• Test for subgroup differences between continuous, intermittent and pulsed antibiotics not significant (P = 0.60; I<sup>2</sup> = 0%)</li> </ul> <p><b>Serious adverse events</b></p> <ul style="list-style-type: none"> <li>• OR 0.88; 95%CI 0.74 to 1.05 (n=2978; studies=9; moderate quality evidence, I<sup>2</sup> = 0%)</li> <li>• Test for subgroup differences between continuous, intermittent and pulsed antibiotics not significant (P = 0.60; I<sup>2</sup> = 0%)</li> <li>• most frequently recorded: gastrointestinal in origin (OR 1.16, 95% CI 0.43 to 3.11; participants = 2522; studies = 6; I<sup>2</sup> = 72%) &gt;&gt; significant heterogeneity among these studies which suggested differences among the antibiotics and their adverse events for each study</li> </ul> <p><b>Any adverse event</b></p> <ul style="list-style-type: none"> <li>• OR 1.07 95%CI 0.69 to 1.67 (n=512; studies=4; moderate quality evidence)</li> <li>• Test for subgroup differences between continuous, intermittent and pulsed antibiotics not significant (P = 0.28), I<sup>2</sup> = 21.9%)</li> </ul> <p><b>Kommentar:</b> Aufschlüsselung spezifischer adverse events: S. 23 Review</p>		

**PDE4-Inhibitoren vs. Placebo**

Zitat	Studiencharakteristika	Population	Methodische Qualität
Chong J. Phosphodiesterase 4 inhibitors for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2017	<p><b>Suchzeitraum:</b> 10/2016</p> <p><b>Fragestellung:</b> efficacy and safety of oral PDE 4 inhibitors in the management of stable COPD.</p> <p><b>Interventionen und Vergleiche:</b></p> <p>1) PDE4 inhibitors vs. Placebo (co-administration of standard COPD therapy allowed)</p> <p><b>Studientyp:</b> RCT</p> <p><b>Eingeschlossene Studien:</b> 34</p> <ul style="list-style-type: none"> <li>• 20 roflumilast, n=17.627;</li> <li>• 14 cilomilast, n=6457</li> </ul>	<p><b>Population:</b> Adults (&gt;18 years of age) with COPD, as defined by ATS, ERS or GOLD</p> <ul style="list-style-type: none"> <li>• moderate to very severe COPD (GOLD grades II-IV), with a mean age of 64 years</li> <li>• excluded participants requiring mechanical ventilation on presentation</li> </ul>	<p>y-n-y-y-y-y-y-n-y-y</p> <p>Score: 9</p>

Zitat	Studiencharakteristika	Population	Methodische Qualität
	<p><b>Studienergebnisse</b></p> <p><u>PDE 4 vs. Placebo</u></p> <p><b>SGRQ</b></p> <ul style="list-style-type: none"> <li>• small improvements (MD -1.06 units, 95%CI -1.68 to -0.43, n=7645; studies=11, moderate-quality evidence due to moderate levels of heterogeneity and risk of reporting bias)</li> <li>• notable: n=2 trials with a duration of one year --&gt; no significant change in QoL (MD0.26, 95%CI -1.18 to 1.69)</li> </ul> <p><b>COPD-related symptoms</b></p> <ul style="list-style-type: none"> <li>• one trial of cilomilast: for breathlessness scored using a Borg scale (MD -0.19, 95% CI 0.33 to -0.05) --&gt; small absolute difference so is of doubtful clinical relevance</li> </ul> <p>Exercise tolerance</p> <ul style="list-style-type: none"> <li>• no significant change</li> </ul> <p><b>COPD exacerbation</b></p> <ul style="list-style-type: none"> <li>• reduced likelihood (OR 0.78, 95% CI 0.73 to 0.83; n=19,948 ; studies=23, high-quality evidence)</li> <li>• number needed to treat for an additional beneficial outcome (NNTB) 20, 95% CI 16 to 26)</li> <li>• Ein Vergleich von Roflumilast 500µg gegen Placebo ergab eine Reduktion an Teilnehmern, die eine oder mehr Exazerbationen hatten (OR 0,0.79 [95% CI 0.73, 0.86]; I<sup>2</sup>= 0%, 13 RCT, n= 14420)</li> <li>• Wenn Roflumilast zusammen mit einem langwirksamen Bronchodilatator verabreicht wurde, zeigte sich ebenfalls eine Reduktion an Teilnehmern mit stattgehabten Exazerbationen (OR 0,69; 95% CI 0,54 - 0,88; I<sup>2</sup>=32%, 2 RCT. n = 1676). Wurde Roflumilast zusammen mit Corticosteroiden gegeben, ergab sich eine OR von 0,81 (95% CI 0,70 - 0,95), 1 RCT, n = 2686)</li> </ul> <p><b>Adverse events (any)</b></p> <ul style="list-style-type: none"> <li>• OR 1.29; 95%CI 1.22 to 1.37 (n=20988; studies=27; moderate quality evidence)</li> </ul> <p><b>Non-serious adverse events</b></p> <ul style="list-style-type: none"> <li>• More participants in the treatment groups experienced non-serious AEs compared with controls, particularly a range of gastrointestinal symptoms such as</li> <li>- diarrhoea (OR 3.13; 95%CI 2.76 to 3.54; n=20181; studies=25; high quality evidence),</li> <li>- nausea (OR 3.78, 95% CI 3.23 to 4.43; n=20627; studies=25)</li> <li>- headache (OR 1.69, 95% CI 1.47 to 1.95; n=18977; studies=22)</li> <li>- vomiting (OR 4.01, 95% CI 2.80 to 5.74; n=5828; studies=11)</li> <li>- dyspepsia (OR 3.17, 95% CI 2.33 to 4.30; n=6216; studies=13)</li> <li>- abdominal pain (OR 2.04, (95% CI 1.63 to 2.55; n=8165; studies=13)</li> <li>• number needed to treat for an additional harmful outcome (NNTH) 15, 95% CI 13 to 17)</li> <li>• Roflumilast in particular was associated with weight loss during the trial period and an increase in insomnia and depressive mood symptoms</li> <li>(Psychiatric adverse events (roflumilast 500µg): OR 2.13; 95%CI 1.79 to 2.54, n=11168; studies=14; moderate quality evidence; Pooled data from FDA website, not individual trial reports)</li> </ul> <p>Non-fatal serious adverse events</p> <ul style="list-style-type: none"> <li>• no significant effect of treatment on non-fatal serious adverse events (OR 0.99, 95% CI 0.91 to 1.07)</li> </ul> <p><b>Mortality</b></p> <ul style="list-style-type: none"> <li>• no significant effect (OR 0.97, 95% CI 0.76 to 1.23; n=19344; studies=23; moderate quality evidence), although mortality was a rare event during the trials.</li> </ul>		

Mukolytika

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Poole P, Sathananthan K, Fortescue R. Mucolytic agents versus placebo for chronic bronchitis or chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2019; (5).</p> <p><a href="http://www.ncbi.nlm.nih.gov/pubmed/31107966">http://www.ncbi.nlm.nih.gov/pubmed/31107966</a>.</p>	<ul style="list-style-type: none"> <li>• <b>primäre Fragestellung:</b>To determine whether treatment with mucolytics reduces exacerbations and/or days of disability in patients with chronic bronchitis or COPD</li> <li>• <b>sekundäre Fragestellungen:</b> To assess whether mucolytics lead to improvement in lung function or quality of life + To determine frequency of adverse effects associated with use of mucolytics</li> <li>• <b>Suchzeitraum:</b> most recently on 23.April 2019</li> <li>• <b>Population:</b> adults with chronic bronchitis or COPD</li> <li>• <b>Einschlusskriterien</b> <ul style="list-style-type: none"> <li>- RCT</li> <li>- adults with chronic bronchitis as defined by the British Medical Research Council or COPD as defined by the criteria of ATS, GOLD, ERS, or WHO</li> <li>- must have received regular treatment with oral mucolytics or placebo for at least two months</li> </ul> </li> <li>• <b>Ausschlusskriterien:</b> <ul style="list-style-type: none"> <li>- people with asthma and cystic fibrosis; children</li> <li>- studies of inhaled mucolytics and combinations of mucolytics with antibiotics and <u>mucolytics with bronchodilators</u>.</li> </ul> </li> </ul>	<p><b>Baseline-Charakteristika</b></p> <ul style="list-style-type: none"> <li>- mean age of participants ranged from 40 to 71 years</li> <li>- All but five studies reported the percentage of current smokers or ex-smokers, which ranged from 55% to 100%</li> <li>- verschiedene Mukolytika in Studien betrachtet; verschiedene Dosierungen</li> </ul> <p><u>Participants with no exacerbations in study period (Follow-up: 8.8 months):</u> Risk with placebo: 386 per 1000 Risk with mucolytic: 521 per 1000 (495 to 545) Peto OR 1.73, 95% CI 1.56 to 1.91; 28 RCTs, 6723 participants; <b>moderate certainty evidence</b></p> <p>&gt;&gt; Generally larger effects in earlier studies of mucolytics in chronic bronchitis and smaller effects in more recent studies in COPD &gt;&gt; The overall number needed to treat with mucolytics for an average of nine months to keep an additional participant free from exacerbations was eight (NNTB 8, 95% CI 7 to 10). &gt;&gt; High heterogeneity was noted for this outcome (<math>I^2 = 62\%</math>) &gt;&gt;The type or dose of mucolytic did not seem to alter the effect size, nor did the severity of COPD, including exacerbation history. &gt;&gt;Longer studies showed smaller effects of mucolytics than were reported in shorter studies.</p> <p><u>Days of disability per participant per month (Follow-up: 8.3 months):</u> Risk with placebo: Mean days of disability per participant per month was 1.57 days Risk with mucolytic: MD 0.43 days lower (0.56 lower to 0.30 lower) 9 RCTs, 2259 participants; <math>I^2 = 61\%</math>; <b>moderate certainty evidence</b></p> <p><u>Health- related quality of life (total score SGRQ) Scale from 1 to 100; lower scores indicate better quality of life (Follow-up: 14.1 months):</u> Risk with placebo: Mean SGRQ total score was 39.02 points Risk with mucolytic: MD 1.37 lower (2.85 lower to 0.11 higher) 7 RCTs; 2721 participants; <math>I^2 = 64\%</math>; <b>moderate certainty evidence</b></p> <p><u>Hospitalisation during study period (Follow-up: 16.6 months):</u> Risk with placebo: 188 per 1000 Risk with mucolytic: 136 per 1000 (107 to 171) Peto OR 0.68 (0.52 to 0.89); 1833 participants; 5 RCTs; <math>I^2 = 58\%</math>; <b>moderate certainty evidence</b></p> <p><u>Adverse effects (Follow-up: 8.2 months):</u></p>	<p>AMSTAR II: low</p>	<p>teilweise große Heterogenität beachten; meist fixed effects model angewendet</p> <p>teilweise unterschiedliche Angaben zu Studien/Teilnehmern in der Darstellung von ein und dem selben Ergebnis (Summary of findings table vs. Ergebnisse im Abstract; Bsp. Hospitalisierung)</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<p>as well as studies of deoxyribonuclease or proteases such as trypsin.</p> <ul style="list-style-type: none"> <li>• <b>Interventionen:</b> oral mucolytic therapy for at least two months</li> <li>• <b>Vergleich:</b> Placebo</li> <li>• <b>eingeschlossene Studien:</b> randomised, placebo-controlled trials; n=38 (10,377 participants) --&gt; betrachtete Mukolytika im Review: N-acetylcysteine (NAC) (n=21 studies) carbocysteine (n = 3) ambroxol (n = 3) erdosteine (n = 2) sobrerol (n = 1) carbocysteinesobrerol (n = 1) carbocysteine-lysine (n = 1) letosteine (n = 1), cithiolone (n = 1) iodinated glycerol (n = 1) N-isobutyrylcysteine (NIC) (n = 1) myrtol (n = 1) cineole and lysozyme (n = 1)</li> </ul>	<p>Risk with placebo: 235 per 1000 Risk with mucolytic: 205 per 1000 (185 to 224) Peto OR 0.84 (0.74 to 0.94); 7264 participants; 24 RCTs; I<sup>2</sup> = 46%; <b>moderate certainty evidence</b> &gt;&gt; pooled effect includes no difference if a random-effects model is used.</p> <p><u>Death during study period (Follow-up: 13.3 months):</u> Risk with placebo: 11 per 1000 Risk with mucolytic: 10 per 1000 (5 to 20) Peto OR 0.98 (0.51 to 1.87); 3527 participants; 11 RCTs; I<sup>2</sup> = 0%; <b>moderate certainty evidence</b> &gt;&gt; 18 deaths on mucolytics and 19 on placebo</p>		

**Betablocker**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
Salpeter SR. Cardioselective beta-blockers for chronic obstructive pulmonary disease. Cochrane Database of	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To assess the effect of cardioselective beta-blockers on respiratory function of patients with COPD.</li> </ul>	<p><u>Cardioselective beta-blockers (single dose (n=131) or longer duration (n=185))</u> - no change in FEV1 compared to placebo -- single dose: MD -2.08 [-5.25, 1.09], 4 RCT, n=108 -- longer duration: MD -4.00 [-8.09, 0.08], 5 RCT, n=121</p>	<p>AMSTAR: y-n-y-n-y-y-n-y-n-n Score: 6</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
Systematic Reviews 2005;(4).	<ul style="list-style-type: none"> <li>• <b>Suchzeitraum:</b> from 1966 to August 2010</li> <li>• <b>Population:</b> patients with COPD</li> <li>• <b>Ein- und Ausschlusskriterien:</b> RCTs (blinded) of single dose or longer duration, studied the effects of cardioselective beta-blockers on FEV1 or symptoms in patients with COPD.</li> <li>• <b>Interventionen:</b> cardioselective beta-blockers</li> <li>• <b>Vergleich:</b> Placebo</li> <li>• <b>eingeschlossene Studien:</b> 11 RCTs (single dose, n=131), 11 RCTs (longer duration, n=185)</li> </ul>	<p>- no Change in respiratory symptoms compared to placebo                      -- single dose: Risk difference 0.0 [-0.04, 0.04], 9 RCT, n=301                      -- longer duration: Risk difference -0.01 [-0.06, 0.04], 10 RCT, n=273</p> <p>- did not affect the FEV1 treatment response to beta2 agonists                      -- Single-dose Beta-agonist treatment effect: MD -1.21 [-10.97, 8.56], 2 RCT. n=50                      -- Longer duration Beta-agonist treatment effect: MD -0.70 [-5.02, 3.63], 3 RCT, n=89</p> <p><u>Subgroup analyses</u>                      - no significant change in results for those participants with severe chronic airways obstruction, those with a reversible obstructive component, or those with concomitant cardiovascular disease.</p> <p><u>Authors' conclusions</u>                      Cardioselective beta-blockers, given to patients with COPD in the identified studies did not produce adverse respiratory effects. Given their demonstrated benefit in conditions such as heart failure, coronary artery disease and hypertension, cardioselective beta-blockers should not be routinely withheld from patients with COPD.</p>	

**Impfungen**

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Walters-Julia AE. Pneumococcal vaccines for preventing pneumonia in chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2017;(1).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001390.pub4/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001390.pub4/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To determine the efficacy of injectable pneumococcal vaccination for preventing pneumonia in persons with COPD.</li> <li>• <b>Suchzeitraum:</b> up to 25 Nov. 2016</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b> RCTs using injectable pneumococcal vaccines</li> <li>• <b>Interventionen:</b> injectable pneumococcal polysaccharide vaccine (PPV) or pneumococcal conjugated vaccine (PCV)</li> <li>• <b>Vergleich:</b> control or alternative vaccine type</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b>                      - average age of participants was 66 years, 67% were male and participants had received a diagnosis of moderate to severe COPD</li> <li>• <b>Ergebnisse: pneumococcal vaccine vs. control</b>  <u>Pneumonia, community acquired</u> (at least 1 episode Follow-up: range 6 to 36 months): OR 0.62 (95% CI 0.43 to 0.89) (n=1372 participants; 6 RCTs;  <b>GRADE: Moderate</b>)                      --&gt; 21 people with COPD (95% CI 15 to 74) would have to be vaccinated to prevent one episode of pneumonia</li> <li><u>Pneumococcal pneumonia</u> (at least 1 episode Follow-up: range 6 to 36 months): OR 0.26 (95% CI 0.05 to 1.31) (n=1158 participants; 3 RCTs; <b>GRADE: Low</b>; Very few confirmed episodes of pneumococcal pneumonia.)</li> <li><u>Death from cardiorespiratory causes</u> (Follow-up: range 24 to 48 months): OR 1.07 (95% CI 0.69 to 1.66) (n=888 participants; 3 RCTs;  <b>GRADE: Moderate</b>)</li> </ul>	<p>AMSTAR-Score: 10/11</p> <p>y-y-y-y-y-y-y-ca-y</p>



Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<p>1. <u>Comparison</u>: pneumococcal polysaccharide vaccine, 23- valent (PPSV-23) OR 14-valent (PPV-14), versus control.</p> <p>2. <u>Comparison</u>: 23-valent pneumococcal polysaccharide vaccine (PPV-23) versus 7-valent diphtheria-conjugated pneumococcal polysaccharide vaccine (PCV-7).</p> <p>• <b>eingeschlossene Studien:</b> 12 RCTs( 2171 participants with COPD)</p>	<p><u>Death from all causes</u> (Follow-up: range 12 to 48 months): OR 1.00 (95% CI (0.72 to 1.40) (n=1053 participants; 5 RCTs; <b>GRADE: Moderate</b>)</p> <p><u>Hospital admission</u> (any cause, at least 1 episode; Follow-up: range 6 to 12 months): OR 0.74 ( 95% CI 0.32 to 1.74) (n=391 participants; 3 RCTs; <b>GRADE: Moderate</b>)</p> <p><u>COPD exacerbation</u> (at least 1 episode; Follow-up: range 6 to 24 months): OR 0.60 (95% CI 0.39 to 0.93) (n=446 participants; 4 RCTs; <b>GRADE: Moderate</b>) --&gt; 8 people with COPD (95% CI 5 to 58) would have to be vaccinated to prevent one person from having an acute exacerbation</p> <p>- one study (n =181) compared the efficacy of different vaccine types - 23-valent PPV versus 7-valent PCV - and reported no differences for CAP, all-cause mortality, hospital admission or likelihood of a COPD exacerbation, but investigators described a greater likelihood of some mild adverse effects of vaccination with PPV-23.</p> <p><b>Authors' conclusions</b> Injectable polyvalent pneumococcal vaccination provides significant protection against community-acquired pneumonia, although no evidence indicates that vaccination reduced the risk of confirmed pneumococcal pneumonia, which was a relatively rare event. Vaccination reduced the likelihood of a COPD exacerbation, and moderate-quality evidence suggests the benefits of pneumococcal vaccination in people with COPD. Evidence was insufficient for comparison of different pneumococcal vaccine types.</p>	

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Kopsaftis Z, Wood-Baker R, Poole P. Influenza vaccine for chronic obstructive pulmonary disease (COPD). Cochrane Database of Systematic Reviews 2018, Issue 6. Art. No.: CD002733. DOI: 10.1002/14651858.CD002733.pub3. <a href="https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD002733.pub3/full">https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD002733.pub3/full</a></p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To determine whether influenza vaccination in people with COPD reduces respiratory illness, reduces mortality, is associated with excess adverse events, and is cost effective.</li> <li>• <b>Suchzeitraum:</b> 12/2017</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b> - RCT, included adults with COPD, -receive at least one annual influenza vaccination. Influenza vaccination may have been one of the following types: live attenuated whole virus, inactivated, or a split-virus type vaccine, and may have been administered by either intramuscular injection or intranasal spray.</li> <li>• <b>Interventionen:</b> live or inactivated virus vaccines, either alone or with another vaccine</li> <li>• <b>Vergleich:</b> placebo</li> <li>• <b>eingeschlossene Studien:</b> 6/11 eingeschlossenen RCT betrachten Patient*innen mit COPD (2469 participants).</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> - Ältere Studien eingeschlossen (alle vor 2004 publiziert)</li> <li>• <b>Ergebnisse:</b> <ul style="list-style-type: none"> <li>• Inaktivierter Impfstoff reduzierte die <u>Gesamtzahl der Exazerbationen</u> pro geimpftem/r Teilnehmer/in im Vergleich zu denen, die Placebo erhielten: MD -0.37 (95% KI -0,64; -0.11); I<sup>2</sup> = 8%, 2 RCT, n = 180, <b>Datenqualität niedrig</b></li> <li>• <u>Hospitalisierungsrate</u> in der Interventionsgruppe im Vergleich zur Kontrollgruppe verringert : 23/1000 vs. 76/1000, OR 0,33 (95% KI 0,09; 1,24), I<sup>2</sup> = 0%, 2 RCT, n = 180, <b>Datenqualität niedrig</b>.</li> <li>• Mortalität: 67/1000 vs. 76/1000, OR 0,87 (95% KI 0,28; 2,70); I<sup>2</sup>=0% , 2 RCT, n = 180, <b>Datenqualität niedrig</b>.</li> <li>• <u>Sicherheit:</u> Two studies evaluating mortality for influenza vaccine versus placebo were too small to have detected any effect on mortality. However, a large study (N=2215) noted that there was no difference in mortality when adding live attenuated virus to inactivated virus vaccination.</li> </ul> </li> </ul>	<p>AMSTAR-II</p> <p>moderat</p>

### Anhang 8.2 Triple-Therapie

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Lee S-D. Efficacy and tolerability of budesonide/formoterol added to tiotropium compared with tiotropium alone in patients</p>	<ul style="list-style-type: none"> <li>• <b>Studientyp:</b> randomized, parallel-group, open-label Phase IV study</li> <li>• <b>Population:</b> patients with severe or very severe COPD (n= 578)</li> <li>• <b>Studienzeitraum:</b> 07/2011 - 06/2013; 12 week trial</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlichliche Alter, geschlecht, Dauer der Erkrankung weitestgehend ausgeglichen; leichte Unterschiede in der Schwere der Erkrankung</li> <li>-ITT comprised 287 patients in the triple therapy group and 290 patients in the tiotropium alone group</li> </ul>	<p><b>Selection bias</b> Randomisierung: <b>unclear</b> Allocation concealment: <b>unclear</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>high</b></p>	<p>kein Protokoll zur Verfügung; keine Angaben zur Methodik auf clinicaltrials.gov</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>with severe or very severe COPD: A randomized, multicentre study in East Asia. <i>Respirology</i> 2016; 21(1):119–27.  <a href="https://www.ncbi.nlm.nih.gov/pubmed/26394882">https://www.ncbi.nlm.nih.gov/pubmed/26394882</a>.</p>	<p>• <b>Intervention:</b>                      - 14-day run-in period: tiotropium 18 µg once daily                      -- Budesonide/Formoterol (Symbicort® Turbuhaler® 160/4.5µg/Inhalation, 2 Inhalations Twice Daily) Added to Tiotropium (Spiriva™ 18 µg/Inhalation, 1 Inhalation Once Daily)                      vs.                      -- Tiotropium (Spiriva™18 µg/Inhalation, 1 Inhalation Once Daily) Alone</p> <p>• <b>Einschlusskriterien:</b>                      - ≥40 years of age; diagnosis of COPD with symptoms &gt; 2 years; a history of at least one COPD exacerbation requiring a course of oral steroids and/or antibiotics within 1-12 months before Visit 2                      - FEV1 ≤50% of predicted normal value, FEV1 / FVC &lt; 70%                      - Total symptom score of 2 or more per day for at least half of run-in period (breathing, cough and sputum scores from the diary card)</p> <p>• <b>Ausschlusskriterien (Auswahl):</b>                      - Asthma, exacerbations within 4 weeks prior to Visit 2 or during run in; relevant cardiovascular disorder</p> <p>• <b>primärer Endpunkt</b>                      - Pre-dose FEV1</p> <p>• <b>sekundäre Endpunkte (Auswahl)</b>                      - Change in COPD Symptoms - Breathing, cough, sputum, exacerbations                      - change in SGRQ</p> <p>• East Asia; multicenter (41 study centres in China, Hong Kong, Indonesia, South Korea and Thailand)</p>	<p>• <b>sekundäre Endpunkte:</b>  <b>Exazerbationen</b>  <u>number of patients with ≥1 COPD exacerbation</u>                      - triple therapy group:n= 40 (13.9%)                      - tiotropium: n= 61 (21.0%)  <u>rate of COPD exacerbations</u>                      The rate of COPD exacerbations per 12weeks was reduced by 40.7% (95% CI: -16.1, -58.1; P = 0.0032) with triple therapy (0.18 (95% CI: 0.14, 0.24)) versus tiotropium alone (0.31 (95% CI: 0.25, 0.38)).</p> <p>Triple therapy significantly prolonged the time to first exacerbation compared with tiotropium alone (38.6% risk reduction (95% CI: -8.4, -58.8), P = 0.017)</p> <p><b>SGRQ-C total score</b>                      - triple therapy mean change from baseline: -10.00 units (95% CI: -12.26, -7.74)                      - tiotropium mean change from baseline: -4.80 units (95% CI: -7.03, -2.56)                      &gt;&gt; LS mean difference: -5.20 units (95% CI: -8.03, -2.38; P = 0.0003)                      A higher proportion of patients in the triple therapy group achieved a clinically meaningful improvement in the SGRQ-C total score (i.e. a change of ≥4 units) versus the tiotropium alone group (59.6 vs 46.2%, respectively; P = 0.0015).</p> <p><b>COPD symptoms</b>                      Triple therapy significantly improved COPD symptoms compared with tiotropium alone, with significant reductions in breathing difficulty, cough and sputum scores</p> <p><u>Breathing</u>                      Triple: n=284 -0.37 (-0.45, -0.29); Tio: n= 286 -0.11 (-0.19, -0.03); treatment difference: -0.26 (-0.36, -0.16); p &lt;0.0001</p> <p><u>Cough</u>                      Triple: n=283 -0.31 (-0.39, -0.23); Tio: n= 286 -0.17 (-0.25, -0.09); treatment difference: -0.14 (-0.25, -0.04); p= 0.0067</p> <p><u>Sputum</u>                      Triple: n=284 -0.22 (-0.30, -0.14); Tio: n= 286 -0.09 (-0.17, -0.01); treatment difference: -0.12 (-0.22, -0.02);</p>	<p><b>Detection bias</b>                      Verblindung der Ergebnisevaluation: <b>unclear</b></p> <p><b>Attrition bias</b>                      Verlust von Studienteilnehmern/ fehlende Daten: <b>unclear</b></p> <p>ITT-Analyse: durchgeführt (siehe Kommentar)</p> <p><b>Reporting bias</b>                      selektive Ergebnisdarstellung: <b>unclear</b></p> <p><b>Andere Biasursachen</b>                      Baseline imbalance: <b>unclear</b></p> <p>Interessenkonflikte/ Sponsoring: Astra Zeneca</p>	

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
		<p>p= 0.0171</p> <ul style="list-style-type: none"> <li>• <b>Sicherheit:</b> <ul style="list-style-type: none"> <li>- Incidence of adverse events was 26% for both groups.</li> <li>- All six deaths were judged by an investigator as unrelated to treatment.</li> </ul> </li> </ul>		
<p>Vestbo J. Single inhaler extrafine triple therapy versus long-acting muscarinic antagonist therapy for chronic obstructive pulmonary disease (TRINITY): A double-blind, parallel group, randomised controlled trial. Lancet 2017; 389(10082):1919–29. <a href="https://www.ncbi.nlm.nih.gov/pubmed/28385353">https://www.ncbi.nlm.nih.gov/pubmed/28385353</a>.</p>	<p><b>TRINITY</b></p> <ul style="list-style-type: none"> <li>• <b>Studientyp:</b> double-blind, parallel group, double-dummy, active-controlled, randomised controlled trial</li> <li>• <b>Population:</b> n= 2691 patients (fixed triple (n=1078), tiotropium (n=1075), open triple (n=538))</li> <li>• <b>Studienzeitraum:</b> 01/2014 - 03-2016; 52 week trial</li> <li>• <b>Intervention:</b> <ul style="list-style-type: none"> <li>- 2-week run-in period: one inhalation per day via single-dose dry-powder inhaler of open-label 18 µg tiotropium</li> <li>- patients were randomised (2:2:1) to tiotropium, fixed triple, or open triple</li> <li>--tiotropium 18 µg</li> <li>-- extrafine beclometasone dipropionate, formoterol fumarate, and glycopyrronium bromide (100 µg BDP/6 µg FF/12,5 µg GB; fixed triple)</li> <li>-- 100 µg BDP/6 µg FF plus tiotropium 18 µg (open triple)</li> </ul> </li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- had COPD, 40 years of age or older; current or ex-smokers; postbronchodilator FEV1 of less than 50%, at least one moderate-to-severe COPD exacerbation in the previous 12 months, and a COPD Assessment Test total score of at least 10</li> <li>- used ICS/LABA, ICS/LAMA; LAMA/LABA or</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Baseline-Patientencharakteristika: hinsichtlich Alter, Geschlecht; Rauchstatus; Blueeosinophilen, Lungenfunktion, Begleiterkrankungen weitestgehend ausgeglichen</li> <li>• sites were a mixture of primary care (17), secondary care (121), tertiary care (48), and specialist investigation units (38)</li> <li>• <b>Statistik:</b> prespecified hierarchical order</li> <li>• <b>completed study:</b> <ul style="list-style-type: none"> <li>- fixed triple: 986/1078</li> <li>- tiotropium: 914/1075</li> <li>- open triple: 496/538</li> </ul> </li> <li>• <b>primärer Endpunkt: moderate-to-severe exacerbation rates</b> <ul style="list-style-type: none"> <li>- fixed triple: 0,46 (95% CI 0,41–0,51)</li> <li>- tiotropium: 0,57 (95% CI 0,52–0,63)</li> <li>- open triple: 0,45 (95% CI 0,39–0,52)</li> <li>&gt;&gt; fixed triple was superior to tiotropium (rate ratio 0,80 [95% CI 0,69–0,92]; p=0-0025)</li> </ul> </li> <li>• <b>Subgruppe: Eosinophile</b> <ul style="list-style-type: none"> <li>- compared with tiotropium monotherapy the effect of the two triple therapies on exacerbation rate was greater in the subgroups with higher eosinophil concentrations <u>eosinophil count of at least 2%</u></li> <li>the triple therapies also reduced exacerbation rates versus tiotropium (RR 0,70 [95% CI 0,58–0,85] for fixed and 0,69 [0,55–0,87] for open triple)</li> <li><u>eosinophil count of &lt;2% subgroup</u></li> <li>corresponding reductions in the &lt;2% subgroup were smaller (0,3 [0,75–1,17] for fixed triple and 0,91 [0,69–1,20] for open triple).</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li><b>Selection bias</b> Randomisierung: <b>low</b> Allocation concealment: <b>low</b></li> <li><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>low</b></li> <li><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>low</b></li> <li><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>unclear</b></li> <li>ITT-Analyse: durchgeführt</li> <li><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>low</b></li> <li><b>Andere Biasursachen</b> Baseline imbalance: <b>low</b></li> <li>Interessenkonflikte/ Sponsoring: Chiesi Farmaceutici SpA. The funder was responsible for the design and analysis of the study, oversaw its conduct and was responsible for preparing the study report.</li> </ul>	<p>Appendix abrufbar</p> <p>BDP/FF/GB: Superiority over Tiotropium</p> <p>open vs. fixed triple: non- inferiority</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<p>LAMA mono for at least 2 month before screening</p> <ul style="list-style-type: none"> <li>• <b>Ausschlusskriterien (relevante )</b></li> <li>- receiving triple therapy of inhaled LABA/LAMA/ICS</li> <li>- diagnosis of asthma, or history of allergic rhinitis or atopy; COPD exacerbation in the 4 weeks before screening or during the run-in period; clinically significant cardiovascular conditions or laboratory abnormalities (including persistent, long-standing, or permanent atrial fibrillation); or unstable concurrent disease; requiring LTOT, requiring antibiotics or systemic steroids or PDE-4 inhibitors in the 4 weeks prior to screening</li> <li>• <b>primärer Endpunkt</b></li> <li>- moderate-to-severe COPD exacerbation rate</li> <li>• <b>sekundäre Endpunkte</b> (Auswahl)</li> <li>- key secondary endpoint was change from baseline in pre-dose FEV1 at week 52</li> <li>- time to first moderate to severe COPD exacerbation, and to first severe COPD exacerbation; rate of severe and of moderate COPD exacerbations throughout 52 weeks of treatment; SGRQ response at weeks 26 and 52; SGRQ total score at all clinic visits; percentage of days without rescue medication use</li> <li>• multicenter: at 224 sites across 15 countries</li> </ul>	<p><u>patients with more than one exacerbation in the previous 12 months</u></p> <p>Additionally, compared with open triple, fixed triple significantly reduced the rate of moderate-to-severe exacerbations in the subgroup of patients with more than one exacerbation in the previous 12 months (0,71 [0,51–1,00]).</p> <ul style="list-style-type: none"> <li>• <b>Sicherheit:</b> Adverse events were reported by 594 (55%) patients with fixed triple, 622 (58%) with tiotropium, and 309 (58%) with open triple.</li> </ul>		
<p>Chapman KR. Long-Term Triple Therapy De-escalation to Indacaterol/Glycopyrronium in Patients with Chronic Obstructive Pulmonary Disease (SUNSET): A Randomized, Double-Blind, Triple-Dummy Clinical Trial. Am J Respir Crit Care</p>	<p><b>SUNSET</b></p> <ul style="list-style-type: none"> <li>• <b>Objective:</b> direct <b>de-escalation</b> from long-term triple therapy to indacaterol/glycopyrronium</li> <li>• <b>Studientyp:</b> randomized, double-blind, triple-dummy clinical trial; parallel group; Nicht-Unterlegenheitsstudie</li> <li>• <b>Population:</b> n=1053 (nach Run-In Phase)</li> <li>• <b>Studienzeitraum:</b> 11/2015 - 07/2017; 26-week trial</li> <li>• <b>Intervention:</b></li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Geschlecht, Alter, Gewicht, Lungenfunktion, Dauer der Erkrankung weitestgehend ausgeglichen.</li> <li>- no differences in the distribution of patients according to their exacerbation history and the baseline blood eosinophil counts</li> <li>- nach Randomisierung: n=456/527 completed in Ind/Gly-group; n=472/526 in triple therapy group</li> <li>• <b>Ergebnisse sekundärer Endpunkt: Exazerbationen</b></li> <li>Patients in the two groups experienced similar annualized</li> </ul>	<p><b>Selection bias</b> Randomisierung: <b>low</b> Allocation concealment: <b>low</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>low</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>low</b></p>	<p>primärer Endpunkt: klinische Relevanz? (nicht durch Leitliniengruppe priorisiert)</p> <p>Ausschluss von Patienten mit eosinophils &gt; 600 cells/µl</p> <p>Ausschluss von Patienten</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Med 2018; 198(3):329–39.  <a href="https://www.ncbi.nlm.nih.gov/pubmed/29779416">https://www.ncbi.nlm.nih.gov/pubmed/29779416</a>.</p>	<p>- 4-week run-in period on standard triple therapy (tiotropium 18 µg once daily + combination of salmeterol/fluticasone propionate 50/500 µg twice daily) --&gt;</p> <p>-- Nach Run-In: Randomisierung (1:1) to                      -- indacaterol/glycopyrronium (110/50 µg) once daily (+ Placebo: triple-Therapy)                      or                      -- triple therapy ( tiotropium plus salmeterol/fluticasone) (+ Placebo: duale Therapie)</p> <p>• Follow-up: 30 d nach Studien-Ende</p> <p>• <b>Einschlusskriterien:</b></p> <p>- nonfrequently exacerbating patients with moderate-to-severe COPD (stable)</p> <p>- patients &gt; 40 years of age</p> <p>- with a postbronchodilator FEV1 of at least 40% to less than 80% predicted, a post-bronchodilator ratio of FEV1 to FVC of less than 0.70, and a smoking history of at least 10 pack-years.</p> <p>- Patients were not frequent exacerbators (i.e., they had a history of no more than one moderate or severe exacerbation in the previous year)</p> <p>- must have received long-term triple therapy (for at least 6 mo) before enrollment</p> <p>• <b>Ausschlusskriterien:</b></p> <p>- a history of asthma</p> <p>- with a blood eosinophil count greater than 600 cells/µl during screening</p> <p>• <b>primärer Endpunkt:</b> noninferiority on change from baseline in trough FEV1</p> <p>• <b>sekundäre Endpunkte:</b></p> <p>- Moderate or severe exacerbations (predefined)</p> <p>- TDI, SGRQ, effect of baseline eosinophil blood level/absolute eosinophil counts</p> <p>• multicenter study</p>	<p>rates of</p> <p>- <u>moderate or severe COPD exacerbations</u> (indacaterol/glycopyrronium vs. tiotropium plus salmeterol/ fluticasone, 0.52 vs. 0.48; rate ratio, 1.08; 95% CI, 0.83 to 1.40)</p> <p>- <u>all (mild, moderate, and severe) exacerbations</u> (4.11 vs. 3.86; rate ratio, 1.07; 95% CI, 0.93 to 1.22).</p> <p>- no difference between treatments in the time to first moderate or severe COPD exacerbation (hazard ratio, 1.11; 95% CI, 0.85 to 1.46)</p> <p>• <b>weitere ausgewählte Ergebnisse:</b></p> <p><u>Exazerbationen und Eosinophile</u></p> <p>- The rate of moderate or severe exacerbations according to baseline blood eosinophils subgroups did not differ between the two treatment arms, with the exception of patients with baseline blood eosinophil counts ≥300 cells/µl who were at increased risk of exacerbations (rate ratio, 1.86; 95% CI, 1.06 to 3.29)</p> <p>- There was no difference in the time to first exacerbation between the two arms in patients with &lt;300 cells/µl (hazard ratio, 0.95; 95% CI, 0.70 to 1.29)</p> <p>- whereas a difference in favor of tiotropium plus salmeterol/fluticasone was observed in patients with ≥300 cells/µl (hazard ratio, 1.80; 95% CI, 0.98 to 3.28)</p> <p><u>Quality of Life (SGRQ)</u></p> <p>The change from baseline in SGRQ-C score at Week 12 was -0.7 and -2.5 units for indacaterol/glycopyrronium and tiotropium plus salmeterol/fluticasone, respectively (Δ = 1.8 units; 95% CI, 0.7 to 3.0); similar changes were observed at Week 26 ( -1.0 and -2.5 units with indacaterol/glycopyrronium and tiotropium plus salmeterol/fluticasone, respectively; Δ = 1.4 units; 95% CI, 0.2 to 2.6 units).</p> <p>• <b>Sicherheit:</b></p> <p>- The incidence of adverse events and serious adverse events were similar across both treatment arms</p> <p>- Adverse events leading to permanent discontinuation of study drug were similar (indacaterol/ glycopyrronium 3.6% and tiotropium plus salmeterol/fluticasone 3.4%)</p>	<p><b>Attrition bias</b></p> <p>Verlust von Studienteilnehmern/ fehlende Daten: <b>unclear</b></p> <p>ITT-Analyse: die sekundären Endpunkte wurden für die Gruppe ausgewertet, die mind. 1 Behandlung erhalten hat, nicht nach Randomisierung</p> <p><b>Reporting bias</b></p> <p>selektive Ergebnisdarstellung: <b>low</b></p> <p><b>Andere Biasursachen</b></p> <p>Baseline imbalance: <b>low</b></p> <p>Interessenkonflikte/ Sponsoring: Novartis (via clinicaltrials.gov NCT 02603393)</p>	<p>enten, welche &gt; 1 moderate oder schwere Exazerbation im letzten Jahr hatten</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Papi A. Extrafine inhaled triple therapy versus dual bronchodilator therapy in chronic obstructive pulmonary disease (TRIBUTE): A double-blind, parallel group, randomised controlled trial. Lancet 2018; 391(10125):1076–84. <a href="https://www.ncbi.nlm.nih.gov/pubmed/29429593">https://www.ncbi.nlm.nih.gov/pubmed/29429593</a>.</p>	<p><b>TRIBUTE</b></p> <ul style="list-style-type: none"> <li>• <b>Studientyp:</b> double-blind, parallel group, double-dummy randomised controlled trial</li> <li>• <b>Population:</b> n= 1532 (BDP/FF/G: n=764; IND/GLY: n=768)</li> <li>• <b>Studienzeitraum:</b> 05/2015 - 07/2017; 52 weeks trials</li> <li>• <b>Intervention:</b> <ul style="list-style-type: none"> <li>- 2 week run in period with one inhalation per day of IND/GLY (85 µg/43 µg)</li> <li>- randomly assigned (1:1) to                             <ul style="list-style-type: none"> <li>-- two inhalations of extrafine beclometasone dipropionate, formoterol fumarate, and glycopyrronium (BDP/FF/G) (87 µg/5 µg/9 µg) twice per day (single-inhaler) or</li> <li>-- one inhalation of indacaterol plus glycopyrronium (IND/GLY) (85 µg/43 µg) per day (single-inhaler)</li> </ul> </li> </ul> </li> <li>• <b>Einschlusskriterien</b> <ul style="list-style-type: none"> <li>- &gt;40 years of age; symptomatic COPD, severe or very severe airflow limitation, at least one moderate or severe exacerbation in the previous year, and were receiving inhaled maintenance medication</li> </ul> </li> <li>• <b>Ausschlusskriterien (Auswahl)</b> <ul style="list-style-type: none"> <li>- Asthma with ICS or OCS therapy</li> <li>- requiring use systemic steroids, antibiotics, PDE4 inhibitors in the 4 weeks prior to screening</li> <li>- treated with non-cardioselective β-blockers for at least 10 days before randomization</li> <li>- requiring LTOT</li> <li>- clinically significant cardiovascular conditions; atrial fibrillation</li> </ul> </li> <li>• <b>primärer Endpunkt</b> <ul style="list-style-type: none"> <li>- rate of moderate-to-severe COPD exacerbations over 52 week treatment</li> </ul> </li> <li>• <b>sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Time and rate of COPD exacerbation</li> <li>- Change from baseline pre-dose morning FEV1, FVC and FEV1 response</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, Geschlecht, Gewicht, Rauchstatus, Blut-Eosinophilen, Dauer der Erkrankung, Begleiterkrankungen weitestgehend ausgeglichen</li> <li>• multicenter: mixture of primary (n=37), secondary (n=104) and tertiary care centres (n=1), and specialised investigation units (n=45)             <ul style="list-style-type: none"> <li>- The study was completed by 666 (87%) of 764 patients assigned to the BDP/FF/G group and 648 (84%) of 768 patients in the IND/GLY group</li> </ul> </li> <li>• <b>primärer Endpunkt: Exazerbationensraten (moderate-to-severe)</b> <ul style="list-style-type: none"> <li>- BDP/FF/G: 0,50 per patient per year (95% CI 0,45–0,57)</li> <li>- IND/GLY: 0,59 per patient per year (0,53–0,67)</li> <li>--&gt; ITT rate ratio of 0,848 (0,723–0,995, p=0,043) in favour of BDP/FF/G (indicating a 15% reduction in the exacerbation rate)</li> </ul> </li> <li>• <b>Subgruppen:</b> <ul style="list-style-type: none"> <li><u>patients with chronic bronchitis</u> <ul style="list-style-type: none"> <li>- BDP/FF/G had a significantly reduced exacerbation rate compared with IND/GLY (rate ratio 0,752, 0,605–0,935, p=0,010)</li> </ul> </li> <li><u>patients with emphysema</u> <ul style="list-style-type: none"> <li>-adjusted rate ratio 0,995 (0,754–1,314, p=0,974)</li> </ul> </li> <li><u>mixed bronchitis and emphysema</u> <ul style="list-style-type: none"> <li>- adjusted rate ratio 0,939 (0,605–1,459, p=0,781)</li> </ul> </li> <li><u>patients with eosinophils of at least 2%</u> <ul style="list-style-type: none"> <li>- BDP/FF/G also significantly reduced the exacerbation rate compared with IND/GLY: rate ratio 0,806, 0,664–0,978; p=0,029</li> </ul> </li> <li><u>patients with eosinophils less than 2%</u> <ul style="list-style-type: none"> <li>- adjusted rate ratio of 0,943 (0,711–1,251, p=0,685)</li> </ul> </li> </ul> </li> <li>- In a second eosinophil subgroup analysis, the adjusted rate ratio was 0,806 (0,646–1,007; p=0,057) in patients with at least 200 cells per µL and 0,872 (0,692–1,098, p=0,244) for patients with &lt;200 cells/µL.</li> </ul>	<ul style="list-style-type: none"> <li><b>Selection bias</b> <ul style="list-style-type: none"> <li>Randomisierung: <b>low</b></li> <li>Allocation concealment: <b>low</b></li> </ul> </li> <li><b>Performance bias</b> <ul style="list-style-type: none"> <li>Verblindung von Teilnehmern und Personal: <b>low</b></li> </ul> </li> <li><b>Detection bias</b> <ul style="list-style-type: none"> <li>Verblindung der Ergebnisevaluation: <b>low</b></li> </ul> </li> <li><b>Attrition bias</b> <ul style="list-style-type: none"> <li>Verlust von Studienteilnehmern/ fehlende Daten: <b>unclear</b></li> </ul> </li> <li>ITT-Analyse: durchgeführt</li> <li><b>Reporting bias</b> <ul style="list-style-type: none"> <li>selektive Ergebnisdarstellung: <b>unclear</b></li> </ul> </li> <li><b>Andere Biasursachen</b> <ul style="list-style-type: none"> <li>Baseline imbalance: <b>low</b></li> </ul> </li> <li>Interessenkonflikte/ Sponsoring: Chiesi Farmaceutici.</li> </ul>	<p>Appendix einsehbar</p> <p>Protokolldaten (Zusammenfassungen) lediglich über clinicaltrialsregister und clinicaltrials.gov --&gt; kein extra Protokoll aufgefunden --&gt; Methodische Bewertung teilweise mit Hilfe dieser Online-Inhalte bewertet)</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<ul style="list-style-type: none"> <li>- Change in SGRQ, CAT, EXACT-PRO score</li> <li>- Use of rescue medication and nocturnal symptoms</li> <li>• multicenter (187 sites across 17 countries)</li> </ul>	<p><b>Quality of life (SGRQ total score defined as <math>\geq 4</math> units decrease from baseline)</b></p> <ul style="list-style-type: none"> <li>- Improvement in mean SGRQ total score was significantly better with BDP/FF/G than with IND/GLY both overall and at all visits</li> <li>Week 26 BDP/FF/G: n=310/764 (41%)</li> <li>Week 26 IND/GLY: n=292/768 (38%) --&gt; OR 1,13 (95% CI 0,92–1,40) p=0,255</li> <li>Week 52 BDP/FF/G: n=311/764 (41%)</li> <li>Week 52 IND/GLY: n=279/768 (36%) --&gt; OR 1,22 (0,99–1,51); p= 0,068</li> <li>• <b>Sicherheit:</b> Adverse events were reported by 490 (64%) of 764 patients receiving BDP/FF/G and 516 (67%) of 768 patients receiving IND/GLY. Pneumonia occurred in 28 (4%) patients receiving BDP/FF/G versus 27 (4%) patients receiving IND/GLY. One treatment-related serious adverse event occurred in each group: dysuria in a patient receiving BDP/FF/G and atrial fibrillation in a patient receiving IND/GLY.</li> </ul>		
<p>Ferguson GT. Triple therapy with budesonide/glycopyrrolate/formoterol fumarate with co-suspension delivery technology versus dual therapies in chronic obstructive pulmonary disease (KRONOS): A double-blind, parallel-group, multicentre, phase 3 randomised controlled trial. <i>Lancet Respir Med</i> 2018; 6(10):747–58. <a href="https://www.ncbi.nlm.nih.gov/pubmed/30232048">https://www.ncbi.nlm.nih.gov/pubmed/30232048</a>.</p>	<p><b>KRONOS</b></p> <ul style="list-style-type: none"> <li>• <b>Studientyp:</b> randomized, double-blind, parallel-group, Phase III, multicenter trial</li> <li>• <b>Population:</b> n=1902</li> <li>• <b>Studienzeitraum:</b> 08/2015 - 01/2018</li> <li>• <b>Intervention:</b> <ul style="list-style-type: none"> <li>- budesonide/glycopyrrolate/formoterol fumarate metered-dose inhaler 320/18/9.6 <math>\mu\text{g}</math> (BGF MDI) (n=640)</li> <li>- glycopyrrolate/ formoterol fumarate metered-dose inhaler 18/9.6 <math>\mu\text{g}</math> (GFF MDI) (n=627)</li> <li>- budesonide/formoterol fumarate metered-dose inhaler 320/9.6 <math>\mu\text{g}</math> (BFF MDI) (n=316)</li> <li>- open-label budesonide/formoterol fumarate dry-powder inhaler 400/12 <math>\mu\text{g}</math> (BUD/ FORM DPI) (n=319)</li> </ul> </li> <li>&gt;&gt; before screening: discontinued prohibited medication</li> <li>&gt;&gt; all patients received ipratropium bromide</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Geschlecht weitestgehend ausgeglichen</li> <li>&gt;&gt; leichte Differenzen in der Verteilung der Ethnizitäten, stattgehabter Exazerbationen im letzten Jahr; median Eosinophilenzahl und der Geschlechter auf die Gruppen (GFF MDI-Gruppe vs. alle anderen Gruppen)</li> <li>• <b>Ergebnisse primärer Endpunkt</b></li> <li>Over 24 weeks, BGF MDI significantly improved FEV1 AUC0-4 versus BFF MDI (least squares mean difference 104 mL, 95% CI 77 to 131; p&lt;0.0001) and BUD/FORM DPI (91 mL, 64 to 117; p&lt;0.0001). BGF MDI also significantly improved pre-dose trough FEV1 versus GFF MDI (22 mL, 4 to 39; p=0.0139) and was non-inferior to BUD/FORM DPI (-10 mL, -36 to 16; p=0.4390). At week 24, patients in the BGF MDI group had a significantly improved FEV1 AUC0-4 compared with patients receiving BFF MDI (116 mL, 95% CI 80 to 152; p&lt;0.0001); there was a non-significant improvement in the change from baseline in morning pre-dose trough FEV1 at week 24 versus GFF MDI (13 mL, -9 to 36</li> </ul>	<p><b>Selection bias</b> Randomisierung: <b>low</b> Allocation concealment: <b>unclear</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>low</b></p> <p><b>Detection bias</b> Verblindung der Ergebnissevaluation: <b>unclear</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>unclear</b></p> <p>ITT-Analyse:modifizierte ITT</p> <p><b>Reporting bias</b></p>	<p>Aussagekraft der primären Endpunkte? Klinischer Nutzen?</p> <p>Verschiedene primäre und sekundäre Endpunkte je nach Land gewählt</p> <p>Baseline imbalance? Ergebnisse des Vergleichs BGF MDI vs. GFF MDI aus klinischer Sicht dennoch vertrauenswürdig?</p> <p>Appendix nicht zur Verfügung</p>



Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<p>(34 µg ex-actuator) 4x/d for maintenance of COPD, and were permitted to continue using ICS during screening &gt;&gt; Ipratropium and ICS were stopped before randomisation.</p> <p>• <b>Einschlusskriterien:</b></p> <ul style="list-style-type: none"> <li>- 40-80 years of age, current or former smokers (with smoking history of &gt;=10 pack-years), had an established clinical history of COPD (mild to very severe: defined post-BD FEV1 less than 80% and 25% or more), and were <u>symptomatic for COPD</u>, despite receiving two or more inhaled maintenance therapies for at least 6 weeks before screening.</li> <li>- <u>without a requirement for a history of exacerbations in the preceding year</u></li> </ul> <p>• <b>Ausschlusskriterien:</b></p> <ul style="list-style-type: none"> <li>- Asthma or any other respiratory disease or condition other than COPD</li> <li>- acute worsening of COPD that required treatment with OCS or antibiotics less than 6 weeks before screening, with less than a 4-week wash-out of corticosteroids or antibiotics before visit 1, or during screening</li> <li>- hospitalised because of COPD within 3 month before or during screening</li> <li>- requiring a spacer divider</li> <li>- unable to perform acceptable spirometry</li> <li>- change in smoking status within 6 weeks before or during screening</li> <li>- need for a long-term oxygen therapy (&lt;15h/day)</li> </ul> <p>• <b>primärer Endpunkt</b></p> <ul style="list-style-type: none"> <li>- FEV1 AUC 0-4 h (for BFG MDI vs. BFF MDI and BFG MDI vs. BUD/FORM DPI over 24 weeks)</li> <li>- and change from baseline in morning pre-dose trough FEV1 for BGF MDI versus GFF MDI and non-inferiority of BFF MDI versus BUD/FORM DPI (margin of -50 mL from lower bound of 95%</li> </ul>	<p>mL; p=0.2375).</p> <p>• <b>sekundärer Endpunkt: Exazerbation</b> The model-estimated rates of moderate or severe exacerbations were</p> <ul style="list-style-type: none"> <li>- 0,46 per year for BGF MDI</li> <li>- 0,95 per year for GFF MDI, rate ratio 0,48 (95%CI 0,37 to 0,64), n=625</li> <li>- 0,56 per year for BFF MDI, rate ratio 0,82 (95%CI 0,58 to 1,17), n=314, and</li> <li>- 0,55 per year for BUD/FORM DPI, rate ratio 0,83 (95%CI 0,59 to 1,18), n=318</li> </ul> <p>The rate of moderate or severe exacerbations was significantly lower during treatment with BGF MDI versus GFF MDI</p> <p>BGF MDI reduced the rate of moderate or severe exacerbations compared with BFF MDI and BUD/FORM DPI, but these reductions were not significant</p> <p>• <b>Subgruppe: Eosinophile</b> The rates of moderate or severe exacerbations with BGF MDI were lower than with GFF MDI for patients in both eosinophil subgroups (&lt;150 cells/mm<sup>3</sup> and ≥150 cells/mm<sup>3</sup>), with locally weighted scatter-plot smoothing showing that treatment differences increased with baseline blood eosinophil concentrations; beginning at approximately 75-100 cells/mm<sup>3</sup>, a level exceeded by more than 75% of patients. No apparent differences were seen between BGF MDI and GFF MDI below these concentration thresholds. Differences between BGF MDI and BFF MDI in the rate of moderate or severe exacerbations were similar across most eosinophil counts</p> <p>• <b>Sicherheit</b> most common treatment-emergent adverse events were</p> <ul style="list-style-type: none"> <li>- nasopharyngitis (n=49 [8%] in the BGF MDI group; n=41 [7%] in the GFF MDI group; n=26 [8%] in the BFF MDI group; and n=30 [9%] in the BUD/FORM DPI group) and</li> <li>- upper respiratory tract infection (n=65 [10%]; n=38 [6%]; n=18 [6%]; and n=22 [7%]).</li> <li>- Pneumonia incidence was low (&lt;2%) and similar across</li> </ul>	<p>selektive Ergebnisdarstellung: <b>unclear</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: <b>unclear</b></p> <p>Interessenkonflikte/ Sponsoring: Pearl (AstraZeneca Group) The funder of the study had a role in study design, data collection, data analysis, data interpretation, and writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.</p>	

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<p>CI) over 24 weeks</p> <ul style="list-style-type: none"> <li>• <b>sekundäre Endpunkte ( Auswahl für Europa und Kanada)</b></li> <li>- change from baseline in morning pre-dose trough FEV<sub>1</sub>, (BGF MDI vs BFF MDI), peak change from baseline in FEV<sub>1</sub>, within 4 h after dosing, rate of moderate or severe COPD exacerbations, TDI focal score (Europe statistical analysis approach only), change from baseline in daily rescue medication use, change from baseline in SGRQ total score, E-RS: COPD total score (RS-Total score), and time to clinically important deterioration (BGF MDI vs GFF MDI, vs BFF MDI, and vs BUD/FORM DPI), all over 24weeks</li> <li>• Canada, China, Japan, and the USA</li> <li>• SGRQ für QoL-Erhebung verwendet</li> </ul>	<p>treatments</p> <ul style="list-style-type: none"> <li>- two treatment-related deaths, both in the GFF MDI group.</li> </ul>		
<p>Lipson DA. Once-Daily Single-Inhaler Triple versus Dual Therapy in Patients with COPD. N Engl J Med 2018; 378(18):1671–80. <a href="https://www.ncbi.nlm.nih.gov/pubmed/29668352">https://www.ncbi.nlm.nih.gov/pubmed/29668352</a>.</p>	<p><b>IMPACT</b></p> <ul style="list-style-type: none"> <li>• <b>Studientyp:</b> randomized, double-blind, parallel-group, Phase III, multicenter trial</li> <li>• <b>Population:</b> n=10.335</li> <li>• <b>Studienzeitraum:</b> June 2014 through July 2017</li> <li>• <b>Intervention:</b> 52 weeks of a once-daily combination of                             <ul style="list-style-type: none"> <li>- fluticasone furoate 100 µg,</li> <li>- umeclidinium 62.5 µg,</li> <li>- vilanterol 25 µg (triple therapy)</li> </ul> <b>vs.</b> <ul style="list-style-type: none"> <li>- fluticasone furoate– vilanterol (100 µg and 25 µg)</li> <li><b>or</b></li> <li>- umeclidinium–vilanterol (62.5 µg and 25 µg)</li> </ul> </li> <li>&gt;&gt; Each regimen was administered in a single Ellipta inhaler</li> <li>&gt;&gt; 2-week run-in period before randomization: continued to take their own medication, which</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Geschlecht, Alter, ehemaliger Raucherstatus; stattgehabte Exazerbationen unterschiedlicher Schwere und Anzahl im letzten Jahr weitestgehend ausgeglichen; in Umeclidinium-Vilanterol-Gruppe halb so viele Teilnehmer (n=2070), wie in den anderen beiden Gruppen</li> <li>• <b>Ergebnisse primärer Endpunkt:</b> <ul style="list-style-type: none"> <li>- <u>rate of moderate or severe exacerbations</u> in the triple-therapy group was 0.91 per year, as compared with 1.07 per year in the fluticasone furoate–vilanterol group (rate ratio with triple therapy, 0.85; 95% CI, 0.80 to 0.90; 15% difference; P&lt;0.001) and 1.21 per year in the umeclidinium–vilanterol group (rate ratio with triple therapy, 0.75; 95% CI, 0.70 to 0.81; 25% difference; P&lt;0.001)</li> <li>- <u>annual rate of severe exacerbations resulting in hospitalization</u> in the triple-therapy group was 0.13, as compared with 0.19 in the umeclidinium–vilanterol group (rate ratio, 0.66; 95% CI, 0.56 to 0.78; 34% difference; P&lt;0.001).</li> </ul> </li> <li>• <b>weitere ausgewählte Ergebnisse: Eosinophile</b> (nicht in hierarchisches statistisches Modell aufgenommen)</li> </ul>	<p><b>Selection bias</b> Randomisierung: <b>unclear</b></p> <p>Allocation concealment: <b>unclear</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>unclear</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>unclear</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>low</b></p> <p>ITT-Analyse: durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>Unclear</b></p>	<p>Drop out-Rate 18; 25; 27%</p>

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	<p>could include a LAMA, a LABA, or an inhaled glucocorticoid alone or in combination</p> <p>• <b>Follow-up Zwischen-Assessment:</b> - Electrocardiographic (ECG) measurements and vital signs were assessed at screening and after 4, 28, and 52 weeks of treatment. - Clinical (chemical and hematologic) assessments were performed at screening and at 16, 28, and 52 weeks.</p> <p>• <b>Einschlusskriterien</b> - &gt; 40 years of age; symptomatic COPD (CAT score <math>\geq 10</math>; range 0 - 40) and - either: FEV1 predicted &lt;50% + history of at least one moderate or severe exacerbation in the previous year - or: FEV1 of 50 to 80% of the predicted normal value and at least two moderate exacerbations or one severe exacerbation in the previous year</p> <p>• <b>primärer Endpunkt:</b> - the annual rate of moderate or severe COPD exacerbations during treatment</p> <p>• <b>sekundäre Endpunkte:</b> hierarchisch 1) FEV1 + change in SGRQ 2) time to the first moderate or severe COPD exacerbation during treatment &gt;&gt; Prespecified protocol-defined secondary outcomes that were not in the hierarchy included the annual rate of moderate or severe exacerbations and the time to the first moderate or severe exacerbation among patients with a blood eosinophil count of at least 150 cells per microliter at baseline, and the annual rate of severe exacerbations.</p>	<p>- annual rate of moderate or severe exacerbations was lower with triple therapy than with either dual-therapy combination, regardless of eosinophil level, although a greater reduction in the exacerbation rate was observed in patients with eosinophil levels of at least 150 cells per microliter</p> <p>- <u>patients with eosinophil levels &lt; 150 cells/<math>\mu</math>l</u>, the annual rate of moderate or severe exacerbations was 0.85 (95% CI, 0.80 to 0.91) with triple therapy, 1.06 (95% CI, 0.99 to 1.14) with fluticasone furoate– vilanterol, and 0.97 (95% CI, 0.88 to 1.07) with umeclidinium–vilanterol</p> <p>- <u>patients with eosinophil levels of <math>\geq 150</math> cells/<math>\mu</math>l</u>, the annual rate was 0.95 (95% CI, 0.90 to 1.01) with triple therapy, 1.08 (95% CI, 1.02 to 1.14) with fluticasone furoate–vilanterol, and 1.39 (95% CI, 1.29 to 1.51) with umeclidinium– vilanterol.</p> <p>• <b>Sicherheit:</b> (ausführlich im Appendix) - There was a higher incidence of pneumonia in the inhaled-glucocorticoid groups than in the umeclidinium–vilanterol group, and the risk of clinician-diagnosed pneumonia was significantly higher with triple therapy than with umeclidinium–vilanterol, as assessed in a time-to-first event analysis (hazard ratio, 1.53; 95% CI, 1.22 to 1.92; <math>P &lt; 0.001</math>). - The incidence of adverse events during treatment that led to discontinuation of trial treatment or withdrawal from the trial was 6% for triple therapy, 8% for fluticasone furoate– vilanterol, and 9% for umeclidinium–vilanterol; the incidence of discontinuation or withdrawal due to an adverse event of COPD was 2%, 2%, and 3%, respectively. Serious adverse events during treatment occurred in 895 patients (22%) receiving triple therapy, 850 (21%) receiving fluticasone furoate–vilanterol, and 470 (23%) receiving umeclidinium–vilanterol. - A serious adverse event of pneumonia occurred in 184 patients (4%), 152 patients (4%), and 54 patients (3%), respectively.</p> <p>• <b>Mortalität:</b> Death during treatment occurred in 50 patients (1%) in the triple-therapy group, 49 patients (1%) in the fluticasone furoate–vilanterol group, and 39 patients (2%) in the umec-</p>	<p><b>Andere Biasursachen</b> Baseline imbalance: <b>low</b></p> <p>Interessenkonflikte/ Sponsoring: Funded by GlaxoSmithKline; the lead author is an employee of the sponsor.</p>	

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		lidinium–vilanterol group. All-cause mortality was significantly lower with the regimens that included the inhaled glucocorticoid fluticasone furoate (triple therapy and fluticasone furoate–vilanterol) than with umeclidinium–vilanterol. The hazard ratio for triple therapy versus umeclidinium–vilanterol was 0.58 (95% CI, 0.38 to 0.88; 42% difference; unadjusted P = 0.01), and the hazard ratio for fluticasone furoate–vilanterol versus umeclidinium– vilanterol was 0.61 (95% CI, 0.40 to 0.93; 39% difference; unadjusted P = 0.02).		
Lipson DA. FULFIL Trial: Once-Daily Triple Therapy for Patients with Chronic Obstructive Pulmonary Disease. Am J Respir Crit Care Med 2017; 196(4):438–46. <a href="https://www.ncbi.nlm.nih.gov/pubmed/28375647">https://www.ncbi.nlm.nih.gov/pubmed/28375647</a> .	<p><b>FULFIL</b></p> <ul style="list-style-type: none"> <li>• <b>Studientyp:</b> Phase 3, randomized, double-blind, double-dummy, parallel group multicenter study</li> <li>• <b>Population:</b> n=1810</li> <li>• <b>Studienzeitraum:</b> 01/2015 - 04/2016; 24 weeks trial; patient subgroup remained on blinded treatment for up to 52 weeks</li> <li>• <b>Intervention:</b> <ul style="list-style-type: none"> <li>- continue maintenance medications unchanged during the 2-week run-in period; randomised (1:1)                             <ul style="list-style-type: none"> <li>-- once-daily triple therapy (fluticasone furoate/umeclidinium/vilanterol 100 µg/ 62.5 µg/ 25 µg) vs.</li> <li>-- twice-daily ICS/LABA therapy (budesonide/formoterol 400 µg/ 12 µg)</li> </ul> </li> </ul> </li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- aged 40 years or older who were defined as being in GOLD group D:                             <ol style="list-style-type: none"> <li>(1) FEV1 less than 50% and COPD Assessment Test score greater than or equal to 10, or</li> <li>(2) patients with FEV1 less than or equal to 50% to less than 80% and COPD Assessment Test score greater than or equal to 10, and either at least two moderate exacerbations or at least one severe exacerbation in the past year.</li> </ol> </li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• Baseline-Patientencharakteristika: hinsichtliche Alter, Geschlecht; Rauchstatus; Lungenfunktion; Exazerbationshistorie weitestgehend ausgeglichen</li> <li>• In the intent-to-treat population (n = 1,810) at Week 24:             <ul style="list-style-type: none"> <li>• <b>mean changes from baseline in SGRQ scores</b> <ul style="list-style-type: none"> <li>- for triple therapy (n = 911): 26.6 units (95% CI, 27.4 to 25.7)</li> <li>- ICS/LABA therapy (n = 899): 24.3 units (95% CI, 25.2 to 23.4)</li> </ul> </li> <li>&gt;&gt; between-group differences in improvement in SGRQ total score was statistically significant for FF/UMEC/VI (22.2 units; 95% CI, 23.5 to 21.0; P&lt;0,001)</li> </ul> </li> <li><b>moderate/severe exacerbation rate</b> <ul style="list-style-type: none"> <li>- The mean annualized rates of moderate/severe exacerbations were 0.22 and 0.34 for FF/UMEC/VI and BUD/FOR, respectively, and the reduction in the annualized rate was statistically significant (35%; 95% CI, 14–51%; P = 0.002) based on data up to 24 weeks in the ITT</li> <li>- The incidence rates of moderate/severe COPD exacerbations over the 24-week treatment period were 10% (n = 95) for FF/UMEC/VI and 14% (n = 126) and BUD/FOR</li> </ul> </li> <li>• <b>Sicherheit:</b> The safety profile of triple therapy reflected the known profiles of the components.             <ul style="list-style-type: none"> <li>&gt;&gt; (SAEs und AEs im Supplement dargestellt)</li> <li>- The incidence rates of on-treatment AEs in the ITT population up to Week 24 were 38.9% in the FF/UMEC/VI group and 37.7% in the BUD/FOR group.</li> </ul> </li> </ul>	<p><b>Selection bias</b> Randomisierung: <b>low</b> Allocation concealment: <b>unclear</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>low</b></p> <p><b>Detection bias</b> Verblindung der Ergebnissevaluation: <b>unclear</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>unclear</b></p> <p>ITT-Analyse: durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>unclear</b></p> <p><b>Andere Biasursachen</b> Baseline imbalance: <b>low</b></p> <p>Interessenkonflikte/ Sponsoring: GlaxoSmithKline</p>	<p>Supplement abrufbar: <a href="https://www.atsjournals.org/doi/suppl/10.1164/rccm.201703-0449OC/suppl_file/lipson_data_supplement.pdf">https://www.atsjournals.org/doi/suppl/10.1164/rccm.201703-0449OC/suppl_file/lipson_data_supplement.pdf</a></p> <p>Protokoll vorhanden <a href="https://s3.amazonaws.com/ctr-gsk-7381/116853/6290c5e2-7f0d-4536-84b9-c08ce4adf390/f90aca32-1e4c-47ff-8f93-3a48b17b7bd9/gsk-116853-protocol-redact-v1.pdf">https://s3.amazonaws.com/ctr-gsk-7381/116853/6290c5e2-7f0d-4536-84b9-c08ce4adf390/f90aca32-1e4c-47ff-8f93-3a48b17b7bd9/gsk-116853-protocol-redact-v1.pdf</a></p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<p>- Subject must be receiving daily maintenance treatment for their COPD for at least 3 months prior to Screening</p> <ul style="list-style-type: none"> <li>• <b>Ausschlusskriterien (Auswahl):</b> <ul style="list-style-type: none"> <li>- current diagnosis of asthma causing their symptoms or if they had unresolved pneumonia or severe COPD exacerbation</li> </ul> </li> <li>• <b>primäre Co-Endpunkte:</b> <ul style="list-style-type: none"> <li>- change from baseline in trough FEV1</li> <li>- change in St. George's Respiratory Questionnaire (SGRQ) total score at Week 24</li> </ul> </li> <li>• <b>sekundäre Endpunkte (Auswahl)</b> <ul style="list-style-type: none"> <li>- TDI, SAEs, AEs</li> </ul> </li> <li>• multicenter</li> </ul>	<p>- For FF/UMEC/VI and BUD/FOR, respectively, the incidence rates of on-treatment SAEs in the ITT population up to Week 24 were 5.4% and 5.7%, and the most common on-treatment SAEs were COPD exacerbation (1.3% and 2.3%) and pneumonia (1.0% and 0.3%).</p> <ul style="list-style-type: none"> <li>• <b>Mortalität:</b> There were 12 on-treatment deaths in this study (6 in each treatment group), which was in line with expectations for patients with advanced COPD and multiple comorbidities</li> </ul>		
<p>Singh D. Single inhaler triple therapy versus inhaled corticosteroid plus long-acting beta2-agonist therapy for chronic obstructive pulmonary disease (TRILOGY): A double-blind, parallel group, randomised controlled trial. Lancet 2016; 388(10048):963–73. <a href="https://www.ncbi.nlm.nih.gov/pubmed/27598678">https://www.ncbi.nlm.nih.gov/pubmed/27598678</a>.</p>	<p><b>TRILOGY</b></p> <ul style="list-style-type: none"> <li>• <b>Studientyp:</b> randomised, parallel group, double-blind, active-controlled study</li> <li>• <b>Population:</b> n= 1368 (BDP/FF/GB n=687; BDP/FF n=681)</li> <li>• <b>Studienzeitraum:</b> 03/2014 - 01/2016; 52 week trial</li> <li>• <b>Intervention</b> <ul style="list-style-type: none"> <li>- 2-week open-label run-in period: beclomethasone dipropionate (100 µg) and formoterol fumarate (6 µg) in two actuations twice daily</li> <li>- then randomly assigned (1:1) to                             <ul style="list-style-type: none"> <li>-- continue BDP (100 µg) and FF (6 µg) or</li> <li>-- step-up to BDP (100 µg), FF (6 µg), and GB (glycopyrronium bromide) (12,5 µg) in two actuations twice daily via pressurised metered-dose inhaler</li> </ul> </li> </ul> </li> <li>• Follow-up (gesamt und Zwischen-Assessments)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, Geschlecht, Gewicht, Rauchstatus, Blut-Eosinophilen, Dauer der Erkrankung, CAT-Score, Exazerbationsrate im letzten Jahr, Begleiterkrankungen weitestgehend ausgeglichen</li> <li>- Statistik: hierachical order--&gt; (1) pre-dose FEV 1 ; (2) 2-h post-dose FEV ; (3) TDI focal score</li> <li>- No association between blood eosinophil concentration and treatment effect was observed</li> <li>• <b>primärer Endpunkt: TDI</b> <ul style="list-style-type: none"> <li>- Mean TDI focal scores at week 26 were 1,71 for BDP/FF/GB and 1,50 for BDP/FF, with a difference of 0,21 (95% CI -0,08 to 0,51; p=0,160); not statistically significant</li> <li>- Increases in TDI focal score were observed in both groups at all visits, with a statistically significant difference between treatments favouring BDP/FF/GB at the two earliest visits (weeks 4 and 12). More than 50% of patients in each group reported clinically relevant improvements (≥1 unit) in TDI focal score at weeks 26 and 52; at week 26, patients were significantly more likely to respond to BDP/FF/GB than BDP/FF; jedoch nicht nach 52 Wochen (s.u.)</li> </ul> </li> </ul>	<p><b>Selection bias</b> Randomisierung: <b>low</b> Allocation concealment: <b>low</b></p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>low</b></p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>low</b></p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>unclear</b></p> <p>ITT-Analyse: durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>low</b></p> <p><b>Andere Biasursachen</b></p>	<p>Protokolldaten (Zusammenfassungen) lediglich über clinicaltrialsregister und clinicaltrials.gov --&gt; kein extra Protokoll aufgefunden --&gt; Methodische Bewertung teilweise mit Hilfe dieser Online-Inhalte bewertet)</p> <p>Appendix nicht zur Verfügung</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<ul style="list-style-type: none"> <li>• ggf. Informationen zu Aufhebung der Verblindung und Cross-over</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- patients with COPD had post-bronchodilator FEV1 &lt; 50%, one or more moderate-to-severe COPD exacerbation in the previous 12 months, COPD Assessment Test total score of 10 or more, and a Baseline Dyspnea Index focal score of 10 or less</li> <li>- used ICS/LABA, ICS/LAMA; LAMA/LABA or LAMA mono for at least 2 month before screening</li> </ul> </li> <li>• <b>Ausschlusskriterien</b> <ul style="list-style-type: none"> <li>- patients received LAMA/LABA/ICS</li> <li>- diagnosis of asthma, or history of allergic rhinitis or atopy; a COPD exacerbation in the 4 weeks before screening or during the run-in period; clinically significant cardiovascular conditions or laboratory abnormalities; or unstable concurrent disease</li> </ul> </li> <li>• <b>primäre Co-Endpunkte:</b> <ul style="list-style-type: none"> <li>- pre-dose FEV1,</li> <li>- 2-h post-dose FEV,</li> <li>- Transition Dyspnea Index (TDI) focal score after 26 weeks</li> </ul> </li> <li>• <b>sekundäre Endpunkte (Auswahl)</b> <ul style="list-style-type: none"> <li>- moderate-to-severe COPD exacerbation rate</li> <li>- SGRQ</li> </ul> </li> <li>• multicenter: 159 sites (mixture of primary, secondary, and tertiary care providers, and specialist investigation units) across 14 countries</li> </ul>	<p>Week 26 BDP/FF/GB: n=394/687 (57%)                      Week 26 BDP/FF: n=352/680 (52%) --&gt; OR 1,28 (95% CI 1,03–1,59); p=0,027                      Week 52 BDP/FF/GB: n=370/687 (54%)                      Week 52 BDP/FF: n=354/680 (52%) --&gt; OR 1,09 (95% CI 0,88–1,36); p=0,430</p> <ul style="list-style-type: none"> <li>• <b>sekundärer Endpunkt: Exazerbationen</b>                      Adjusted annual moderate-to-severe exacerbation frequencies were 0,41 for BDP/FF/GB and 0,53 for BDP/FF (rate ratio 0,77 [95% CI 0,65–0,92]; p=0,005), corresponding to a 23% reduction in exacerbations with BDP/FF/GB compared with BDP/FF --&gt;indicating a significant 23% reduction in the rate with BDP/FF/GB</li> <li>• <b>Subgruppe Exazerbationshistorie: <u>history of more than one exacerbation</u></b> <ul style="list-style-type: none"> <li>- significant 33% reduction in the rate of moderate-to-severe exacerbations with BDP/FF/GB compared with BDP/FF (rate ratio 0,67 [95% CI 0,48–0,94]; p=0,019)</li> <li>- adjusted exacerbation frequency: 0,65 and 0,97 in the BDP/FF/GB and BDP/FF group</li> </ul> </li> <li>• <b>Subgruppe Exazerbationshistorie: <u>history of one exacerbation</u></b> <ul style="list-style-type: none"> <li>- treatment reduction appeared to be slightly lower (0,83 [0,67–1,02]; p=0,074)</li> <li>- adjusted exacerbation frequency in patients was 0,37 and 0,44 in the BDP/FF/GB and BDP/FF groups</li> </ul> </li> </ul> <p>The frequency of both moderate and severe exacerbations was lower in the BDP/FF/GB group than the BDP/FF group. Furthermore, BDP/FF/GB significantly prolonged the time to first moderate-to-severe exacerbation compared with BDP/FF (hazard ratio 0,80 [95% CI 0,67–0,97]; p=0,020)</p> <ul style="list-style-type: none"> <li>• <b>sekundärer Endpunkt: SGRQ:</b>                      Week 26 BDP/FF/GB: n=321/687 (47%)                      Week 26 BDP/FF: n= 246/680 (36%) --&gt; OR 1,52 (95% CI 1,21–1,91); p&lt;0,001                      Week 52 BDP/FF/GB: n=297/687 (43%)                      Week 52 BDP/FF: n= 244/680 (36%) --&gt; OR 1,33 (95% CI 1,06–1,66); p=0,014</li> </ul>	<p>Baseline imbalance: <b>low</b></p> <p>Interessenkonflikte/ Sponsoring: Chiesi Farmaceutici SpA: The funder of the study was responsible for the design and analysis of the study, oversaw its conduct, and was responsible for the study report preparation.</p>	

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
		<ul style="list-style-type: none"> <li>• <b>Sicherheit</b> Adverse events were reported by 368 (54%) patients with BDP/FF/GB and 379 (56%) with BDP/FF. One serious treatment-related adverse event occurred (atrial fibrillation) in a patient in the BDP/FF/GB group.</li> </ul>		

### Anhang 8.3 Kardiale Nebenwirkungen LABA oder LAMA

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Jara M. A new user cohort study comparing the safety of long-acting inhaled bronchodilators in COPD. <i>BMJ Open</i> 2012; 2(3).</p> <p><a href="https://www.ncbi.nlm.nih.gov/pub-med/22619266">https://www.ncbi.nlm.nih.gov/pub-med/22619266</a>.</p> <ul style="list-style-type: none"> <li>• nicht zitiert</li> </ul>	<ul style="list-style-type: none"> <li>• <b>UK</b></li> <li>• <b>Studiendesign:</b> retrospektive Kohortenstudie (Registerdaten; UK healthcare system general practitioner electronic medical record database)</li> <li>• <b>Fragestellung:</b> To investigate a possible increased risks of stroke and other adverse events, including angina and myocardial infarction, with tiotropium use in chronic obstructive pulmonary disease</li> <li>• <b>Population:</b> <ul style="list-style-type: none"> <li>- Patient*innen mit COPD oder COPD/Asthma</li> <li>- n=10 840 patients</li> </ul> </li> <li>• <b>Vergleich</b> <ul style="list-style-type: none"> <li>- New users of LAMA therapy (tiotropium HandiHaler powder formulation) were compared with new users of LABA monotherapy (Salmeterol oder Formoterol)</li> </ul> </li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- at least 40 years old, and not</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika</b> <ul style="list-style-type: none"> <li>- hinsichtlich Alter, Geschlecht, Gewicht weitestgehend ausgeglichen</li> <li>- diagnosis of COPD and asthma: 38% of tiotropium patients and 55% of LABA patients</li> <li>- diagnosis of COPD only: 51% of tiotropium patients and 32% of LABA patients</li> <li>- More LABA patients than tiotropium patients had an asthma codiagnosis (42% vs 63%)</li> <li>- newly prescribed tiotropium (n=4767) or single-ingredient LABA (n=6073); 95% salmeterol</li> <li>- Mean duration of exposure was 212 days for tiotropium patients and 139 days for LABA patients</li> </ul> </li> <li>• <b>Ergebnisse:</b> <ul style="list-style-type: none"> <li>• Tiotropium was associated with increased rates of                             <ul style="list-style-type: none"> <li>- stroke (HR=1.49, 95% CI 0.91 to 2.45)</li> <li>- angina (HR=1.38, 95% CI 0.88 to 2.16)</li> <li>- myocardial infarction (HR=1.26, 95% CI 0.72 to 2.21)</li> </ul> </li> <li>• There were similar rates between treatment groups of                             <ul style="list-style-type: none"> <li>- aneurysm (HR=0.96, 95% CI 0.44 to 2.05)</li> <li>- atrial fibrillation or flutter (HR=0.99, 95% CI 0.71 to 1.38)</li> <li>- coronary artery disease (HR=1.11, 95% CI 0.84 to 1.47)</li> <li>- hypertension (HR=1.03, 95% CI 0.81 to 1.29)</li> <li>- syncope (HR=0.94, 95% CI 0.57 to 1.55)</li> <li>- tachycardia (HR=1.08, 95% CI 0.48 to 2.41)</li> </ul> </li> <li>• There was a decrease in the tiotropium group in the rate of</li> </ul> </li> </ul>	<p>(In Anlehnung an NOS)</p> <p><u>I. Selektion der Studienteilnehmer</u></p> <ol style="list-style-type: none"> <li>1. exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition: ja</li> <li>2. nicht-exponierte Kohorte repräsentativ, adäquat ausgewählt: ja</li> <li>3. valide Erfassung der Exposition: ja (Registerdaten)</li> <li>4. wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war: unklar</li> </ol> <p><u>II. Vergleichbarkeit</u></p> <ol style="list-style-type: none"> <li>1. Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben: ja</li> </ol> <p><u>III. Endpunkterfassung</u></p> <ol style="list-style-type: none"> <li>1. valide Erfassung der Endpunkte: ja</li> <li>2. Konnte in der Beobachtungszeit der Endpunkt auftreten: ja</li> <li>3. fehlende Daten adäquat berücksichtigt: k.A.</li> </ol> <p><u>IV. Col/ Funding</u></p> <p>Funding: Boehringer Ingelheim Pharmaceuticals. Two of the authors were employees of Boehringer Ingelheim.</p>	<p>Patienten mit erstmaliger Nutzung von LABA oder LAMA</p> <p>Einige nutzten jedoch bereits vorab:</p> <ul style="list-style-type: none"> <li>- LAMAs</li> <li>- LABAs</li> <li>- ICS</li> <li>- OCS</li> <li>- Theophyllines</li> <li>- Cromoglycates</li> </ul>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<p>having asthma as their only respiratory illness.</p> <ul style="list-style-type: none"> <li>- Patients had to have at least one prescription for tiotropium or LABA from November 2002 (the earliest use of tiotropium) until January 2007.</li> </ul> <p>• <b>Studienzeitraum:</b> from 11/ 2002 until 01/ 2007</p> <p>• <b>Statistik:</b> propensity scores were used to control confounding</p> <p>• <b>Endpunkte:</b></p> <ul style="list-style-type: none"> <li>- included various cardiovascular adverse events (aneurysm, atrial fibrillation, cardiac arrest, coronary artery disease, angina, MI, heart failure, hypertension, stroke, syncope, tachycardia and ventricular tachycardia)</li> <li>- respiratory events and other AEs</li> </ul>	<ul style="list-style-type: none"> <li>- heart failure (HR=0.85, 95% CI 0.63 to 1.14)</li> <li>- allcause mortality (HR=0.70, 95% CI 0.56 to 0.89)</li> </ul> <p>• <b>receiving long-acting bronchodilator therapy for at least 6 months.</b> effect estimates increased for</p> <ul style="list-style-type: none"> <li>- stroke (HR=1.63, 95% CI 0.83 to 3.17)</li> <li>- angina (HR=1.42, 95% CI 0.78 to 2.59)</li> <li>- MI (HR=1.65, 95% CI 0.63 to 4.27)</li> </ul> <p>• The difference between groups in rates of total mortality diminished (HR=0.90, 95% CI 0.58 to 1.38).</p> <p>• Associations for other cardiovascular events were weaker, including</p> <ul style="list-style-type: none"> <li>- aneurysm (HR=0.82, 95% CI 0.27 to 2.45)</li> <li>- atrial fibrillation/ flutter (HR=1.17, 95% CI 0.70 to 1.94)</li> <li>- heart failure (HR=0.77, 95% CI 0.47 to 1.24)</li> <li>- hypertension (HR=1.07, 95% CI 0.79 to 1.45)</li> <li>- syncope (HR=0.79, 95% CI 0.36 to 1.70) and</li> <li>- tachycardia (HR=0.98, 95% CI 0.32 to 3.04).</li> </ul> <p>With regard to concomitant asthma diagnosis, the association with angina was stronger in patients with asthma and COPD (HR=1.91, 95% CI 1.00 to 3.63) than patients with only COPD (HR=0.93, 95% CI 0.49 to 1.77), while the association with MI was stronger in patients who had only COPD (HR=1.94, 95% CI 0.77 to 4.94).</p>	<p>Data sets for this study are the property of Boehringer Ingelheim and not currently available.</p>	
<p>Vogelmeier C. Effect of tiotropium vs. salmeterol on exacerbations: GOLD II and maintenance therapy naïve patients. <i>Respir Med</i> 2013; 107(1):75–83. <a href="https://www.ncbi.nlm.nih.gov/pub-med/23102611">https://www.ncbi.nlm.nih.gov/pub-med/23102611</a>.</p> <p>• nicht zitiert</p>	<p>• <b>Deutschland, Italien</b></p> <p>• <b>Fragestellung:</b> To explore the relative effects of therapy with tiotropium or salmeterol on exacerbation outcomes further, we conducted <u>prespecified subgroup analyses</u> of the POET-COPD study cohort in patients with moderate (GOLD stage II) disease, and those who were maintenance naïve.</p> <p>• <b>Studiendesign:</b> Subgruppenanalyse eines randomized, double blind, doubledummy, 1-year trial</p> <p>• <b>Population:</b> Patient*innen mit</p>	<p>siehe Tabelle 2: Incidence for Cardiac disorders (nicht näher beschrieben)</p> <p>&gt;&gt; Subgruppe: Maintenance therapy naïve patients:                  Tiotropium (n=672): 1,8%                  Salmeterol (n=671): 1,5%</p>	<p><u>Selection bias</u>                  Randomisierung: gering</p> <p>Allocation concealment: gering</p> <p><u>Performance bias</u>                  Verblindung von Teilnehmern und Personal: ja</p> <p>Detection bias                  Verblindung der Ergebnisevaluation: unklar</p> <p><u>Attrition bias</u>                  Verlust von Studienteilnehmern/ fehlende Daten: hoch</p> <p>ITT-Analyse: nein</p> <p><u>Reporting bias</u></p>	<p>Patients were considered “maintenance naïve” if they were exclusively using short-acting b2-agonists, or none of the following maintenance medications at baseline: ICS, systemic corticosteroids, xanthines, anticholinergics (shortor long-acting), and LABAs.</p> <p>Für die methodische Bewertung wurden die Referenzen 9 Vogelmeier C, Hederer B, Glaab T, et al. <i>Tiotropium versus salmeterol for the prevention of exacerbations of COPD. N Engl J Med</i> 2011;364:1093e103.</p>



Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<p>COPD</p> <ul style="list-style-type: none"> <li>• <b>Interventionen:</b> tiotropium 18 µg once daily (via HandiHaler ) plus placebo twice daily (via HFA-pMDI), or salmeterol 50 µg twice daily (via HFA-pMDI) plus placebo once daily (via HandiHaler).</li> <li>• <b>relevante Einschlusskriterien</b> - history of at least 1 COPD exacerbation within the past year requiring treatment with antibiotics and/or systemic steroids and/or requiring hospitalization</li> <li>• <b>Endpunkt sekundär:</b> serious adverse events</li> <li>• <b>Studienzeitraum:</b> 01/2008</li> </ul>		<p>selektive Ergebnisdarstellung: gering Baseline imbalance: gering Interessenkonflikte/ Sponsoring: Boehringer Ingelheim.</p>	<p>10 <i>Beeh KM, Hedere B, Glaab T, et al. Study design considerations in a large COPD trial comparing effect of tiotropium with salmeterol on exacerbations. Int J Chron Obstruct Pulmon Dis 2009;4:119e25.</i></p> <p>inklusive Supplements herangezogen</p>
<p>Gershon A. Cardiovascular safety of inhaled long-acting bronchodilators in individuals with chronic obstructive pulmonary disease. <i>JAMA Intern Med</i> 2013; 173(13):1175–85. <a href="https://www.ncbi.nlm.nih.gov/pub-med/23689820">https://www.ncbi.nlm.nih.gov/pub-med/23689820</a>.</p> <p>• nicht zitiert</p>	<ul style="list-style-type: none"> <li>• <b>Kanada</b></li> <li>• <b>Studiendesign:</b> population-based, nested case-control analysis of a retrospective cohort study (Health care databases from Ontario)</li> <li>• <b>Fragestellung:</b> to clarify the relative cardiovascular risk of LABA compared with LAA in older patients with COPD.</li> <li>• <b>Population:</b> ältere Patient*innen mit COPD</li> <li>• <b>Vergleich:</b> New use of an inhaled long-acting beta-agonist or</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> zwischen Cases und Controls: ausgeglichen</li> <li>• n=191.005 eligible patients</li> <li>• n= 53.532 (28.0%) with hospitalization or an emergency department visit for a cardiovascular event</li> <li>• n=26.628 (49,7%) were matched to a control</li> <li>- Cases were more likely than controls to have a history of diabetes mellitus and hypertension, to be taking some medications, and to have had a recent hospitalization and/or emergency department visit</li> <li>• Newly prescribed long-acting inhaled beta-agonists and anticholinergics were associated with a higher risk of an event compared with nonuse of those medications:</li> <li>- LABA: adjusted OR 1.31 [95% CI, 1.12-1.52; p &lt; .001] and</li> <li>- LA[M]A: adjusted OR 1.14 [1.01-1.28; p = 0.03]).</li> </ul>	<p>(In Anlehnung an NOS)</p> <p><u>I. Selektion der Studienteilnehmer</u></p> <ol style="list-style-type: none"> <li>1. exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition: ja</li> <li>2. nicht-exponierte Kohorte repräsentativ, adäquat ausgewählt: ja</li> <li>3. valide Erfassung der Exposition: ja (Registerdaten)</li> <li>4. wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war: unklar</li> </ol> <p><u>II. Vergleichbarkeit</u></p> <ol style="list-style-type: none"> <li>1. Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben: ja</li> </ol> <p><u>III. Endpunkterfassung</u></p>	<p>Definitionen:</p> <ul style="list-style-type: none"> <li>• cardiovascular event defined as - acute coronary syndrome (including acute myocardial infarction)</li> <li>- heart failure</li> <li>- ischemic stroke</li> <li>- or cardiac arrhythmia</li> <li>• New use of LABA or LAMA constituted the primary exposure. --&gt; defined as receiving a prescription within 90 days of the index date and not having received</li> </ul>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<p>long-acting anticholinergic (dry tiotropium inhalation powder).</p> <p>• <b>relevante Ein- und Ausschlusskriterien:</b>                      - All individuals 66 years or older meeting a validated case definition of COPD, based on health administrative data, and treated for COPD                      - were entered into study once they received at least 1 prescription a SABA, LABA, LA[M]A, ICS or Methylxanthine</p> <p>• <b>Studienzeitraum:</b> 01/2003 - 03/2009</p> <p>• <b>Endpunkte:</b>                      - Emergency department visit or a hospitalization for a cardiovascular event.</p>	<p>• We found no significant difference in events between the 2 medications:                      - adjusted OR of LABAs compared with anticholinergics: OR 1.15 [95% CI, 0.95-1.38; p = 0.16]).</p> <p>• Cardiovascular events in cases newly taking LABAs or LA[M]As appeared to be highest in the first 2 to 3 weeks after medication was prescribed.</p> <p>• Cardiovascular risk associated with new use of LA[M]A relative to LABA did not appear to differ by sex, preexisting cardiovascular disease, or COPD severity.</p> <p><u>Separate cardiovascular outcomes</u>                      Compared with nonuse of either medication, LABA and LA[M]A use were associated with an increased risk of acute coronary syndrome and heart failure but not cardiac arrhythmias or stroke.</p> <p>• ACS including acute MI:                      - New use of LAMA: OR 1.30 [95% CI, 1.04-1.62; p = 0.02]                      - New use of LABA: OR 1.43 [95% CI, 1.08-1.89; p = 0.01]</p> <p>• Heart failure:                      - New use of LAMA: OR 1.31 [95% CI, 1.08-1.60; p = 0.006]                      - New use of LABA: OR 1.42 [95% CI, 1.10-1.83; p = 0.008]</p> <p>• Arrhythmias                      - New use of LAMA: OR 1.26 [95% CI, 0.91-1.75; p = 0.17]                      - New use of LABA: OR 1.17 [95% CI, 0.74-1.83; p = 0.50]</p> <p>• Ischemic stroke                      - New use of LAMA: OR 0.68 [95% CI, 0.50-0.91; p = 0.01]                      - New use of LABA: OR 1.17 [95% CI, 0.78-1.74; p = 0.58]</p> <p>A protective effect for ischemic strokes were observed with new LA[M]A but not new LABA use, resulting in 73% increased risk of stroke in new users of LABAs compared with new users of LA[M]As.</p>	<p>1. valide Erfassung der Endpunkte: ja                      2. Konnte in der Beobachtungszeit der Endpunkt auftreten: ja                      3. fehlende Daten adäquat berücksichtigt: ja</p> <p><u>IV. Col/ Funding</u>                      Government of Ontario; Institute for Clinical Evaluative Sciences; Ministry of Health and Longterm Care, Canadian Institute of Health Research; Institute of Nutrition</p>	<p>any prescriptions for the same medication in the previous year</p>
Dong Y-H. Comparative Cardiovascular and Cerebrovascular Safety of Inhaled Long-Acting Bron-	<p>• <b>Taiwan</b></p> <p>• <b>Studiendesign:</b> Retrospective cohort study, population-based (Taiwan National Health Insurance Research Database)</p>	<p>• <b>Baseline-Patientencharakteristika</b>                      - mean age 70.2 years; 80% male                      - initiators of LABA alone: waren jünger, mehr Frauen, hatten mehr ambulante Besuche und erhielten mehr SABAs, ICS, OCS oder orale B2 Agonisten</p>	<p>(In Anlehnung an NOS)  <u>I. Selektion der Studienteilnehmer</u>                      1. exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition: ja</p>	<p>Selbe Datenbank wie RefID 29331; teilweise überlappender Untersuchungszeitraum: 1997 - 2008 vs. 2001 - 2010</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>chodilators in Patients with Chronic Obstructive Pulmonary Disease: A Population-Based Cohort Study. <i>Pharmacotherapy</i> 2016; 36(1):26–37. <a href="https://www.ncbi.nlm.nih.gov/pubmed/26799347">https://www.ncbi.nlm.nih.gov/pubmed/26799347</a>.</p> <p>• nicht zitiert</p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> to compare the cardiovascular and cerebrovascular risks of LAMA alone, LABA alone, and LABA/LAMA combination</li> <li>• <b>Population:</b> Patient*innen mit COPD &gt; 40 years of age</li> <li>• <b>Vergleich:</b> <ul style="list-style-type: none"> <li>- LAMA (Tiotropium; dry powder)</li> <li>- LABA</li> <li>- LABA/LAMA</li> </ul> </li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- Individuals with COPD <u>who initiated</u> LAMAs alone, LABA alone, and LABA and LAMA in combination</li> </ul> </li> <li>• <b>Ausschlusskriterien:</b> <ul style="list-style-type: none"> <li>- patients who received LABA or LAMA within 1 year before index date from the analysis</li> <li>- older 100 years</li> <li>- lack of continuous insurance coverage the year before drug initiation</li> <li>- patients with asthma co-diagnosis</li> </ul> </li> <li>• <b>Studienzeitraum:</b> 2001 - 2010</li> <li>• <b>Follow up:</b> mean duration of 3.1 years (1 day to 10.0 years)</li> </ul>	<p><u>composite cardiovascular outcome</u> (hospitalization for acute myocardial infarction, congestive heart failure, and cerebrovascular diseases) &gt;&gt; LABA alone (n=2363) and LAMA alone (n=1004) were associated with similar risks of the composite outcome (adjusted HR 1.09; 95% CI 0.87-1.37; crude HR 0.94; 95% CI 0.76 - 1.16)</p> <p><u>Subgroup analyses</u> (Table4) for risk of composite cardiovascular events comparing LABA alone with LAMA as reference:</p> <ul style="list-style-type: none"> <li>- Age ≥ 65 yrs (n=2432): adjusted HR 1.08 (95% CI 0.85 - 1.38)</li> <li>- Age &lt; 65 yrs (n=1138): aHR 1.07 (95% CI 0.52 - 2.2.0)</li> <li>- male (n=2834): aHR 1.08 (95% CI 0.84 - 1.38)</li> <li>- female (n=736): aHR 0.77 (95% CI 0.40 - 1.46)</li> <li>- with preexisting cardiovascular histories (n=2176): aHR 1.08 (95% CI 0.83 - 1.39)</li> <li>- without preexisting cardiovascular histories (n=1138): aHR 1.12 (95% CI 0.66 - 1.90)</li> </ul>	<ul style="list-style-type: none"> <li>2. nicht-exponierte Kohorte repräsentativ, adäquat ausgewählt: ja</li> <li>3. valide Erfassung der Exposition: ja (Registerdaten)</li> <li>4. wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war: unklar</li> </ul> <p><u>II. Vergleichbarkeit</u></p> <ul style="list-style-type: none"> <li>1. Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben: ja</li> </ul> <p><u>III. Endpunkterfassung</u></p> <ul style="list-style-type: none"> <li>1. valide Erfassung der Endpunkte: ja (Registerdaten)</li> <li>2. Konnte in der Beobachtungszeit der Endpunkt auftreten: ja</li> <li>3. fehlende Daten adäquat berücksichtigt: ja</li> </ul> <p><u>IV. Col/ Funding</u></p> <ul style="list-style-type: none"> <li>- partly supported by the Taiwan Department of Health Grant</li> <li>- 1 author: grant Novartis</li> </ul>	
<p>Suissa S. Long-Acting Bronchodilator Initiation in COPD and the Risk of Ad-</p>	<ul style="list-style-type: none"> <li>• <b>Kanada (Daten aus UK)</b></li> <li>• <b>Studiendesign:</b> population-based comparative Safety Study; retrospektive Kohortenstudie</li> </ul>	<ul style="list-style-type: none"> <li>- base cohort: n=463.899 patients</li> <li>- Study cohort of incident users of LABA (n = 88.955) or tiotropium (n = <b>26.442</b>) (For analysis of AMI, CHF and stroke)</li> <li>- Study sub-cohort of incident users of LABA (n = 55,123) or tiotropium (n = <b>15,427</b>) (For analysis of arrhythmia and pneumonia)</li> </ul>	<p>(In Anlehnung an NOS)</p> <p><u>I. Selektion der Studienteilnehmer</u></p> <ul style="list-style-type: none"> <li>1. exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition: ja</li> </ul>	

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>verse Cardiopulmonary Events: A Population-Based Comparative Safety Study. Chest 2017; 151(1):60–7. <a href="https://www.ncbi.nlm.nih.gov/pub-med/27554300">https://www.ncbi.nlm.nih.gov/pub-med/27554300</a>.</p> <p>• nicht zitiert</p>	<p>(United Kingdom's Clinical Practice Research Datalink = primary care database)</p> <p>• <b>Fragestellung:</b> assessed the comparative safety of COPD treatment initiation with tiotropium relative to a LABA on the incidence of acute myocardial infarction (MI), stroke, heart failure, and arrhythmia as well as pneumonia</p> <p>• <b>Population:</b> - cohort of new users of long-acting bronchodilators - Patient*innen mit COPD - age 55 or older</p> <p>• <b>Ausschlusskriterien:</b> - Patients initiating treatment with both bronchodilators on the same date</p> <p>• <b>Vergleich:</b> tiotropium vs. LABA</p> <p>• <b>Follow-up:</b> 1 year from cohort entry, with follow-up ending, for each studied outcome, at the earliest of the date of the cardiovascular or pneumonia outcome, 1 year after cohort entry, date of death</p> <p>• <b>Studienzeitraum:</b> 2002 - 2012</p>	<p>&gt;&gt; wurden jeweils gematcht</p> <p><b>Tiotropium initiation relative to LABA initiation:</b> - acute myocardial infarction: HR 1.10 (95% CI, 0.88-1.38), - stroke HR: 1.02 (95% CI, 0.78-1.34) - arrhythmia 0.81 (95% CI, 0.60-1.09) - heart failure 0.90 (95% CI, 0.79-1.02).</p> <p>• initiation of COPD treatment with tiotropium or with a LABA is associated with similar rates of cardiovascular events in the first year of use.</p>	<p>2. nicht-exponierte Kohorte repräsentativ, adäquat ausgewählt: ja 3. valide Erfassung der Exposition: ja (Registerdaten) 4. wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war: unklar</p> <p><u>II. Vergleichbarkeit</u> 1. Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben: ja</p> <p><u>III. Endpunkterfassung</u> 1. valide Erfassung der Endpunkte: ja (Registerdaten) 2. Konnte in der Beobachtungszeit der Endpunkt auftreten: ja 3. fehlende Daten adäquat berücksichtigt: k.A.</p> <p><u>IV. Col/ Funding</u> Canadian Institutes of Health Research, Canadian Foundation for Innovation, and Boehringer-Ingelheim</p>	
<p>Wang M-T. Association of Cardiovascular Risk With Inhaled Long-Acting Bronchodilators in Patients With Chronic Obstructive Pulmonary Disease: A</p>	<p>• <b>China</b></p> <p>• <b>Studiendesign:</b> Nested Case-Control Study; retrospektive Kohortenstudie (Taiwan National Health Insurance Research Database for health care claims)</p>	<p>Baseline-Patientencharakteristika: hinsichtlich Alter und Geschlecht ausgeglichen; leichte Unterschiede bei Vorerkrankungen - mean age, 71.4 years; 68.9% men - 37 719 patients with CVD (mean age, 75.6 years; 71.6% men) and 146 139 matched controls (mean age, 75.2 years; 70.1% men) were identified</p> <p>&gt;&gt; New LABA and LAMA use in COPD was associated with a 1.50-</p>	<p>(In Anlehnung an NOS)</p> <p><u>I. Selektion der Studienteilnehmer</u> 1. exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition: ja 2. nicht-exponierte Kohorte repräsentativ, adäquat ausgewählt: ja 3. valide Erfassung der Exposition:</p>	<p>vermutlich selbe Datenbank wie RefID 29331 und 29329 teilweise überlappender Untersuchungszeitraum: 1997 - 2008 vs. 2001 - 2010 vs. 2007 - 2011</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Nested Case-Control Study. JAMA Intern Med 2018; 178(2):229–38. <a href="https://www.ncbi.nlm.nih.gov/pub-med/29297057">https://www.ncbi.nlm.nih.gov/pub-med/29297057</a>.</p> <p>• nicht zitiert</p>	<p>• <b>Fragestellung:</b> Does the duration since initial use and new use of inhaled LABAs or LAMAs for the treatment of COPD act as important determinants of the risk of cardiovascular disease?</p> <p>• <b>Population:</b> 280 000 patients with COPD; LABA-LAMA-naïve; at least 40 years old</p> <p>• <b>Ausschlusskriterien:</b> received any LABA-LAMA therapy or who lacked continuous health insurance coverage for 1 year preceding cohort entry.</p> <p>• <b>Follow-up:</b> mean 2.0 years</p> <p>• <b>Studienzeitraum:</b> from 2007 to 2011</p> <p>• <b>Matching:</b> Cases with inpatient or emergency care visits for <u>coronary artery disease, heart failure, ischemic stroke, or arrhythmia</u> were identified and individually matched to 4 randomly selected controls.</p>	<p>fold (95% CI, 1.35-1.67; P &lt; .001) and a 1.52-fold (95% CI, 1.28-1.80; P &lt; .001) increased cardiovascular risk <u>within 30 days of initiation</u>, respectively, whereas the risk was absent, or even reduced with prevalent use [of these medications; siehe Tabelle 2].</p> <p>&gt;&gt; Individual LABA agents, LAMA dosage forms, and concomitant COPD regimens did not differ in the CVD risks.</p> <p>&gt;&gt; new LABA use vs new LAMA use yielded no difference in the risk of CVDs (P = .93)</p> <p><u>Auszug: e-Table 2: Cardiovascular events/subtypes</u></p> <p><b>Coronary artery disease</b> LABA new use vs nonuse: adjusted OR 2.01 (95% CI 1.71-2.38) ; p&lt;0.001 LAMA new use vs nonuse: aOR 1.89 (95% CI 1.45-2.46); p &lt;0.001 Both new use vs nonuse: aOR 3.25 (95% CI 1.97-5.36); p &lt;0.001 New LAMA vs New LABA: aOR 0.95 (95% CI 0.70-1.29); p= 0.74</p> <p><b>Heart failure</b> LABA new use vs nonuse: aOR 1.42 (95% CI 1.16-1.75); p= 0.001 LAMA new use vs nonuse: aOR 1.56 (95% CI 1.14-2.14)p= 0.006 Both new use vs nonuse: aOR 1.72 (95% CI 0.79-3.75); p= 0.17 New LAMA vs New LABA: aOR 1.09 (95% CI 0.75-1.59); p= 0.64</p> <p><b>Ischemic stroke</b> LABA new use vs nonuse: aOR 1.06 (95% CI 0.81-1.37); p= 0.69 LAMA new use vs nonuse: aOR 0.93 (95% CI 0.58-1.51); p= 0.78 Both new use vs nonuse: aOR 0.38 (95% CI 0.09-1.67); p= 0.20 New LAMA vs New LABA: aOR 0.87 (95% CI 0.50-1.50); p= 0.61</p> <p><b>Cardiac arrhythmia</b> LABA new use vs nonuse: aOR 1.27 (95% CI 0.94-1.72); p= 0.12 LAMA new use vs nonuse: aOR 1.67 (95% CI 1.02-2.76); p= 0.042 Both new use vs nonuse: aOR 1.87 (95% CI 0.68-5.13); p= 0.23 New LAMA vs New LABA: aOR 1.31 (95% CI 0.73-2.33); p= 0.36</p>	<p>ja (Registerdaten) 4. wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war: unklar (teilweise kardiovaskuläre Anamnese; siehe Tabelle 1)</p> <p><u>II. Vergleichbarkeit</u> 1. Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben: ja</p> <p><u>III. Endpunkterfassung</u> 1. valide Erfassung der Endpunkte: ja (Registerdaten) 2. Konnte in der Beobachtungszeit der Endpunkt auftreten: ja 3. fehlende Daten adäquat berücksichtigt: k.A.</p> <p><u>IV. Col/ Funding</u> This study was supported by grants from the Ministry of Science and Technology, ROC; Col: non reported</p>	

Anhang 8.4 Eosinophile

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar zur Methodik
<p>Bafadhel M. Blood eosinophils to direct corticosteroid treatment of exacerbations of chronic obstructive pulmonary disease: A randomized placebo-controlled trial. Am J Respir Crit Care Med 2012; 186(1):48–55.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pub-med/22447964">https://www.ncbi.nlm.nih.gov/pub-med/22447964</a></p>	<ul style="list-style-type: none"> <li>• <b>Ort:</b> UK</li> <li>• <b>Studiendesign:</b> diagnostischer RCT, Nichtunterlegenheitsstudie</li> <li>• <b>Intervention:</b> biomarkergesteuerte Therapie                             <ul style="list-style-type: none"> <li>- ≤ 2% Eosinophile im Blut: Placebo (14d) + amoxicillin or doxycycline (7d)</li> <li>- &gt; 2% Eosinophile im Blut: 30 mg Prednisolon (14d) + Antibiotika (7d)</li> </ul> </li> <li>Vergleich: biomarkerunabhängige Therapie                             <ul style="list-style-type: none"> <li>- ≤ 2% Eosinophile im Blut: 30 mg Prednisolon (14d) + Antibiotika (7d)</li> <li>- &gt; 2% Eosinophile im Blut: 30 mg Prednisolon (14d) + Antibiotika (7d)</li> </ul> </li> <li>• <b>Follow-up:</b> 2 (posttherapy) and 6 (recovery) weeks after exacerbation</li> <li>• <b>Cross-over:</b> ja</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- COPD</li> </ul> </li> <li>• <b>Studienzeitraum:</b> k.A.</li> <li>• <b>Definitionen und Messmethoden:</b> <ul style="list-style-type: none"> <li>- pre- and post-bronchodilator spirometry;</li> <li>- health quality questionnaires using the Chronic Respiratory Disease Interviewer-Administered Standardized Questionnaire (CRQ)</li> <li>- symptom assessment of cough, breathlessness, sputum production</li> <li>- sputum purulence using the visual analog scale (VAS)</li> <li>- cell differential and C-reactive protein; and sputum for analysis of bacteria, colony-forming units (CFU), virus, and sputum cell differential</li> </ul> </li> <li>• <b>Primärer Endpunkt:</b> (1) noninferiority in the health status score after treatment between the</li> </ul>	<p><b>Baseline-Patientencharakteristika:</b> ausgeglichen, n= 109</p> <ul style="list-style-type: none"> <li>• <b>primärer Endpunkt:</b> <ul style="list-style-type: none"> <li>- noninferiority of health status in the standard therapy and biomarker-directed groups after 2 weeks of treatment was achieved (CRQ mean score change, 0.8 vs. 1.1; mean difference, 0.3; 95% CI, 0.0; 0.6; p = 0.05</li> <li>- similar reduction in the CRQ score from baseline to exacerbation in the biomarker-directed and standard therapy arms (0.9 vs. 0.9; MD 0.0; 95% CI, 20.3; 0.3; p = 0.97).</li> </ul> </li> <li>• <b>ausgewählte weitere Ergebnisse</b> <ul style="list-style-type: none"> <li>- treatment failures associated with worsening symptoms of COPD after treatment: 14 (standard: 10 vs. biomarker-directed 4)</li> <li>- demonstrating at least equivalence with a trend favoring the biomarker-directed arm as there were fewer treatment failures (13 vs. 5%; 95% CI, 21; 16; P = 0.07).</li> </ul> </li> </ul>	<p><b>Selection bias:</b> Randomisierung: low; Allocation concealment: unclear</p> <p><b>Performance bias:</b> Verblindung von Teilnehmern und Personal: low</p> <p><b>Detection bias:</b> Verblindung der Ergebnisevaluation: unclear</p> <p><b>Attrition bias:</b> Verlust von Studienteilnehmern/ fehlende Daten: unclear</p> <p>ITT-Analyse: high</p> <p><b>Reporting bias:</b> selektive Ergebnisdarstellung: unklar</p> <p><b>Andere Biasursachen:</b> Baseline imbalance: low</p> <p>Interessenkonflikte/ Sponsoring: Medical Research Council (UK) and Astra-Zeneca, Col-Erklärungen der Autoren liegen vor</p>	<ul style="list-style-type: none"> <li>- einige Limitationen im RoB-Tool</li> <li>- positiv hervorzuheben ist das RCT-Design in einer diagnostischen Studie</li> <li>- am ehesten Strategiedesign</li> <li>- die Ergebnisbewertung wird dadurch gemindert, dass nicht hinsichtlich der Patientenzahl sondern der Exazerbationen ausgewertet wurde</li> </ul> <p>Fehlende Definition der Ein- und Ausschlusskriterien</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar zur Methodik
	<p>standard therapy and biomarker-directed therapy</p> <p>• <b>Weitere Endpunkte:</b> (2) equivalence in the proportions of exacerbations associated with treatment failure (defined as need to start or repeat treatment within 30 days of randomization, hospitalization for any cause, or death (3) demonstration of a reduction in corticosteroid therapy prescription in the biomarker-directed therapy study group.</p>			
<p>Brightling CE. Sputum eosinophilia and the short term response to inhaled mometasone in chronic obstructive pulmonary disease. Thorax 2005; 60(3):193–8.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pub-med/15741434">https://www.ncbi.nlm.nih.gov/pub-med/15741434</a></p>	<p>• <b>UK</b></p> <p>• <b>Studientyp:</b> RCT mit Cross-over</p> <p>• <b>Intervention:</b> ICS Mometasone furate (800 µg/day)</p> <p>• <b>Vergleich:</b> Placebo</p> <p>• <b>Design:</b> - 4-week run-in period; treatment periods separated by a 4-week washout</p> <p>• <b>Population:</b> n=60</p> <p>• <b>Einschlusskriterien:</b> - symptoms of chronic airflow obstruction, postbronchodilator FEV1 &lt; 70% predicted, FEV1/FVC ratio &lt; 70%. - no significant improvement in FEV1 after 200 µg inhaled salbutamol</p> <p>• <b>Ausschlusskriterien:</b> - asthma, a history of childhood respiratory disorders, variability in symptoms not associated with infections, history of acute wheeze, or deterioration associated with allergens, exacerbation within 6 weeks of trial entry. - taking regular OCS</p>	<p>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Geschlecht, Alter weitestgehend ausgeglichen; Rauchstatus: in mittlerer Terzile doppelt so viele Raucher*innen, wie in den anderen beiden Terzilen</p> <p>• <b>Einteilung nach Baseline eosinophil count tertiles:</b> - &lt;1,0 (n=20) - 1,0–3,9 (n=20) - &gt;3,9 (n=20)</p> <p>• <b>primäre Endpunkte</b> The mean paired difference between mometasone and placebo treatment for the change in primary outcomes for the <b>whole group</b> were: - post-bronchodilator FEV1 0.04 l (95% CI 20.03 to 0.11; p=0.24) - CRQ total 20.025 (95% CI 20.23 to 0.18; p=0.8).</p> <p>The group geometric mean sputum eosinophil count decreased after mometasone from 2.20% to 1.58%, but this change was not significantly different from the change after placebo (2.32% to 1.96%; 1.17-fold decrease after mometasone compared with placebo (95% CI 0.7 to 1.4), p=0.38)</p> <p><u>Auswertung entsprechend der Baseline Eosinophilen im</u></p>	<p><b>Selection bias:</b> Randomisierung: unclear; Allocation concealment: unclear</p> <p><b>Performance bias:</b> Verblindung von Teilnehmern und Personal: low</p> <p><b>Detection bias:</b> Verblindung der Ergebnisevaluation: unclear</p> <p><b>Attrition bias:</b> Verlust von Studienteilnehmern/ fehlende Daten: low</p> <p>ITT-Analyse: low</p> <p><b>Reporting bias:</b> selektive Ergebnisdarstellung: unclear</p> <p><b>Andere Biasursachen:</b> Baseline imbalance: unclear bis high</p>	- Endpunkte klinisch relevant?

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar zur Methodik
	<p>- taking ICS: drugs discontinued for at least 1 month before randomisation.</p> <p>- withdrew patients from the study if they had a moderate exacerbation requiring ICS or antibiotics, a severe exacerbation needing OCS, or a severe intercurrent illness</p>	<p><u>Sputum:</u></p> <ul style="list-style-type: none"> <li>- peripheral blood eosinophil count and total IgE concentration was higher in the most eosinophilic tertile (p&lt;0.05)</li> <li>- There was a progressive increase in the mean difference between mometasone and placebo from the least to the most eosinophilic tertiles for change in post-bronchodilator FEV1 and total CRQ</li> <li>- ITT: The mean change in post-bronchodilator FEV1 with mometasone compared with placebo in the <b>highest tertile</b> was 0.11 l (95% CI 0.03 to 0.19; p=0.02). Similarly, an improvement in pre-bronchodilator FEV1 was only observed in those subjects in the highest tertile (0.096 l (95% CI 0.00 to 0.19); p=0.05).</li> <li>- posthoc: re-analysed the data including n= 49 subjects who completed the study --&gt; The findings were very similar to the intention-to-treat analysis with a mean improvement in post-bronchodilator FEV1 after mometasone compared with placebo of 0.11 l (95% CI 0.002 to 0.21; p=0.046).</li> </ul> <p><u>ausgewählte weitere Ergebnisse:</u></p> <ul style="list-style-type: none"> <li>- no significant reduction in the sputum eosinophil count in the two tertiles with the highest baseline eosinophil count and in the lowest tertile the sputum eosinophilic count increased after mometasone compared with placebo, although this represented a very small change in the absolute sputum eosinophil count in this group</li> </ul> <p>• <b>Sicherheit:</b> nicht betrachtet</p> <p>&gt;&gt; An increased sputum eosinophil count is related to an improvement in post-bronchodilator FEV(1) following treatment with inhaled mometasone in COPD, but the improvement is not associated with a reduction in the sputum eosinophil count.</p>	<p>Interessenkonflikte/ Sponsoring: angegeben: Funded by an unrestricted grant from Schering-Plough, UK</p>	



Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar zur Methodik
<p>Brightling CE. Sputum eosinophilia and short-term response to prednisolone in chronic obstructive pulmonary disease: A randomised controlled trial. Lancet 2000; 356(9240):1480–5.</p> <p><a href="https://www.ncbi.nlm.nih.gov/pub-med/11081531">https://www.ncbi.nlm.nih.gov/pub-med/11081531</a></p>	<ul style="list-style-type: none"> <li>• <b>Studientyp:</b> RCT mit Cross-over</li> <li>• <b>Intervention:</b> Prednisolon</li> <li>• <b>Vergleich:</b> Placebo</li> <li>• <b>Design:</b> <ul style="list-style-type: none"> <li>- 4-week run-in period; treatment periods separated by a 4-week washout</li> </ul> </li> <li>• <b>Population:</b> n=67</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- symptoms of chronic airflow obstruction, postbronchodilator FEV1 &lt; 70% predicted, FEV1/FVC ratio &lt; 70%.</li> <li>- no substantial improvement in FEV1 after 2,5 mg nebulised albutamol</li> </ul> </li> <li>• <b>Ausschlusskriterien:</b> <ul style="list-style-type: none"> <li>- asthma, a history of childhood respiratory disorders, variability in symptoms not associated with infections, history of acute wheeze, breathlessness, or deterioration associated with allergens, exacerbation within 6 weeks of trial entry.</li> <li>- taking regular OCS</li> <li>- taking ICS: drugs discontinued for at least 1 month before randomisation.</li> <li>- withdrew patients from the study if they had a moderate exacerbation requiring ICS or antibiotics, a severe exacerbation needing OCS, or a severe intercurrent illness</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Geschlecht, Alter, Rauchstatus weitestgehend ausgeglichen</li> <li>• Einteilung nach Baseline eosinophil count tertiles: <ul style="list-style-type: none"> <li>- &lt;1,3 (n=22)</li> <li>- 1,3–4,5 (n=23)</li> <li>- &gt;4,5 (n=22)</li> </ul> </li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>mean paired difference between prednisolone and placebo treatment for the change in primary outcomes for the <b>whole group</b> were: <ul style="list-style-type: none"> <li>- postbronchodilator FEV1 0,07 L (95% CI 0,01–0,14)</li> <li>- total score on CRQ 0,32 (0,17–0,47)</li> <li>- shuttle walk distance 12 m (3–21)</li> </ul> </li> </ul> </li> <li><u>Auswertung entsprechend der Baseline Eosinophilen im Sputum:</u> <ul style="list-style-type: none"> <li>- Mean difference between prednisolone and placebo increased progressively from the lowest to the highest eosinophilic tertile for FEV1 and CRQ</li> <li>- in the <b>highest tertile:</b> mean change in postbronchodilator FEV1 0,19 L (0,06–0,32), CRQ scores 0,62 (0,31–0,93), and shuttle walk distance 20 m (5–35) with prednisolone compared with placebo</li> </ul> </li> <li>• <b>ausgewählte weitere Ergebnisse:</b> <ul style="list-style-type: none"> <li>- mean sputum eosinophil count: significantly decreased after treatment with prednisolone from 2,4% to 0,4% [95% CI 3,1–11,4], p&lt;0,0001)</li> <li>- 29 (43%) patients had a baseline eosinophil differential count higher than the normal range in our laboratory (&gt;3%).</li> </ul> </li> <li>• <b>Sicherheit:</b> nicht betrachtet</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Selection bias:</b> <ul style="list-style-type: none"> <li>Randomisierung: unclear; Allocation concealment: low</li> </ul> </li> <li>• <b>Performance bias:</b> <ul style="list-style-type: none"> <li>Verblindung von Teilnehmern und Personal: low</li> </ul> </li> <li>• <b>Detection bias:</b> <ul style="list-style-type: none"> <li>Verblindung der Ergebnisevaluation: unclear</li> </ul> </li> <li>• <b>Attrition bias:</b> <ul style="list-style-type: none"> <li>Verlust von Studienteilnehmern/ fehlende Daten: unclear.</li> <li>ITT-Analyse: unclear</li> </ul> </li> <li>• <b>Reporting bias:</b> <ul style="list-style-type: none"> <li>selektive Ergebnisdarstellung: unclear</li> </ul> </li> <li>• <b>Andere Biasursachen:</b> <ul style="list-style-type: none"> <li>Baseline imbalance: unclear bis high</li> <li>Interessenkonflikte/ Sponsoring: ja, grant from Trent Regional Research Scheme; Astra-Zeneca;</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>- Endpunkte klinisch relevant?</li> <li>- führen die Ein- und Ausschlusskriterien zu einem Verzerrungsrisiko? (z.B. Run-in-Phase: Absetzen von ICS, dann Ausschluss bei Exazerbation)</li> </ul>

### Anhang 8.5 Roflumilast

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Devi M K. A clinical study on safety and efficacy of formoterol and tiotropium combination compared to formoterol and tiotropium combination compared to formoterol and tiotropium with roflumilast combination in treatment of moderate to severe chronic obstructive pulmonary disease patients. Asian J Pharm Clin Res 2018; 11(3):184. <a href="http://innovareacademics.in/journals/index.php/aj-pcr/article/view/21871">innovareacademics.in/journals/index.php/aj-pcr/article/view/21871</a>.</p> <p>• Nicht zitiert</p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> to assess the safety and efficacy of formoterol and tiotropium combination compared to formoterol and tiotropium with roflumilast combination in treatment of moderate-to-severe chronic obstructive pulmonary disease (COPD) patients on inhaled combination therapy.</li> <li>• <b>Studiendesign:</b> comparative randomized control study</li> <li>• <b>Population:</b> moderate-to-severe COPD; n=61 patients</li> <li>• <b>Intervention:</b> formoterol and tiotropium combination (group A)</li> <li>• <b>Vergleich:</b> formoterol and tiotropium with roflumilast (group B)</li> <li>• 12 weeks</li> <li>• <b>Einschlusskriterien:</b> genders aged more than 40 years, moderate-to-severe COPD patient, current or ex-smokers, with a smoking history, patient with other comorbid conditions</li> <li>• <b>Studienzeitraum:</b> October 2016 to March 2017</li> <li>• Indien (single center)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> <ul style="list-style-type: none"> <li>- average age: 57.63±8.3 years.</li> <li>- Differenzen hinsichtlich Alter und Komorbiditäten zwischen den Gruppen (aufgrund geringer Fallzahlen)</li> </ul> </li> <li>• Comparison of spirometry reports before and after drug administration in both groups was done. FEV1 and FVC were found to be statistically significant between the study group (0.001, p&lt;0.05). The average mean change of FEV1 before and after treatment in Group B was found to be improved as compared to Group B (0.66).</li> <li>• <b>Sicherheit:</b> adverse drug reaction: diarrhea in 10% of patients, weight loss (23.3%), headache (3.3%), back pain (3.3%), insomnia (10%), and decreased appetite (13.3%) were observed in Group B patients treated with roflumilast.</li> </ul>	<ul style="list-style-type: none"> <li><b>Selection bias</b> Randomisierung: unklar Allocation concealment: unklar</li> <li><b>Performance bias</b> Verblindung von Teilnehmern und Personal: unklar</li> <li><b>Detection bias</b> Verblindung der Ergebnisevaluation: unklar</li> <li><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: gering</li> <li>ITT-Analyse: nicht durchgeführt</li> <li><b>Reporting bias</b> selektive Ergebnisdarstellung: unklar</li> <li><b>Andere Biasursachen</b> Baseline imbalance: hoch</li> <li><b>Interessenkonflikte/ Sponsoring:</b> nicht angegeben</li> </ul>	<ul style="list-style-type: none"> <li>• keine durch die Leitliniengruppe NVL COPD priorisierten Endpunkte beschrieben</li> <li>• Methodik in Publikation kaum beschrieben</li> <li>• geringe Fallzahl: n=61</li> </ul>

### Anhang 8.6 Wirksamkeit von Instruktionen in Inhalationssysteme (NVL Asthma)

Zitat	AMSTAR	Studiencharakteristika (Patienten, Intervention, Vergleich, Studientypen)	Ergebnisse (inklusive Datenqualität)
<p>27137 Normansell R. Interventions to im-</p>	11	<p>Suchzeitraum: 11/2016 Ziel: assess impact of interventions to improve inhaler technique [...]</p>	<p><b>enhanced inhaler technique education vs control or usual care:</b> <u>1. Inhaler technique:</u> Erwachsene: correct in intervention group (69/100) vs. control group (31/100) (OR 5.00, 95% CI 1.83 to 13.65; n=258; 3 studies; I<sup>2</sup> = 57%; moderate quality)</p>

Zitat	AMSTAR	Studiencharakteristika (Patienten, Intervention, Vergleich, Studientypen)	Ergebnisse (inklusive Datenqualität)
<p>prove inhaler technique for people with asthma. Cochrane Database Syst Rev 2017;3:CD012286 <a href="http://www.ncbi.nlm.nih.gov/pub-med/28288272">http://www.ncbi.nlm.nih.gov/pub-med/28288272</a></p>		<p>P: adults and children with asthma, diagnosed according to national or international guidelines or by a healthcare professional. I: primarily aimed at improving inhaler technique C: 1. Usual care/ No additional intervention 2. intervention that did not primarily aim to improve inhaler technique (e.g. asthma education only vs asthma education plus an inhaler technique demonstration). 3. intervention of different type or intensity, also aimed at improving inhaler technique (e.g. written instructions only vs written instructions plus physical demonstration). S: parallel and cluster- (RCTs); any duration; in any setting</p>	<p>Kinder: no significant differences between groups, with CI including both potential harm and benefit of the intervention (OR 1.29, 95% CI 0.70 to 2.36; n=175; 2 studies; I<sup>2</sup> = 0%; low-quality). <u>2. Asthmakontrolle:</u> benefit in favour of educational intervention but with a lower CI, including no difference (SMD 0.48, 95%CI -0.29; 1.24; n= 247; 2 studies; I<sup>2</sup> = 88%; very low-quality) <u>3. Exazerbationen:</u> similar number of participants (adults) in each group experienced an exacerbation requiring at least OCS treatment (10 vs 8), Datenqualität: very low <u>4. QoL:</u> SMD 0.52, 95%CI -0.04 to 1.09; n= 247; 2 studies; I<sup>2</sup> = 78%; low-quality, zu Gunsten Instruktion <b>multi-media training vs control or usual care:</b> <u>1. Inhaler technique:</u> benefit in favour of multi-media intervention when compared with a patient information leaflet and a verbal explanation, but the lower CI does not rule out benefit for the control group (OR 2.15, 95%CI 0.84 to 5.50; n= 164; 2 studies; I<sup>2</sup> = 49%; moderate-quality) <u>2. Asthmakontrolle:</u> one study in children using the ACT, as endpoint score and as change from baseline and found no significant between group differences, with confidence intervals excluding the established minimal clinically important difference (MCID) of 3 (low quality). <b>feedback device vs control or usual care:</b> <u>1. Inhaler technique:</u> - benefit in favour of the feedback device, but the effect was very imprecise (OR 18.26, 95% CI 2.22 to 150.13; n = 71; 1 study; low-quality) - Use of an inhaler feedback device in addition to verbal training (pharmacists) increased the odds of achieving the correct technique (OR 4.80, 95% CI 1.87 to 12.33; n= 97; 1 study; low-quality). 51/ 100 in control vs 83/ 100 in intervention (95% CI 66 to 93). <u>2. Asthmakontrolle:</u> - Erwachsene: found no differences between groups and confidence intervals, excluding the MCID of 0.5 (MD -0.10, 95% CI - 0.46 to 0.26; 97 participants; one study; low-quality). - Kinder: no between-group differences, with confidence intervals again excluding theMCID of 0.5 (MD -0.02, 95% CI -0.35 to 0.32; n= 98; 2 studies; I<sup>2</sup> = 0%; moderate-quality). <u>3. QoL:</u> - Erwachsene: analysis suggests benefit of device feedback over usual care; below the MCID of 0.5, lower CI includes no difference (MD 0.38, 95%CI -0.01 to 0.77; n= 100; 2 studies; I<sup>2</sup> = 0%; low quality).</p>
<p>27138 Gillette C. Inhaler Technique in Children With Asthma: A Systematic Review. Acad Pediatr 2016;16(7):605-15.</p>	6	<p>Suchzeitraum: 2015/08 Fragestellung: 1) the prevalence of correct inhaler technique among children with asthma 2) are educational interventions associated with improved rates of correct inhalation technique</p>	<p>Ergebnisse zur Frage 1 nicht Inhalt der von uns gestellten Frage <b>Fragestellung 2:</b> - Overall, teaching how to correctly use an inhaler: associated with improved inhaler technique, regardless of who did the coaching - All but 1 study: communication was associated with improved inhaler technique and the more often the child received instruction, the better the technique. - technique should be continuously assessed even in children who have previously demonstrated correct technique</p>

Zitat	AMSTAR	Studiencharakteristika (Patienten, Intervention, Vergleich, Studientypen)	Ergebnisse (inklusive Datenqualität)
<p><a href="http://www.ncbi.nlm.nih.gov/pub-med/27130811">http://www.ncbi.nlm.nih.gov/pub-med/27130811</a></p> <p>- nicht eingeschlossen</p>		<p>3) is improved inhaler technique associated with improved asthma outcomes</p> <p>P: 6 through 18 years of age</p> <p>I und C: nicht definiert</p> <p>S: experimental and observational studies</p> <p>&gt;&gt; narrative Synthese und tabellarische Darstellung erfolgt</p>	<p>- 2 studies: repeated instruction about inhaler technique is associated with improved technique over time.</p> <p>- 2 studies reported: children demonstrate correct use of the inhaler was also associated with correct inhaler technique.</p> <p>- more intensive training in which each child's technique was checked and rechecked until the educator was satisfied were also more likely to use their inhaler correctly.</p> <p>- 4 studies: examined effects of telemedicine by pharmacists: improved technique in children</p> <p>- prerecorded video (3 minutes): the improvement in technique was not sustained 1 month later</p> <p><b>Fragestellung 3:</b> in 8 Primärstudien untersucht; 3 directly examined how inhaler technique was associated with asthma outcomes: heterogene Ergebnisse</p> <p>Selbstmanagement: in 7 Studien untersucht; All studies reported increases in asthma knowledge, quality of life, and self-efficacy</p>

### Anhang 8.7 Mukolytika

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Zeng Z. Effect of carbocisteine on patients with COPD: A systematic review and meta-analysis. 2017.</p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> we investigated the efficacy of carbocisteine on stable COPD.</li> <li>• <b>Suchzeitraum:</b> up to September 1, 2016</li> <li>• <b>Population:</b> stable COPD</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- RCT</li> <li>- oral carbocisteine for a period of at least 3 months</li> <li>- adults with COPD</li> </ul> </li> <li>• <b>Interventionen:</b> oral carbocisteine 1.500 mg daily - (1 study: carbocisteine lysine 2,700 mg daily = equivalent to carbocisteine 1,500 mg daily)</li> <li>• <b>Vergleich:</b> placebo</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Exacerbation rates (total number)</b> <ul style="list-style-type: none"> <li>- significant decrease in the rate of exacerbations in the carbocisteine group compared with the placebo group (3 studies: n=1,215; MD -0.43; 95% confidence interval [CI] -0.57, -0.29, I<sup>2</sup>=60%, P,0.00001)</li> </ul> </li> <li>• <b>Number of patients with at least one exacerbation</b> <ul style="list-style-type: none"> <li>- 3 three studies reported the outcome of the number of patients with at least one exacerbation.</li> <li>- One study showed no difference in the risk of the outcome.</li> <li>- significant difference in number of patients with at least one exacerbation compared with placebo (3 studies: n=1,215; relative risk [RR] 0.86; 95% CI 0.78, 0.95, I<sup>2</sup>=84%, P=0.002).</li> <li>- NNT = 12</li> </ul> </li> <li>• <b>Quality of life (SGRQ)</b> <ul style="list-style-type: none"> <li>- significant decrease was seen in the rate of exacerbations in the carbocisteine group compared with the placebo group (2 studies: n=849; MD -6.29; 95% CI -9.30, -3.27, I<sup>2</sup>=61%, P&lt;0.0001; tota SGRQ)</li> </ul> </li> <li>• <b>Adverse effects</b> <ul style="list-style-type: none"> <li>- most common adverse events reported were gastrointestinal problems</li> <li>- No significant difference was seen with carbocisteine compared with placebo (3 studies: n=1,201; RR 1.02; 95% CI 0.73, 1.43, I<sup>2</sup>=61%,</li> </ul> </li> </ul>	<p>AMSTAR-II: low</p>	<p>&gt;&gt; geringe Studienanzahl</p> <p>&gt;&gt; RoB der eingeschlossenen Studien: wurde durchgeführt, kann jedoch nicht dargestellt werden, da "supplemental material" auf einer asiatischen Internetseite hinterlegt ist</p> <p>&gt;&gt; substantial heterogeneity was detected in some outcomes. The conclusion needs to be used with caution</p> <p>&gt;&gt; Publication bias may be seen in this review. It may cause overestimate outcomes</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<ul style="list-style-type: none"> <li>• <b>eingeschlossene Studien:</b> 4 RCTs; 1357 Participants</li> </ul>	<p>P=0.75)</p> <ul style="list-style-type: none"> <li>- no significant difference in the adverse effects of gastrointestinal problems (3 studies: n=1,201; RR 1.38; 95% CI 0.71, 2.66, I<sup>2</sup>=77%, P=0.34).</li> <li>- No fatal adverse effects were found in the four studies.</li> <li>• <b>Rates of hospitalization</b></li> <li>- No significant difference was seen in it (1 study: n=352; RR 9.52; 95% CI 0.52, 175.57, P=0.13).</li> <li>• <b>Rates of mortality</b></li> <li>- 2 studies: no one died</li> <li>• <b>Subgruppen-Analysen: rate of exacerbations</b></li> <li>- subgroup with the population of non-Chinese showed a large reduction in the carbocisteine group (2 studies: n=508, MD =-0.34; 95% CI -0.90, -0.40, I<sup>2</sup>=2%, P,0.00001) compared to placebo.</li> <li>- subgroup with the population of Chinese showed no difference in the risk of the outcome (1: n=707, MD =-0.34; 95% CI -0.51, -0.17, P,0.0001)</li> </ul>		
<p>Cazzola M. The therapeutic efficacy of erdosteine in the treatment of chronic obstructive bronchitis: A meta-analysis of individual patient data. Pulm Pharmacol Ther 2010; 23(2):135–44. <a href="https://www.ncbi.nlm.nih.gov/pub-med/19854285">https://www.ncbi.nlm.nih.gov/pub-med/19854285</a>.</p> <p>• Nicht zitiert.</p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> to test the available evidence for the efficacy of erdosteine in adults with stable or exacerbated CB/COPD.</li> <li>• <b>Suchzeitraum:</b> nicht angegeben (Individual patient data from the published and unpublished studies in patients with CB submitted for European marketing approval in 2005 were considered.)</li> <li>• <b>Population:</b> Patient*innen mit chronischer Bronchitis/COPD</li> <li>- either at occurrence of an acute exacerbation or during the stable phase of the disease</li> <li>• <b>Interventionen:</b></li> <li>- Erdosteine (300 mg capsule) vs. placebo or mucolytics (ambroxol, N-acetylcysteine, carbocysteine, sobrerol)</li> <li>- 7-10 days of treatment</li> <li>- 2-3x/day on top of background therapy</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b></li> <li>- individual data from 1046 patients from 15 RCTs (12 on exacerbated and 3 on stable CB/COPD) were obtained.</li> <li>• <b>Ergebnisse (Erdosteine vs. Mucolytics)</b></li> <li>- <u>cGEI:</u> erdosteine induced a significant reduction of cGEI versus comparators (-1.02; 95% CI: from -1.60 to -0.44; p = 0.0006; n= 1046 patients).</li> <li>- <u>cough intensity:</u> the effect of erdosteine was significant vs. mucolytics (- 0.26; 95% CI: from -0.43 to -0.10; p = 0.002; n=496 Participants).</li> <li>- <u>expectoration difficulty</u> ( 13 RCTs involving 992 patients): Erdosteine significantly improved this symptom vs. mucolytics (-0.19; 95% CI: from -0.34 to 0.03; p = 0.02)</li> <li>- <u>Dyspnoe:</u> keine signifikanten Effekte hinsichtlich Dyspnoe (Erdosteine vs. mucolytics)</li> <li>• <b>Sicherheit:</b> Erdosteine (n=295) versus Placebo (n=292)</li> <li><u>No. Patients reporting AEs (n Erdosteine/ n Placebo):</u></li> <li>Gastrointestinal: 21/24</li> <li>Taste Loss: 1/0</li> </ul>	<p>AMSTAR-II: - critically low</p>	<ul style="list-style-type: none"> <li>- Individual patient data were provided by the manufacturer of erdosteine, Edmond Pharma (Milano, Italy)</li> <li>&gt;&gt; Furthermore, the manufacturer of erdosteine (Edmond Pharma s.r.l., Italy) was contacted and asked for any additional non-indexed publications and relevant unpublished studies. Individual patient data from the published and unpublished studies in patients with CB submitted for European marketing approval in 2005 were considered.</li> <li>- gemischte Population eingeschlossen: COPD und chron. Bronchitis (Patients with stable COPD disease accounted for 26.3% of the study population)</li> <li>- Ergebnisse werden für den</li> </ul>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<ul style="list-style-type: none"> <li>• <b>eingeschlossene Studien:</b> n=15 RCTs (n=1046 participants)</li> <li>• <b>RoB der eingeschlossenen Studien:</b> n= 6 RCTs JADAD 1-2; n=9 RCTs JADAD 3-5 Score</li> <li>• cumulative global efficacy index = cGEI (the sum of all assessed respiratory symptom scores)</li> </ul>	<p>Allergic reactions: 2/3 Miscellaneous: 11/5 Total: 35 (11.9%)/32 (11.0%)</p> <ul style="list-style-type: none"> <li>• <b>Sicherheit:</b> Erdosteine (n=234) versus Mucolytics (n=225) <u>No. Patients reporting AEs (n Erdosteine/ n Mucolytics):</u> Gastrointestinal: 11/19 Taste Loss: 0/0 Allergic reactions: 1/0 Miscellaneous: 7/6 Total: 19 (8.1%)/25 (11.1%)</li> </ul>		Vergleich Erdostein vs. Mukolytika dargestellt. Für den Vergleich Erdostein vs. Placebo wurde ein Review identifiziert, welche die hier eingeschlossenen Studien um drei weitere ergänzt und metaanalysiert hat (Ref ID 29801)
<p>Cazzola M. Impact of erdosteine on chronic bronchitis and COPD: A meta-analysis. Pulm Pharmacol Ther 2018; 48:185–94. <a href="https://www.ncbi.nlm.nih.gov/pub-med/29233650">https://www.ncbi.nlm.nih.gov/pub-med/29233650</a>.</p> <ul style="list-style-type: none"> <li>• Nicht zitiert.</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To clarify the real impact of erdosteine in improving the clinical score of patients with chronic bronchitis and/or COPD, and the use of this drug in preventing chronic bronchitis/COPD exacerbations.</li> <li>• <b>Suchzeitraum:</b> up to July 31, 2017</li> <li>• <b>Population:</b> patients with chronic bronchitis and/or COPD</li> <li>• <b>Interventionen:</b> - Erdosteine vs. placebo - maximale Tagesdosis zwischen 600mg und 900 mg - 2-3x/Tag</li> <li>• <b>eingeschlossene Studien:</b> 10 clinical studies (n=8 RCTs) involving 1278 patients</li> <li>• RoB der eingeschlossenen Studien: n= 8 studies JADAD ≥3; n=2 studies JADAD &lt;3</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> - 6 studies on chronic bronchitis; 3 studies on COPD and 1 study on patients suffering from both chronic bronchitis and COPD</li> <li>• <b>Effektivität: Treatment with erdosteine:</b> <u>clinical score (studies mixed: patients with CB or COPD)</u> - significantly (p&lt;0.001) improved clinical score of patient with no differences (p&gt;0.05) to subanalysis (only high quality studies included) - only high quality studies included: SMD -0.44; 95% CI -0.70 to -0.18; I<sup>2</sup> 80%; p&lt;0.001; <b>GRADE: MODERATE</b></li> <li><u>clinical condition (only studies on COPD)</u> - significantly improved clinical condition - SMD all studies -0.56; 95%Ci -0.94 to -0.17; I<sup>2</sup> 85%; p&lt;0.001; <b>GRADE: HIGH</b> - SMD high quality studies -0.28; 95%Ci -0.50 to -0.06; I<sup>2</sup> 53%; p=0.12</li> <li><u>COPD exacerbation</u> - significantly (P &lt; .01 to P &lt; .001) reduced overall risk of CB/COPD exacerbations and risk of experiencing at least one exacerbation vs. control - risk of COPD exacerbation: RR 0.74 95% CI 0.61 -0.89, I<sup>2</sup> 31%, P = .24; <b>GRADE: HIGH</b> - risk of experiencing at least one COPD exacerbation: RR 0.78, 95%CI 0.64 - 0.96, I<sup>2</sup> 6%, P=0.35; <b>GRADE: HIGH</b></li> </ul>	<p>AMSTAR-II: - critically low</p>	Update des Cazzola Reviews von 2010 (ID 29809); hier ausschließlich Studien: Erdostein vs. Placebo inkludiert

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Cazzola M. Influence of N-acetylcysteine on chronic bronchitis or COPD exacerbations: A meta-analysis. Eur Respir Rev 2015; 24(137):451–61. <a href="https://www.ncbi.nlm.nih.gov/pub-med/26324807">https://www.ncbi.nlm.nih.gov/pub-med/26324807</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> whether NAC is effective in preventing COPD exacerbations, and whether the effects are dose related</li> <li>• <b>Suchzeitraum:</b> up to July 31, 2014</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Interventionen:</b> <ul style="list-style-type: none"> <li>- oral administration of NAC</li> </ul> </li> <li>• <b>Vergleich:</b> <ul style="list-style-type: none"> <li>- Placebo or control subjects</li> </ul> </li> <li>• <b>eingeschlossene Studien:</b> n=13 studies (RCTs &amp; observational studies)                             <ul style="list-style-type: none"> <li>- 4155 COPD patients (NAC n=1933; placebo or controls n=2222)</li> </ul> </li> <li>• RoB der eingeschlossenen Studien: für 12 RCTs: 8/12 Studien &gt; 3 JADAD score</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- NAC treatment ranged from 4 to 36 months.</li> <li>- 10 trials were double-blind, randomised placebo-controlled, one trial was single-blind, randomised placebo-controlled, one trial was open, randomised and controlled and one study was a retrospective cohort investigation</li> </ul> </li> <li>• <b>Exazerbationen</b> <ul style="list-style-type: none"> <li>- relative risk 0.75, 95% CI 0.66-0.84; p &lt; 0.01 (n=13 studies): at patients treated with NAC had significantly and consistently fewer exacerbations of chronic bronchitis or COPD , although this protective effect was more apparent in patients without evidence of airway obstruction.</li> </ul> </li> <li>• <b>subgroup with Jadad score ≤3</b> <ul style="list-style-type: none"> <li>- decrease in the risk of exacerbation (six studies: treated n=986, placebo n=1267; relative risk 0.64, 95% CI 0.56–0.74; p=0.07),</li> </ul> </li> <li>• <b>subgroup with Jadad score &gt;3</b> <ul style="list-style-type: none"> <li>- significant reduction in the risk of exacerbation was detected in the subgroup of RCTs with Jadad score &gt;3 (seven studies: treated n=957, placebo n=955; relative risk 0.85, 95% CI 0.74–0.98; p&lt;0.01).</li> </ul> </li> <li>• <b>Low Doses of NAC</b> <ul style="list-style-type: none"> <li>- NAC administered at low doses (patients from 10 studies: treated n=1298, placebo or controls n=1614) significantly protected against COPD exacerbations (relative risk 0.76, 95% CI 0.65–0.89; p&lt;0.01)</li> <li>- the reduction of exacerbation risk was less extensive (relative risk 0.90, 95% CI 0.84–0.96; p&lt;0.01) in the analysis of those RCTs where COPD was diagnosed using PFT (patients from five studies: treated n=444, placebo n=433)</li> </ul> </li> <li>• <b>High Doses NAC</b> <ul style="list-style-type: none"> <li>- NAC at high doses included patients from four studies (treated n=635, placebo or controls n=1362) and showed a significant reduction of COPD exacerbation rate (relative risk 0.65, 95% CI 0.49–0.88; p=0.03)</li> <li>- confirmed by the results of the subgroup of RCTs enrolling COPD patients using PFT according to ATS/ERS or GOLD guidelines (two studies: treated n=534, placebo n=538; relative risk 0.75, 95% CI 0.68–0.82; p=0.04)</li> </ul> </li> </ul>	<p>AMSTAR-II: - critically low</p>	<ul style="list-style-type: none"> <li>• random effects model genutzt, jedoch keinerlei Untersuchungen bezüglich möglicher Heterogenität zwischen den einzelnen Studien durchgeführt</li> <li>• sehr schwache methodische Qualität</li> </ul>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
		<ul style="list-style-type: none"> <li>• <b>Sicherheit</b> <ul style="list-style-type: none"> <li>- NAC was well tolerated and the risk of adverse reactions was not dose-dependent</li> <li>-- low doses relative risk 0.93, 95% CI 0.89-0.97; p = 0.40</li> <li>-- high doses relative risk 1.11, 95% CI 0.89-1.39; p = 0.58</li> </ul> </li> </ul>		
<p>Fowdar K. The effect of N-acetylcysteine on exacerbations of chronic obstructive pulmonary disease: A meta-analysis and systematic review. 2017 Mar - Apr.</p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To investigate the effects of NAC on COPD exacerbation and changes in lung function parameters in patients with COPD.</li> <li>• <b>Suchzeitraum:</b> 09/2015</li> <li>• <b>Population:</b> patients with stable COPD</li> <li>• <b>Interventionen:</b> orally administered N-acetylcysteine (NAC) for &gt;4 weeks in addition to standard therapy</li> <li>• <b>Vergleich:</b> Placebo or standard therapy (e.g. <math>\beta</math>2-agonists, anticholinergics, and theophylline)</li> <li>• <b>eingeschlossene Studien:</b> 12 RCTs (n=2691 participants: NAC n=1339; control group n=1352)</li> <li>• <b>RoB der eingeschlossenen Studien:</b> 11/12 Studien &gt; 3 JADAD score</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika:</b> <ul style="list-style-type: none"> <li>- NAC doses ranged from 257 mg/daly to 1800 mg/day</li> <li>- NAC treatment durations ranged from 3 months to 36 months</li> </ul> </li> <li>• <b>Exacerbation prevalence</b> <ul style="list-style-type: none"> <li>- High-dose (RR = 0.90, 95% CI = 0.82-0.996, P = 0.041, 3 RCTs, n=1237) and low-dose (RR = 0.83, 95% CI = 0.69-0.99, P = 0.043, 6 RCTs, n=805) NAC reduced COPD exacerbation prevalence.</li> <li>- Long-term (<math>\geq</math>6 months), but not short-term, NAC reduced exacerbation prevalence (RR = 0.85, 95% CI = 0.74-0.98, P = 0.024, 7 RCTs, n=1741).</li> </ul> </li> <li>• <b>Hospital admission</b> (n=3 Studien; nicht gepoolt aufgrund Heterogenität) <ul style="list-style-type: none"> <li>- one study: significantly lower in NAC group (37/50 participants) than in control group (55/50 participants)</li> <li>- two other studies: similar but not significant results (NAC 26/52 vs. placebo 45/56; and NAC 33/482 vs. placebo 36/482).</li> </ul> </li> <li>• NAC did not affect exacerbation rate, forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), or inspiratory capacity (IC). Long-term NAC therapy may reduce risk of COPD exacerbation.</li> <li>• <b>Sicherheit</b> (n=6 Studien; nicht gepoolt aufgrund Heterogenität) <ul style="list-style-type: none"> <li>- mentioned in six studies involving 1777 participants (NAC n=857; control n=872)</li> <li>- No significant difference in adverse drug effects was observed between NAC-treated patients and controls (RR = 1.13, 95% CI = 0.86 - 1.48, P= 0.384)</li> <li>- No significant differences in adverse effects were obtained in our dose and treatment duration subgroup analyses (fixed effects models)</li> </ul> </li> <li>- Participants who received NAC therapy reported gastrointestinal disorders ( e.g., nausea and vomiting, abdominal pain and diarrhea, indigestion and epigastric discomfort) 5/6 studies: average frequency</li> </ul>	<p>AMSTAR-II: - critically low</p>	



Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
		<p>6% in NAC group vs, 5% in control group).</p> <ul style="list-style-type: none"> <li>- Skin disorders were reported in two studies: average frequency 1,3% in NAC group vs. 0.6% in control group.</li> <li>- Central nervous system disorders, dry mouth, joint pain, and muscle pain were reported in a few patients</li> </ul>		
<p>Cazzola M. Impact of Mucolytic Agents on COPD Exacerbations: A Pair-wise and Network Meta-analysis. COPD 2017; 14(5):552–63. <a href="https://www.ncbi.nlm.nih.gov/pub-med/28753070">https://www.ncbi.nlm.nih.gov/pub-med/28753070</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To investigate the impact of mucoactive agents on the risk of COPD exacerbations</li> <li>• <b>Suchzeitraum:</b> 03/2017</li> <li>• <b>Population:</b> Patient*innen mit COPD (not chronic bronchitis)</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- RCTs lasting at least 3 months</li> <li>- und Ausschlusskriterien</li> </ul> </li> <li>• <b>Interventionen:</b> oral                             <ul style="list-style-type: none"> <li>- ambroxol (150gm) or</li> <li>- carbocysteine (1500mg) or</li> <li>- erdosteine (600mg) or</li> <li>- iodinated glycerol and N-acetylcysteine (600 mg/1200mg)</li> </ul> </li> <li>• <b>Vergleich:</b> Placebo</li> <li>• <b>eingeschlossene Studien:</b> n=11 RCTs (n=3.164 patients: n=1.587 treated with a mucolytic agent, n=1.577 treated with placebo)</li> </ul>	<ul style="list-style-type: none"> <li>• 6 RCT on NAC , 3 on carbocysteine, 1 on erdosteine, and 1 on ambroxol</li> <li>• Mucolytics significantly reduced the odds of exacerbation vs. placebo (11 studies analyzed: odds ratio (OR) 0.51, 95% confidence interval (CI) 0.39-0.67; p &lt; 0.001).</li> <li>• Only N-acetylcysteine 1,200 mg/day significantly protected against exacerbations vs. placebo (2 studies analyzed: OR 0.56, 95% CI 0.35-0.92; p &lt; 0.05; high quality of evidence).</li> <li>• NAC at lower dose (600 mg/day) did not significantly improve the odds of COPD exacerbations vs. placebo (2 high-quality studies analyzed: OR 0.95, 95% CI 0.85-1.07; p ≥ 0.05)</li> <li>• A signal of effectiveness was detected for carbocysteine (2 studies analyzed: OR 0.45, 95% CI 0.20-1.01; p ≥ 0.05; moderate quality of evidence; no significant reduction).</li> <li>- After adjusting for the significant confounders detected in the meta-regression model, therapy with mucolytic agents remained as a statistically significant treatment against COPD exacerbations (nonadjusted p &lt; 0.001; adjusted for Jadad score p &lt; 0.01; adjusted for studies duration p &lt; 0.05; adjusted for history of exacerbation rate p &lt; 0.001).</li> <li>- The sensitivity analysis identified greater effectiveness of mucolytics agents in studies lasting ≥ 1 year vs. shorter RCTs (OR 0.61, 95% CI 0.47 - 0.79 vs. OR 0.29, 95%CI 0.14 - 0.60).</li> <li>• <b>Qualität der Evidenz (GRADE); mucolytic agents and COPD exacerbations, Anticipated absolute effects</b> <ul style="list-style-type: none"> <li>- overall (all studies): MODERATE</li> <li>-- Risk with placebo 317 per 1000</li> <li>-- Risk difference with mucolytic agents 125 fewer per 1000 (164 fewer to 80 fewer)</li> <li>- <u>N-acetylcysteine, high-dose</u> (high-quality studies with Jaded score ≥ 3): HIGH</li> <li>-- Risk with placebo 256 per 1000</li> <li>-- Risk difference with mucolytic agents 94 fewer per 1000 (178 fewer</li> </ul> </li> </ul>	<p>AMSTAR-II: low</p>	<p>2 weitere Studien (2x Carbocysteine) eingeschlossen, die nicht im Poole-Review von 2019 inkludiert wurden</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
		to 16 fewer)  - <u>N-acetylcysteine, low-dose</u> (high-quality studies with Jaded score $\geq$ 3): HIGH -- Risk with placebo 281 per 1000 -- Risk difference with mucolytic agents 10 fewer per 1000 (34 fewer to 14 more)  - <u>Carbocysteine</u> (high-quality studies with Jaded score $\geq$ 3): MODERATE -- Risk with placebo 317 per 1000 -- Risk difference with mucolytic agents 144 fewer per 1000 (231 fewer to 1 more)  - <u>Erdosteine</u> (high-quality studies with Jaded score $\geq$ 3): VERY LOW -- Risk with placebo 515 per 1000 -- Risk difference with mucolytic agents 164 fewer per 1000 (from 59 fewer to 256 fewer)  - <u>Ambroxol</u> (high-quality studies with Jaded score $\geq$ 3): VERY LOW -- Risk with placebo 118 per 1000 -- Risk difference with mucolytic agents 6 fewer per 1000 (from 41 fewer to 40 more)		
Poole P. Mucolytic agents versus placebo for chronic bronchitis or chronic obstructive pulmonary disease. 2019 May 20.	<ul style="list-style-type: none"> <li>• <b>primäre Fragestellung:</b> To determine whether treatment with mucolytics reduces exacerbations and/or days of disability in patients with chronic bronchitis or COPD</li> <li>• <b>sekundäre Fragestellungen:</b> To assess whether mucolytics lead to improvement in lung function or quality of life + To determine frequency of adverse effects associated with use of mucolytics</li> <li>• <b>Suchzeitraum:</b> most recently on 23. April 2019</li> <li>• <b>Population:</b> adults with chronic bronchitis or COPD</li> </ul>	<b>Baseline-Charakteristika</b> - mean age of participants ranged from 40 to 71 years - All but five studies reported the percentage of current smokers or ex-smokers, which ranged from 55% to 100% - verschiedene Mukolytika in Studien betrachtet; verschiedene Dosierungen  <u>Participants with no exacerbations in study period (Follow-up: 8.8 months):</u> Risk with placebo: 386 per 1000 Risk with mucolytic: 521 per 1000 (495 to 545) Peto OR 1.73, 95% CI 1.56 to 1.91; 28 RCTs, 6723 participants; <b>moderate certainty evidence</b> >> Generally larger effects in earlier studies of mucolytics in chronic bronchitis and smaller effects in more recent studies in COPD >> The overall number needed to treat with mucolytics for an aver-	AMSTAR-II: - low	<ul style="list-style-type: none"> <li>• Ausschlusskriterien irreführend:                          We <b>excluded studies</b> of inhaled mucolytics and combinations of mucolytics with antibiotics and <b>mucolytics with bronchodilators</b>, as well as studies of deoxyribonuclease or proteases such as trypsin.</li> <li>&gt;&gt; irreführende Formulierung: es wurden doch Studien eingeschlossen, welche Einnahme von langwirksamen Bronchodilatoren erlauben (Bsp. Bachh 2007; Tabelle 2) --&gt; deshalb</li> </ul>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<ul style="list-style-type: none"> <li>• <b>Einschlusskriterien</b></li> <li>- RCT</li> <li>- adults with chronic bronchitis as defined by the British Medical Research Council or COPD as defined by the criteria of ATS, GOLD, ERS, or WHO</li> <li>- must have received regular treatment with oral mucolytics or placebo for at least two months</li> <li>• <b>Ausschlusskriterien:</b></li> <li>- people with asthma and cystic fibrosis; children</li> <li>- studies of inhaled mucolytics and combinations of mucolytics with antibiotics and mucolytics with bronchodilators, as well as studies of deoxyribonuclease or proteases such as trypsin.</li> <li>• <b>Interventionen:</b> oral mucolytic therapy for at least two months</li> <li>• <b>Vergleich:</b> Placebo</li> <li>• <b>eingeschlossene Studien:</b> randomised, placebo-controlled trials; n=38 (10,377 participants) --&gt; betrachtete Mukolytika im Review: N-acetylcysteine (NAC) (n=21 studies) carbocysteine (n = 3) ambroxol (n = 3) erdosteine (n = 2) sobrerol (n = 1) carbocysteinesobrerol (n = 1) carbocysteine-lysine (n = 1) letosteine (n = 1), cithiolone (n = 1) iodinated glycerol (n = 1) N-isobutyrylcysteine (NIC) (n = 1) myrtol (n = 1) cineole and lysozyme (n = 1)</li> </ul>	<p>age of nine months to keep an additional participant free from exacerbations was eight (NNTB 8, 95% CI 7 to 10). &gt;&gt; High heterogeneity was noted for this outcome (<math>I^2 = 62%</math>) &gt;&gt;The type or dose of mucolytic did not seem to alter the effect size, nor did the severity of COPD, including exacerbation history. &gt;&gt;Longer studies showed smaller effects of mucolytics than were reported in shorter studies.</p> <p><u>Days of disability per participant per month (Follow-up: 8.3 months):</u> Risk with placebo: Mean days of disability per participant per month was 1.57 days Risk with mucolytic: MD 0.43 days lower (0.56 lower to 0.30 lower) 9 RCTs, 2259 participants; <math>I^2 = 61%</math>; <b>moderate certainty evidence</b></p> <p><u>Health-related quality of life (total score SGRQ) Scale from 1 to 100; lower scores indicate better quality of life (Follow-up: 14.1 months):</u> Risk with placebo: Mean SGRQ total score was 39.02 points Risk with mucolytic: MD 1.37 lower (2.85 lower to 0.11 higher) 7 RCTs; 2721 participants; <math>I^2 = 64%</math>; <b>moderate certainty evidence</b></p> <p><u>Hospitalisation during study period (Follow-up: 16.6 months):</u> Risk with placebo: 188 per 1000 Risk with mucolytic: 136 per 1000 (107 to 171) Peto OR 0.68 (0.52 to 0.89); 1833 participants; 5 RCTs; <math>I^2 = 58%</math>; <b>moderate certainty evidence</b></p> <p><u>Adverse effects (Follow-up: 8.2 months):</u> Risk with placebo: 235 per 1000 Risk with mucolytic: 205 per 1000 (185 to 224) Peto OR 0.84 (0.74 to 0.94); 7264 participants; 24 RCTs; <math>I^2 = 46%</math>; <b>moderate certainty evidence</b> &gt;&gt; pooled effect includes no difference if a random-effects model is used.</p> <p><u>Death during study period (Follow-up: 13.3 months):</u> Risk with placebo: 11 per 1000 Risk with mucolytic: 10 per 1000 (5 to 20) Peto OR 0.98 (0.51 to 1.87); 3527 participants; 11 RCTs; <math>I^2 = 0%</math>; <b>moderate certainty evidence</b> &gt;&gt; 18 deaths on mucolytics and 19 on placebo</p>		<p>doch E und Abgleich mit anderen Reviews (Einschluss Primärstudien), welche E sind</p>

Anhang 8.8 Selektiv eingebrachte Literatur

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Dransfield MT. Metoprolol for the Prevention of Acute Exacerbations of COPD. N Engl J Med 2019; 381(24):2304-14.  <a href="http://www.ncbi.nlm.nih.gov/pub-med/31633896">http://www.ncbi.nlm.nih.gov/pub-med/31633896</a></p>	<ul style="list-style-type: none"> <li>• <b>Studiendesign:</b> prospective, randomized trial, multicenter, placebo-controlled</li> <li>• <b>Population:</b> patients with COPD, n = 532</li> <li>• <b>Intervention:</b> Metoprolol (Metoprolol succinate extended release tablets (50 mg) starting dose followed by a dose titration procedure (resulting in a final dose of 25mg (1/2 of one tablet daily), 50 mg, or 100 mg (two tablets daily))</li> <li>• <b>Vergleich:</b> matching Placebo</li> <li>• <b>Follow-up:</b> 1 year</li> <li>• ggf. Informationen zu Aufhebung der Verblindung und Cross-over</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- age 40-85, clinical history of COPD, moderate airflow limitation and an increased risk of exacerbations (evidenced by a history of exacerbations during the previous year or the prescribed use of supplemental oxygen)</li> </ul> </li> <li>• <b>Ausschlusskriterien:</b> <ul style="list-style-type: none"> <li>- already taking a beta-blocker or who had an established indication for the use of such drugs</li> </ul> </li> <li>• <b>Studienzeitraum:</b> 5/2016 - 03/2019</li> <li>• multicenter: 26 center United States</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, Geschlecht, Lungenfunktion, COPD-Medikation, Rauchstatus, HF und RR weitestgehend ausgeglichen <ul style="list-style-type: none"> <li>- mean age: 65.0±7.8 years;</li> </ul> </li> <li>• <b>Effektivität / Sicherheit:</b> <ul style="list-style-type: none"> <li>- trial was stopped early because of futility with respect to the primary end point and safety concerns.</li> <li>- no significant betweengroup difference in the median time until the first exacerbation (202 days in the metoprolol group and 222 days in the placebo group; hazard ratio for metoprolol vs. placebo, 1.05; 95% CI, 0.84 to 1.32; P = 0.66)</li> <li>- Metoprolol was associated with a higher risk of exacerbation leading to hospitalization (hazard ratio, 1.91; 95% CI, 1.29 to 2.83)</li> <li>- frequency of side effects that were possibly related to metoprolol was similar in the two groups, as was the overall rate of nonrespiratory serious adverse events.</li> <li>- during treatment period: 11 deaths in the metoprolol group and 5 in the placebo group, with unadjusted and adjusted hazard ratios for death of 2.18 (95% CI, 0.76 to 6.29) and 2.13 (95% CI, 0.69 to 6.42)</li> <li>- The majority of deaths in the metoprolol group were attributed to COPD (7, vs. 1 in the placebo group)</li> <li>- after treatment period: 3 additional deaths in the metoprolol group (at 10 to 277 days after the last dose) and 4 additional deaths in the placebo group (at 10 to 26 days after the last dose)</li> </ul> </li> <li>• <b>CAT (COPD assessment test):</b> <ul style="list-style-type: none"> <li>The patients in the metoprolol group had a greater increase (indicating worse control) from baseline in the score on the COPD Assessment Test than those in the placebo group, with a difference of 1.13 points (95% CI, 0.06 to 2.20) at day 112 and a difference of 1.47 points (95% CI, 0.32 to 2.62) at day 336</li> </ul> </li> <li>• <b>SOBQ (San Diego Shortness of Breath Questionnaire):</b> <ul style="list-style-type: none"> <li>The metoprolol group had a greater increase in SOBQ scores from baseline, indicating a worsening in shortness of breath. The between-group difference in the change from baseline was 3.47 points (95%</li> </ul> </li> </ul>	<p><b>Selection bias</b>  Randomisierung: gering  Allocation concealment: gering</p> <p><b>Performance bias</b>  Verblindung von Teilnehmern und Personal: gering</p> <p><b>Detection bias</b>  Verblindung der Ergebnisevaluation: unklar</p> <p><b>Attrition bias</b>  Verlust von Studienteilnehmern/ fehlende Daten: gering</p> <p>ITT-Analyse: alle Analysen ITT-basiert</p> <p><b>Reporting bias</b>  selektive Ergebnisdarstellung: unklar</p> <p><b>Andere Biasursachen</b>  Baseline imbalance: gering</p> <p>Interessenkonflikte/ Sponsoring:  Funded by the Department of Defense/ Sponsor: University of Minnesota</p>	<p>Studie vorzeitig abgebrochen u.a. aufgrund von Sicherheitsbedenken</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
		CI, 0.42 to 6.52) at day 112 and 4.80 points (95% CI, 1.52 to 8.07) at day 336		
<p>Rabe KF, Martinez FJ, Ferguson GT, et al. Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD. N Engl J Med 2020; 383(1):35–48. DOI: 10.1056/NEJMoa1916046.</p> <p><a href="http://www.ncbi.nlm.nih.gov/pub-med/32579807">http://www.ncbi.nlm.nih.gov/pub-med/32579807</a>.</p>	<p><b>ETHOS</b></p> <ul style="list-style-type: none"> <li>• <b>Studientyp:</b> randomized, double-blind, multi-center, parallel-group study</li> <li>• <b>Population:</b> moderate-to very-severe COPD and at least one exacerbation in the past year; n=8509 (n=8588 randomisiert)</li> <li>• <b>Studienzeitraum:</b> 2015 - 2019</li> <li>• <b>Interventionen:</b> 1:1:1:1 ratio                     <ul style="list-style-type: none"> <li>- twice-daily inhaled doses of triple therapy</li> <li>-- inhaled glucocorticoid (<b>320 µg or 160 µg</b> of budesonide), a LAMA (18 µg of glycopyrrolate), and a LABA (9.6 µg of formoterol) or</li> <li>- one of two dual therapies:                             <ul style="list-style-type: none"> <li>-- 18 µg of glycopyrrolate plus 9.6 µg of formoterol or</li> <li>-- 320 µg of budesonide plus 9.6 µg of formoterol</li> </ul> </li> </ul> </li> <li>• <b>primärer Endpunkt:</b> annual rate (the estimated mean number per patient per year) of moderate or severe COPD exacerbations</li> <li>• <b>sekundäre Endpunkte:</b> time to the first moderate or severe COPD exacerbation, the change from baseline in average daily use of rescue medication over 24 weeks, the percentage of patients who had a St. George's Respiratory Questionnaire (SGRQ) response (defined as a decrease from baseline in the total score on the SGRQ of ≥4 points at week 24), the annual rate of</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> hinsichtlich Alter, Geschlecht, Rauchstatus, stattgehabte Exazerbationen weitestgehend ausgeglichen; etwas weniger Patienten mit Baseline ≥300 cells/mm<sup>3</sup> Eosinophilen in LAMA/LABA-Gruppe (13,8% vs. 14,5%; 15,0%; und 15,6%)</li> <li>• <b>Ergebnisse primärer Endpunkt:</b> <u>annual rates of moderate or severe exacerbations</u> <ul style="list-style-type: none"> <li>- 320-µg-budesonide triple-therapy group (n=2137 patients): 1.08</li> <li>- 160 µg-budesonide triple-therapy group (n=2121 patients): 1.07</li> <li>- glycopyrrolate-formoterol group (n=2120 patients): 1.42</li> <li>- budesonide-formoterol group (n=2131 patients): 1.24</li> </ul> </li> </ul> <p>The rate was significantly lower with 320-µg-budesonide triple therapy than with glycopyrrolate-formoterol (24% lower: rate ratio, 0.76; 95% confidence interval [CI], 0.69 to 0.83; P&lt;0.001) or budesonide-formoterol (13% lower: rate ratio, 0.87; 95% CI, 0.79 to 0.95; P = 0.003). Similarly, the rate was significantly lower with 160 µg-budesonide triple therapy than with glycopyrrolate-formoterol (25% lower: rate ratio, 0.75; 95% CI, 0.69 to 0.83; P&lt;0.001) or budesonide-formoterol (14% lower: rate ratio, 0.86; 95% CI, 0.79 to 0.95; P = 0.002).</p> <ul style="list-style-type: none"> <li>• <b>Eosinophile:</b> (siehe Figure 4 Supplement)</li> <li>• <b>Sicherheit:</b> (siehe Supplement)                     <ul style="list-style-type: none"> <li>- The incidence of any adverse event was similar across the treatment groups (range, 61.7 to 64.5%); the incidence of confirmed pneumonia ranged from 3.5 to 4.5% in the groups that included inhaled glucocorticoid use and was 2.3% in the glycopyrrolate-formoterol group.</li> <li>- The most frequently reported adverse events overall were nasopharyngitis (10.5%), COPD (10.4%), and upper respiratory tract infection (5.6%)</li> </ul> </li> <li>• <b>risk of death from any cause (sekundärer Endpunkt):</b> <ul style="list-style-type: none"> <li>- in 320-µg-budesonide tripletherapy group was 46% lower than that in the glycopyrrolate-formoterol group (28 vs. 49 deaths; hazard ratio, 0.54; 95% CI, 0.34 to 0.87) and 22% lower than that in the</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li><b>Selection bias</b> Randomisierung: <b>low</b> Allocation concealment: <b>low</b></li> <li><b>Performance bias</b> Verblindung von Teilnehmern und Personal: <b>low</b></li> <li><b>Detection bias</b> Verblindung der Ergebnisevaluation: <b>unclear</b></li> <li><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: <b>low</b></li> <li>ITT-Analyse:modifizierte ITT (with the use of on-treatment data only)</li> <li><b>Reporting bias</b> selektive Ergebnisdarstellung: <b>unclear</b></li> <li><b>Andere Biasursachen</b> Baseline imbalance: <b>low</b></li> <li>Interessenkonflikte/ Sponsoring: Funded by AstraZeneca</li> </ul>	<p>Selektiv eingebrachte Literatur</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	severe COPD exacerbations, and time to death from any cause. <ul style="list-style-type: none"> <li>• 26 countries</li> <li>• 52-week, phase 3</li> </ul>	budesonide–formoterol group (28 vs. 34 deaths; hazard ratio, 0.78; 95% CI, 0.47 to 1.30). The risk of death from any cause in the 160- $\mu$ g–budesonide triple-therapy group was lower than that in the glycopyrrolate–formoterol group (39 vs. 49 deaths; hazard ratio, 0.79; 95% CI, 0.52 to 1.20) but higher than that in the budesonide–formoterol group (39 vs. 34 deaths; hazard ratio, 1.13; 95% CI, 0.72 to 1.80)		

## Anhang 9 Evidenztabelle Medizinische Rehabilitation

### Anhang 9.1 Cochrane Reviews Rehabilitation

Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>McCarthy B. Pulmonary rehabilitation for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2015;(2).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003793.pub3/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003793.pub3/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n= 65 eingeschlossene RCTs für Metaanalyse ( n= 3822 eingeschlossene Patient*innen)</li> <li>• <b>Suchzeitraum:</b> current as of 04/2014</li> <li>• <b>Population:</b></li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- participants had COPD</li> <li>- any or all participants were on continuous oxygen</li> </ul> </li> <li>• <b>Ausschlusskriterien:</b> <ul style="list-style-type: none"> <li>- who were mechanically ventilated; or</li> <li>- who had an acute exacerbation within four weeks before commencement of the intervention</li> </ul> </li> <li>• <b>Interventionen:</b> <p><u>Pulmonary rehabilitation</u> (Any in-patient, out-patient, community-based or home-based rehabilitation programme of at least four weeks' duration that included exercise therapy with or without any form of education and/or psychological support delivered to patients with exercise limitation attributable to COPD. We included any exercise therapy that included physical activity considered to be aerobically demanding.) vs. <u>Usual Care</u> (without education or additional interventions)</p> </li> <li>• <b>Primäre Endpunkte:</b> <p><u>Disease-specific health-related quality of life (HRQoL)</u></p> <ul style="list-style-type: none"> <li>- Chronic Respiratory Disease Questionnaire (CRQ)</li> <li>- St. George's Respiratory Questionnaire (SGRQ)</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Functional exercise capacity assessments</li> <li>- Six-minute walk test/distance (6MWT/6MWD)</li> <li>- Incremental shuttle walk test (ISWT)</li> </ul> </li> </ul>	<p>&gt;&gt; This review highlights that pulmonary rehabilitation improves the health-related quality of life of people with COPD. Results strongly support inclusion of pulmonary rehabilitation as part of the management and treatment of patients with COPD.</p> <p><u>QoL - Change in CRQ (dyspnoea)</u> CRQ Questionnaire.(Higher is better and 0.5 unit is an important difference), n=1283 (19 RCTs), <b>GRADE: Moderate</b> Usual care: Median change = 0 units Rehabilitation versus usual care: Mean QoL - change in CRQ (Dyspnoea) in the intervention groups was <b>0.79 units higher</b> (0.56 to 1.03 higher) MD 0.79, 95%CI 0.56 to 1.03; I<sup>2</sup>= 63%</p> <p><u>QoL - Change in CRQ (fatigue)</u> MD 0.68 (95%CI 0.45, 0.92), I<sup>2</sup>= 64%, 19 RCT, n = 1291, <b>GRADE:low</b></p> <p><u>QoL - Change in CRQ (Emotional funtion)</u> MD 0.56 (95%CI 0.34, 0.78), I<sup>2</sup>=58% , 19 RCT, n = 1291, <b>GRADE: nicht angegeben</b></p> <p><u>QoL - Change in CRQ (Mastery)</u> MD 0.71 (95%CI 0.47, 0.95), I<sup>2</sup>=63%,19 RCT, n = 1212, <b>GRADE:low</b></p> <p><u>QoL - Change in SGRQ (total)</u> (Lower is better and 4 units is an important difference), I<sup>2</sup>=59%, n=1146 (19 RCTs), <b>GRADE: Moderate</b> Usual care: Median change = 0.42 units Rehabilitation versus usual care: Mean QOL - change in SGRQ (total) in the intervention groups was <b>6.89 units lower</b> (-6.89 (95%CI -9.26; -4.52)</p> <p><u>Change in maximal exercise</u> (Incremental Shuttle walk test (ISWT)), n=694 (8 RCTs); <b>GRADE: Moderate</b> Usual care: Median change = 1 metre Rehabilitation versus usual care: Mean maximal exercise (incremental shuttle walk test) in the intervention groups was <b>39.77 metres higher</b> (22.38 to 57.15 higher)</p> <p><u>Change in functional exercise capacity</u> (6MWT)), n=1879 (38 RCTs), <b>GRADE: Very low</b> Usual care: Median change = 3.4 metres</p>	<p>AMSTAR-Score: 10/11</p> <p>y-y-y-y-y-y-y-y-n</p>

Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<ul style="list-style-type: none"> <li>◦ Endurance shuttle walk test (ESWT)</li> <li>- Maximal exercise tests</li> <li>◦ Incremental cycle ergometry</li> </ul>	<p>Rehabilitation versus usual care: Mean functional exercise capacity (6MWT)) in the intervention groups was <b>43.93 metres higher</b> (32.64 to 55.21 higher)</p> <p><u>Aussagen des Reviews zu Home-based Rehabilitation:</u></p> <ul style="list-style-type: none"> <li>• Only six studies reported patient-based programmes, three of which were combined with a home-based follow-up component. Thirty-seven studies were hospital out-patient based; eight of these included a home-based element. In all, 21 programmes were community based, 11 of which were entirely home based, and one programme combined community- and home-based components.</li> </ul> <p><u>Rehabilitation versus usual care (subgroup analysis hospital versus community-based pulmonary rehabilitation)</u></p> <ul style="list-style-type: none"> <li>• In total, 39 included studies were considered to have a hospitalbased PR intervention delivered on an in-patient or out-patient basis. A total of 25 studies focused on programmes that were delivered in the community at community centres or in individuals' homes. One study had both a community-based and an out-patient- based intervention group, so it was excluded from the subgroup analysis (Mendes De Oliveira 2010).</li> <li>• In the subgroup analysis for the CRQ domain outcomes, the 'community' subgroup included nine studies and the 'hospital group' included 10 studies. For SGRQ outcomes, the community subgroup included nine studies and the hospital subgroup included 10 studies.</li> <li>• Evidence suggested a significant difference in treatment effect between subgroups for all domains of the CRQ, with higher mean values, on average, in the PR group in hospital than in the community- based group (Analysis 2.1; Analysis 2.2; Analysis 2.3; Analysis 2.4). No subgroup differences were reported for any of the SGRQ domains (Analysis 2.5; Analysis 2.6; Analysis 2.7; Analysis 2.8).</li> </ul> <p>&gt;&gt; hier: homebased &amp; community-based Therapien zusammen betrachtet; kein direkter Vergleich.</p>	
<p>Puhan MA. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2016;(12).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005305.pub4/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005305.pub4/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=20 eingeschlossene RCTs für Metaanalyse ( n= 1477 eingeschlossene Patient*innen)</li> <li>• <b>Suchzeitraum:</b> current as of 10/2015; handsearches up to 4/016</li> <li>• <b>Population:</b> Patient*innen mit COPD nach Exazerbation</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- Participants with COPD after inpatient or out-patient care for acute exacerbation. This review required that more than 90% of study participants were patients with COPD.</li> <li>- The rehabilitation programme must commence</li> </ul> </li> </ul>	<p><u>Hospital readmission</u> (to end of follow-up, median 9 months), high risk for 1-year readmission, n=810 (8 RCTs), <b>GRADE: Moderate</b>                  Control: 500 per 1000                  Rehabilitation: 306 per 1000 (174 to 476)                  -reduced hospital readmissions (OR 0.44, 95% CI 0.21 to 0.91; I2 = 77%).</p> <p><u>Mortality</u> (to end of follow-up, median 12 months), High risk for 1-year mortality, n=670 (6 RCTs), <b>GRADE: Low</b>                  Control: 150 per 1000                  Rehabilitation: 107 per 1000 (47 to 228)                  (Comment: None of the trials used mortality as a primary outcome, and none of the trials was powered to detect a meaningful effect of rehabilitation on mortality)</p>	<p>AMSTAR-Score: 11/11</p> <p>y-y-y-y-y-y-y-y-y-y</p>



Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<p>immediately after initiation of exacerbation treatment or within three weeks of initiation of exacerbation treatment.</p> <ul style="list-style-type: none"> <li>• <b>Interventionen:</b> Any inpatient and/or outpatient pulmonary rehabilitation programme, including at least physical exercise (endurance or strength exercise, or both), delivered to patients who have received acute care for an exacerbation of COPD vs. usual care control groups</li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Hospital admissions (at least one hospital admission during follow-up)</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- HRQL (SF-36, CRQ, SGRQ)</li> <li>- Exacerbation rates (after discharge)</li> <li>- Number of outpatient visits</li> <li>- Length of readmissions</li> <li>- Mortality</li> <li>- Functional exercise capacity as measured by two-, three-, four-, six- or 12-minute-walk test, or by a shuttle walk test</li> <li>- Maximal exercise capacity</li> <li>- Exercise endurance</li> <li>- Withdrawals</li> <li>- Adverse events</li> <li>- Costs</li> </ul> </li> </ul>	<p>- OR 0.68, 95% CI 0.28 to 1.67), I2 = 59%.</p> <p><u>health-related quality of life (SGRQ)</u>, n=1003 (8 RCTs), <b>GRADE: High</b>                  Control: SGRQ score at beginning of rehabilitation was typically around 65                  Rehabilitation: Mean change from baseline in SGRQ Total score in the intervention group was <b>7.80 units lower</b> (95%CI -12.12 to -3.47)                  - SGRQ total score (MD) -7.80, 95% CI -12.12 to -3.47; I2 = 64%.</p> <p><u>Change from baseline in 6-minute walking test</u> (to end of follow-up, median 3 months). n=819 (13 RCTs), <b>GRADE: High</b>                  Control: 6-Minute walking distance at beginning of rehabilitation was typically around 300 metres                  Rehabilitation: Mean change from baseline in 6-minute walking test in the intervention group was <b>62.38 metres more</b> (95%CI 38.45 to 86.31)</p> <p><u>Adverse events</u>                  Five studies involving 278 participants explicitly recorded adverse events, four studies reported no adverse events during rehabilitation programmes and one study reported one serious event.</p> <p><b>&gt;&gt; Quality of life and exercise capacity were improved by rehabilitation, and the effect was substantially larger than the minimal important difference. Results for hospital readmissions and mortality were diverse, with some studies showing that pulmonary rehabilitation reduced hospital admissions and mortality compared with usual community care (no rehabilitation), and other studies not showing such effects.</b></p>	
<p>McCabe C. Computer and mobile technology interventions for self-management in chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2017;(5).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/">http://onlinelibrary.wiley.com/doi/10.1002/</a></p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=3 eingeschlossene RCTs für Metaanalyse ( n=557 eingeschlossene Patient*innen)</li> <li>• <b>Suchzeitraum:</b> 11/2016</li> <li>• <b>Population:</b> Patient*innen mit COPD (alle Schweregrade)</li> <li>• <b>Einschlusskriterien:</b> adult &gt; 18y</li> <li>- We included participants who live at home or in a non-healthcare residential setting (sheltered</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b> <ul style="list-style-type: none"> <li>- mean age: 64 years;</li> <li>- men=307 (64.9%)</li> <li>- n= 319 received smart technology to support self-management, and n=238 received face-to-face verbal/written or digital information and education about self-management</li> </ul> </li> <li><u>Hospital admission</u>, n=239 (1 RCT), <b>GRADE: Low</b> <ul style="list-style-type: none"> <li>- Hospital admission not reported at 4 months. At 12 months. smart technology did not significantly impact the number of hospital admissions</li> </ul> </li> </ul>	<p>AMSTAR-Score: 9/11</p> <p>y-n-y-y-y-y-y-y-y-n</p>

Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
14651858.CD011425.pub2/abstract	<p>housing) and who use, or have access to, technology, for example, personal computer, tablet, or smart phone, to help them manage their illness.</p> <p><b>• Interventionen:</b></p> <ul style="list-style-type: none"> <li>- remote and Web 2.0-based interventions delivered via technologies that give patients access to ehealth information to change behaviours towards self-management of COPD. These technologies include personal computers (PCs) and applications (apps) for mobile technology such as iPad, Android tablets, smart phones, and Skype.</li> </ul> <p><b>vs.</b></p> <ul style="list-style-type: none"> <li>- face-to-face and/or hard copy/digital documentary educational/self management support</li> </ul> <p><b>• Primäre Endpunkte:</b></p> <ul style="list-style-type: none"> <li>- Hospital admissions</li> <li>- Acute exacerbations requiring general practitioner (GP) visit or additional treatment, or both</li> <li>- Health-related quality of life (HRQoL)</li> </ul> <p><b>• Sekundäre Endpunkte:</b></p> <ul style="list-style-type: none"> <li>- Self-efficacy</li> <li>- Cost-effectiveness</li> <li>- Functional capacity</li> <li>- Lung function</li> <li>- Anxiety and depression</li> <li>- Sustained behaviour change (smoking cessation and increased physical activity)</li> </ul>	<p><u>Acute exacerbations</u> requiring general practitioner (GP) visit and/ or additional treatment, n= 239 (1 RCT), <b>GRADE: Low</b></p> <ul style="list-style-type: none"> <li>- Acute exacerbations were not reported at 4 months. At 12 months, smart technology did not significantly impact the number of acute exacerbations</li> </ul> <p><u>Health-related quality of life</u> (HRQoL) assessed with SGRQ and CCQ, n=472 (3 RCTs), <b>GRADE: Low</b></p> <ul style="list-style-type: none"> <li>- Risk with face- to- face/ digital and/or written support: Mean HRQoL ranged across control groups from 0.08 to 1.686</li> <li>- Risk with smart technology: SMD in HRQoL in the intervention group was <b>0.22 lower</b> (0.44 to 0.03 lower) (Lower scores on both SGRQ and CCQ indicate better HRQoL.)</li> </ul> <p><u>Self-efficacy</u> was not measured in any of the included studies</p> <p><u>Functional capacity</u> (6- minute walking test or similar): None of the included studies measured this outcome</p> <p>&gt;&gt; People who received smart technology showed greater improvement in self management and quality of life and increased physical activity compared with people who received face-to-face/digital and/or written support over a four-week to six-month period. Also, hospital admissions and exacerbations of COPD did not differ between those who used smart technology and those who did not. Only one study provided information about people who stopped smoking and reported no differences between groups.</p>	
McLean S. Telehealthcare for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2011;(7).	<p><b>• Body of Evidence:</b> n=10 RCTs eingeschlossen (n=1004 patients)</p> <p><b>• Suchzeitraum:</b> up to January 2010</p> <p><b>• Population:</b> participants with COPD</p> <p><b>• Einschlusskriterien:</b></p> <ul style="list-style-type: none"> <li>- COPD, as diagnosed by a clinician</li> <li>- with no exclusions on the basis of age, gender, ethnicity or language spoken</li> </ul>	<p><b>Total exacerbations (2 studies)</b></p> <ul style="list-style-type: none"> <li>- Bourbeau 2003 (telephone system used): 362 acute exacerbations of COPD in the control group (n = 95) and 299 exacerbations in the intervention group (n = 96) over a 12 month period. (p = 0.06)</li> <li>- Vitacca 2009 (used Internet; n=240 participants,n=101 with COPD): mean number of exacerbations per month was significantly higher in controls than in the telehealthcare group (0.78±0.77 and 0.23±0.38; p&lt;0.0001).</li> </ul>	AMSTAR-Score: 9/11 y-n-y-y-y-y-y-y-ca

Referenz	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<ul style="list-style-type: none"> <li>• <b>Ausschlusskriterien:</b> <ul style="list-style-type: none"> <li>- people with asthma only</li> </ul> </li> <li>• <b>Interventionen:</b> telehealthcare vs. usual face-to-face care                             <ol style="list-style-type: none"> <li>1. Video or telephone links with healthcare professionals in real time or using store and forward technologies.</li> <li>2. Systems of care using Internet-based telecommunication with healthcare professionals.</li> <li>3. Systems of care using both wired and wireless telemetry for telemonitoring of spirometry (FEV1/FVC), respiratory rate, blood pressure and oxygen saturations involving feedback to the patient, which has been processed or a thorised by a healthcare professional.</li> <li>4. Other systems of remote healthcare.</li> <li>5. Complex intervention studies if it is possible to tease out the individual tele-healthcare elements.</li> <li>6. Interventions in all settings and from all types of healthcare provider.</li> </ol> </li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Total exacerbations</li> <li>- Quality of life (e.g. SGRQ)</li> <li>- Emergency Department visits</li> <li>- Hospitalisations</li> <li>- Deaths</li> </ul> </li> <li>• <b>Sekundäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- FEV1; FVC; Patient satisfaction; Study withdrawal; Costs; Cost effectiveness</li> </ul> </li> </ul>	<p><b>Quality of life (SGRQ)</b></p> <ul style="list-style-type: none"> <li>- Telehealthcare was associated with a clinically significant increase in quality of life</li> <li>--&gt; mean difference -6.57 (95%CI -13.62 to 0.48; n=2 studies, 253 participants ; minimum clinically significant difference is a change of -4.0) (Wide CI)</li> <li>- QoL with CRQ assessed: Nguyen 2008 dyspnoea management(face to face vs. electronic web-networked interface)--&gt; minimal clinically important difference is 0.5 (CRQ used)</li> </ul> <p><b>Emergency department visits</b></p> <ul style="list-style-type: none"> <li>- Telehealthcare showed a significant reduction in the number of patients with one or more emergency department attendances over 12 months;</li> <li>--&gt; OR 0.27 (95% CI 0.11 to 0.66; n=3 trials, n=449 participants)</li> </ul> <p><b>Hospitalisations</b></p> <ul style="list-style-type: none"> <li>- having one or more admissions to hospital over 12 months:</li> <li>--&gt; OR 0.46 (95% CI 0.33 to 0.65, n=4 trials with 604 participants)</li> </ul> <p><b>Death</b></p> <p>There was no significant difference in the OR for deaths over 12 months for the telehealthcare group as compared to the usual care group:</p> <p>--&gt; OR 1.05 (95% CI 0.63 to 1.75), n=3 trials, 503 participants</p> <p>&gt;&gt; verschiedene Arten von Telehealthcare in den verschiedenen Studien, jedoch dennoch gepoolt!</p>	

### Anhang 9.2 Gerätebasiertes Training

Zitat	Studiencharakteristika	Interventionen	Studienergebnisse
Duruturk N. A comparison of calisthenic and cycle exercise training in	<ul style="list-style-type: none"> <li>• Studientyp: RCT</li> <li>• 6-Wochen Programm; Assesment at baseline + after intervention</li> </ul>	<ul style="list-style-type: none"> <li>• Setting: evtl. Rehabilitation; in a physical therapy clinic under supervision of a physiotherapist</li> <li>• formal education session was provided to all participants before starting the interventions</li> </ul>	<ul style="list-style-type: none"> <li>• Baseline-Patientencharakteristika: hinsichtlich Alter, Gewicht, Lungenfunktion weitestgehend ausgeglichen; Geschlecht: etwas mehr Frauen in Cycle exercise group (4/11), als in den anderen Gruppen (calisthenic 1/13; control 2/11)</li> </ul>

Zitat	Studiencharakteristika	Interventionen	Studienergebnisse
<p>chronic obstructive pulmonary disease patients: A randomized controlled trial. Expert Rev Respir Med 2016; 10(1):99–108. <a href="https://www.ncbi.nlm.nih.gov/pubmed/26616764">https://www.ncbi.nlm.nih.gov/pubmed/26616764</a>.</p>	<ul style="list-style-type: none"> <li>Population: n= 47 patients with COPD; Studienende n=42</li> <li><b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>diagnosis of stage II or II COPD according to GOLD</li> <li>clinical stable patient</li> </ul> </li> <li><b>Ausschlusskriterien</b> <ul style="list-style-type: none"> <li>patients clinically unstable</li> <li>CVD or malignant disorders</li> <li>non-compliant with treatment or unable to perform lung function testing, cardiopulmonary exercise testing, or exercise training</li> </ul> </li> <li><b>primärer Endpunkt</b> Quality of life (Saint George Respiratory Questionnaire)</li> <li><b>sekundäre Endpunkte</b> pulmonary functions, cardiopulmonary exercise testing, Fitness Testing, and Hospital Anxiety-Depression, Modified Medical Research Council Dyspnea, Fatigue Severity, Fatigue Impact Scale</li> <li>Studienzeitraum: keine Angaben</li> <li>Türkei</li> </ul>	<ul style="list-style-type: none"> <li>6-week intervention period</li> <li><b>3 randomisierte Gruppen:</b> <ul style="list-style-type: none"> <li>Calisthenic (3x/Woche für 6 Wochen)                             <ul style="list-style-type: none"> <li>included strengthening and stretching of lower and upper extremity muscles (siehe S. 2 [100] der Publikation); 20-45 Minuten; kontinuierliche Steigerung der Wiederholungen</li> </ul> </li> <li>Cycle ergometer exercise (3x/Woche für 6 Wochen)                             <ul style="list-style-type: none"> <li>50-70% of VO2max obtained from cycle ergometer testing; 20-30 Minuten; kontinuierliche Steigerung der Intensität</li> </ul> </li> <li>Control group: no exercise (nur Schulung und Weiterführen ihrer medikamentösen Behandlung)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li><b>Ergebnisse primärer Endpunkt: SGRQ (total) (mean ± SD)</b> Cycle exercise group: baseline: 49,3 ± 19,6 6 weeks: 28,7 ± 12,9 difference: -20,7 ± 11,4  Calisthenic exercise group: baseline: 49,9 ± 19,6 6 week: 26,7 ± 15,9 difference: -22,6 ± 10,4</li> <li><b>ausgewählte weitere Ergebnisse: 6MWDt (m) (mean ± SD)</b> Cycle exercise group: baseline: 448,7 ± 60,9 6 weeks: 514,2 ± 59,3 difference: 65,4 ± 21,7  Calisthenic exercise group: baseline: 395,6 ± 98,2 6 week: 482,3 ± 65,4 difference: 86,7 ± 44,5</li> <li>Physical fitness, QoL, anxiety-depression, dyspnea and fagtigue changed significantly in exercise groups</li> <li>no between-group differences; p=0,66 für SRGQ total; p=0,31 für 6MWDt</li> <li>no significant improvements in control group</li> <li>&gt;&gt;&gt; main finding: cycle ergometer and calisthenic exercise training were similarly effective in improving quality of life, exercise capacity, physical fitness psychosocial status and reducing respiratory symptoms in patients with COPD</li> </ul>

**Selection bias**

Randomisierung: gering

Allocation concealment: gering

**Performance bias**

Verblindung von Teilnehmern und Personal: nicht anwendbar

**Detection bias**

Verblindung der Ergebnisevaluation: unklar

**Attrition bias**

Zitat	Studiencharakteristika	Interventionen	Studienergebnisse
<p>Verlust von Studienteilnehmern/ fehlende Daten: gering                      ITT-Analyse: keine ITT-Analyse durchgeführt;  <b>Reporting bias</b>                      selektive Ergebnisdarstellung: unklar                      Andere Biasursachen                      Kommentar: Vertrauenswürdigkeit der Ergebnisdarstellung: Baseline-Daten für SGRQ (total) sind für beide Interventionsgruppen exakt gleich.                      Interessenkonflikte/ Sponsoring: funded by Baskent University; writing assistance by EDANZ editing service</p>			
<p>Baseline-Daten für SGRQ (total) sind für beide Interventionsgruppen exakt gleich.                      Frage: ist dies eher unwahrscheinlich? Vertrauenswürdig?</p>			

Zitat	Studiencharakteristika	Interventionen	Studienergebnisse
<p>Greulich T. A randomized clinical trial to assess the influence of a three months training program (gym-based individualized vs. calisthenics-based non-individualized) in COPD-patients. Respir Res 2014; 15:36. <a href="https://www.ncbi.nlm.nih.gov/pub-med/24666558">https://www.ncbi.nlm.nih.gov/pub-med/24666558</a>.</p>	<ul style="list-style-type: none"> <li>• <b>Studientyp:</b> RCT</li> <li>• <b>Assessments:</b> At the beginning and after three months</li> <li>• <b>Population:</b> patients with mild to very severe COPD (n=61 randomized; n=34 patients completed the study)</li> <li>• <b>Einschlusskriterien:</b> stable COPD; diagnostic criteria published by GOLD</li> <li>• <b>Endpunkte</b> (keine Unterscheidung zwischen primär und sekundär)                             <ul style="list-style-type: none"> <li>- 6-minute walking test (6-MWT)</li> <li>- health-related quality of life using SGRQ and CAT</li> <li>- ultrasound measurement of M. rectus femoris cross-sectional area (M. rect. fem.)</li> <li>- serum level measurements of myokines and inflammatory markers</li> </ul> </li> <li>• Studienzeitraum: 01/2009 - 12/2012</li> <li>• Deutschland</li> </ul>	<p>Setting: outpatient</p> <ul style="list-style-type: none"> <li>• Individualisiertes Gerätetraining vs. nicht-individualisierte Calisthenics</li> <li>• 3 - 4 months ambulatory training program ; both low-intensity training approaches</li> <li>• jeweils 1x/Woche 1 Stunde; at least 12 trainings sessions</li> </ul> <p>“Individualized Training” (IT):</p> <ul style="list-style-type: none"> <li>- patients participated in a weekly individualized gym-based outpatient exercise training.</li> <li>- included all components of exercise training suggested by ACCP/AACVPR clinical practice guidelines.</li> <li>- Each patient received an individual training schedule at the beginning of the training period based on his maximal force and endurance time in different approaches</li> <li>- special focus on the following muscle groups: thigh muscles (especially the quadriceps femoris), lateral hip and trunk stabilizers, anterior shoulder muscles, rotator cuff muscles, different muscles of the upper extremities and dorsal trunk and scapular stabilizers</li> <li>- Endurance training was done on the ergometer</li> </ul> <p>“Non-individualized Training” (NT):</p> <ul style="list-style-type: none"> <li>- patients participated once weekly as part of a group in different forms of exercise (calisthenics).</li> <li>- training unit was divided into three parts: warm-up (free movements, stretching) for ten minutes; the main part was a forty minute training which included collectively performed exercises like ball games, stepping, thera-band training</li> </ul>	<ul style="list-style-type: none"> <li>• Baseline-Patientencharakteristika: hinsichtlich Geschlecht, Alter, Gewicht, Schwere der COPD weitestgehend ausgeglichen (no statistical significant differences)</li> <li>- Comorbidities: Patients in all groups reported a high number of comorbidities; no statistical significant differences between groups</li> </ul> <p><b>exercise capacity (6-MWT)</b></p> <ul style="list-style-type: none"> <li>- IT group: significant change of the walking distance (M1 = 407 ± 105.44 m, M2 = 439.37 ± 122.89 m; p = 0.012)</li> <li>- NT group: no significant change was observed (M1 = 411.79 ± 64.74 m, M2 = 427.5 ± 84.57 m; p = 0.116)</li> <li>- No significant between group differences could be observed.</li> </ul> <p><b>Quality of life</b></p> <p>We were not able to detect significant differences of SGRQ and CAT between measurement 1 and 2 in any of the groups. (keine weiteren Daten hierzu angegeben)</p> <p>When considering only patients that entered the training period we observed a differential dropout, with significantly more subjects stopping NT than IT (13/27 vs. 5/25; p = 0.04). Assessing possible reasons for this phenomenon, the main causes were not significantly different between both groups [...] In summary, patients with a worse baseline condition had a higher probability to drop out.</p>

Zitat	Studiencharakteristika	Interventionen	Studienergebnisse
		and dumbbells. The training period was finalized by a ten minute relaxing exercises period. - Disease-specific techniques (body positions, different breath and cough techniques, like the pursed lips breathing) were communicated to the group.  • in both group: same physiotherapist • All patients were encouraged to perform domestic workout. However, it was not systematically assessed, to which extent this recommendation was followed	
<p><b>Selection bias</b>  <b>Randomisierung:</b> gering  <b>Allocation concealment:</b> gering.  <b>Performance bias</b>                      Verblindung von Teilnehmern und Personal: nicht anwendbar  <b>Detection bias</b>                      Verblindung der Ergebnisevaluation: gering  <b>Attrition bias</b>                      Verlust von Studienteilnehmern/ fehlende Daten: hoch                      ITT-Analyse: : keine ITT-Analyse durchgeführt;  <b>Reporting bias</b>                      selektive Ergebnisdarstellung: unklar  <b>Andere Biasursachen</b>                      Baseline imbalance: gering                      Interessenkonflikte/ Sponsoring: Teilweise durch pharmakol. Unternehmen gesponsert (The project was supported by the German Centre for Lung Research (DZL). The study has been funded partially by GSK. No further conflict of interest has to be acknowledged.)</p> <p>Setting: outpatient training program (3 months ambulatory training program)</p>			

Zitat	Studiencharakteristika	Interventionen	Studienergebnisse
Normandin EA. An evaluation of two approaches to exercise conditioning in pulmonary rehabilitation. Chest 2002; 121(4):1085–91.	<ul style="list-style-type: none"> <li>• Studientyp: prospective, randomized, unblinded, 8-week-trial</li> <li>• Assessments: before/during the first week of PR + immediately after the 8-week program</li> <li>• Population: n=40 patients with COPD referred for pulmonary rehabilitation</li> <li>• Ein- und Ausschlusskriterien:</li> </ul>	Setting: hospital-based outpatient pulmonary rehabilitation program  • compared the short-term effectiveness of a high-intensity, lower extremity endurance program vs. a low-intensity, multicomponent calisthenics program	<ul style="list-style-type: none"> <li>• Baseline-Patientencharakteristika: hinsichtlich Geschlecht, Alter, Gewicht weitestgehend ausgeglichen</li> <li>Lungenfunktion + CRQ at baseline: Baseline FEV1 was significantly lower in the high-intensity group (p=0,03), and the CRQ total score tended to be higher in this group (p=0,16)</li> <li>Patients in the high-intensity group showed greater increases in treadmill endurance and greater reductions in exertional dyspnea, whereas those in the low-intensity group showed greater increases in arm-endurance testing. Both groups had</li> </ul>

Zitat	Studiencharakteristika	Interventionen	Studienergebnisse
<p><a href="https://www.ncbi.nlm.nih.gov/pubmed/11948036">https://www.ncbi.nlm.nih.gov/pubmed/11948036</a>.</p>	<p>1) symptomatic COPD                      2) ability to perform aerobic treadmill and stationary bicycle training and peripheral muscle training                      3) absence of a significant comorbid disease                      4) no formal PR within the past 12 months</p> <p>• <b>primärer Endpunkt:</b> health status (measured using Chronic Respiratory Disease Questionnaire; CRQ)                      • <b>sekundäre Endpunkte (Auswahl):</b> exertional dyspnea, treadmill endurance time, number of sit-to-stand repetitions and arm lifts in 1 minute, overall dyspnea, questionnaire-rated functional status</p> <p>• Studienzeitraum: nicht angegeben                      • USA</p>	<ul style="list-style-type: none"> <li>• before exercising: all patients received education</li> <li>• high-intensity group trained predominantly on the stationary bicycle and treadmill, with a goal of exercising at <math>\geq 80\%</math> of maximal level determined from incremental testing for 30 minutes per session</li> <li>• low-intensity group performed predominantly classroom exercises for approximately 30 minutes per session</li> <li>• beide Gruppen trainierten 2x/Woche für insgesamt 8 Wochen</li> </ul>	<p>similar improvements in overall dyspnea, functional performance, and health status.</p> <p><b>health status</b>                      both groups showed significant improvements in CRQ scores after rehabilitation (no significant group differences in change)                      - high-intensity group increased <math>11,5 \pm 2,9U</math> (<math>p &lt; 0,001</math> vs. baseline)                      - low-intensity group increased <math>18,8 \pm 2,9U</math> (<math>p &lt; 0,001</math> vs. baseline)                      - 8/20 patients (40%) in high-intensity group had clinically meaningful changes in CRQ vs 14/20 patients (70%) in the low-intensity group</p> <p><b>functional performance (questionnaire)</b>                      PFSS function and emotion scores both showed significant improvements from baseline (no significant group differences in change)                      - <b>high-intensity group:</b> PFSS function <math>2,8 \pm 0,7 U</math> ; <math>p &lt; 0,001</math>                      PFSS emotion: <math>3,1 \pm 1,2</math>; <math>p = 0,01</math>                      - <b>low-intensity group:</b> PFSS function: <math>3,9 \pm 0,7</math>; <math>p &lt; 0,001</math>                      PFSS emotion: <math>5,8 \pm 1,2</math>; <math>p &lt; 0,001</math></p> <p><b>Overall dyspnea (TDI)</b>                      - high-intensity group: <math>2,9 \pm 0,5</math>; <math>p &lt; 0,001</math>                      - low-intensity group: <math>3,2 \pm 0,5</math>; <math>p &lt; 0,001</math></p>
<p><b>Selection bias</b>                      Randomisierung: unklar                      Allocation concealment: unklar</p> <p><b>Performance bias</b>                      Verblindung von Teilnehmern und Personal: nicht anwendbar</p> <p><b>Detection bias</b>                      Verblindung der Ergebnisevaluation: gering (für primären Endpunkt)</p> <p><b>Attrition bias</b>                      Verlust von Studienteilnehmern/ fehlende Daten: unklar                      ITT-Analyse: keine ITT-Analyse durchgeführt;</p> <p><b>Reporting bias</b>                      selektive Ergebnisdarstellung: unklar</p> <p><b>Andere Biasursachen</b>                      Baseline imbalance: unklar                      Interessenkonflikte/ Sponsoring: Funding beschrieben (funded in part by [...] Hoffman foundation)</p> <p>Setting: hospital-based outpatient pulmonary rehabilitation program</p>			

Zitat	Studiencharakteristika	Interventionen	Studienergebnisse
<p>Probst VS. Effects of 2 exercise training programs on physical activity in daily life in patients with COPD. <i>Respir Care</i> 2011; 56(11):1799–807. <a href="https://www.ncbi.nlm.nih.gov/pubmed/22035826">https://www.ncbi.nlm.nih.gov/pubmed/22035826</a>.</p>	<ul style="list-style-type: none"> <li>• Studientyp: prospective randomized trial</li> <li>• Studiendesign: keine Angaben zur Randomisierung</li> <li>• Population: n=40 Patient*innen mit COPD; (n=63 consecutive patients initially included)</li> <li>• <b>Einschlusskriterien:</b> <ul style="list-style-type: none"> <li>- COPD diagnosis according GOLD criteria;</li> <li>- stable condition (no exacerbations or infections in the preceding 3 months);</li> <li>- no severe/unstable cardiac disease (eg, left-ventricular failure or atrial fibrillation);</li> <li>- no comorbidities that might influence the execution of the tests and/or the exercise training programs;</li> <li>- had not attended a pulmonary rehabilitation program in the last year;</li> <li>- able to attend the out-patient clinic 3 times per week.</li> </ul> </li> <li>&gt;&gt; Pharmacologic treatment was not changed during the course of the study</li> <li>• <b>primärer Endpunkt:</b> effects on physical activity in daily life</li> <li>• <b>sekundäre Endpunkte:</b> exercise capacity, (respiratory and peripheral) muscle force, health-related quality of life, functional status</li> <li>• Studienzeitraum: July 2006 to July 2009</li> <li>• Brasilien</li> </ul>	<ul style="list-style-type: none"> <li>• <u>Setting:</u> out-patient clinic</li> <li>high-intensity whole-body endurance and-strength program vs. low-intensity calisthenics-and-breathing-exercises program</li> <li>&gt;&gt; Both groups: 3 sessions per week for 12 weeks</li> <li>&gt;&gt; Activity monitoring in daily life was performed with 2 brands of motion sensor: DynaPort Activity Monitor and SenseWear multisensor</li> <li>&gt;&gt; Assesment 1x before and 1x after exercise programs</li> <li><u>The low-intensity calisthenics-and-breathing program</u> consists of 5 sets of exercises: <ul style="list-style-type: none"> <li>- breathing exercises (diaphragmatic breathing and pursed-lips breathing)</li> <li>- strengthening of the abdominal muscles (crunches)</li> <li>- calisthenics (trunk rotation and flexion, associated with pursed lips breathing and prolonged expiration)</li> </ul> </li> <li>&gt;&gt; Exercises were performed in various body positions: supine, side-lying, sitting, kneeling, and standing. Each set consisted of 12 different exercises, repeated 15 times each.</li> <li><u>The high-intensity whole-body endurance and strength exercise training</u> included: <ul style="list-style-type: none"> <li>- cycling ergometry: training intensity was initially set at 60% of the initial maximum work rate</li> <li>- treadmill walking: training intensity was initially set at 75% of the average walking speed during the baseline 6-min walk test</li> <li>- strength training for the quadriceps, biceps, and triceps muscle groups: training intensity was initially set at 70% of the baseline one-repetition maximum test</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>• hinsichtlich Geschlecht, Alter, Gewicht, Lungenfunktion, Rauchstatus weitestgehend ausgeglichen</li> <li>• <u>Ergebnisse primärer Endpunkt (effects on physical activity in daily life)</u> <b>Time spent standing, sitting, and lying and energy expenditure</b> in daily life were not significantly altered in either group. <ul style="list-style-type: none"> <li><u>Time spent standing (min)</u> <ul style="list-style-type: none"> <li>niedrige Intensität: 270 ± 139</li> <li>hohe Intensität: 248 ± 95</li> </ul> </li> <li><u>Time spent sitting (min)</u> <ul style="list-style-type: none"> <li>niedrige Intensität: 283 ± 121</li> <li>hohe Intensität: 296 ± 91</li> </ul> </li> <li><u>Time spent lying (min)</u> <ul style="list-style-type: none"> <li>niedrige Intensität: 108 ± 100</li> <li>hohe Intensität: 113 ± 101</li> </ul> </li> <li><u>energy expenditure (kcal)</u> <ul style="list-style-type: none"> <li>niedrige Intensität: 1,331 ± 596</li> <li>hohe Intensität: 1,295 ± 635</li> </ul> </li> </ul> </li> <li>In <b>time spent walking</b>, the endurance-and-strength group had no significant change, whereas a reduction was observed in the calisthenics-and-breathing group.</li> <li><u>weitere Ergebnisse</u> <ul style="list-style-type: none"> <li>- <b>Exercise capacity and muscle force</b> significantly improved only in the endurance-and-strength group. (p=0.02 )</li> <li>- The change in the endurance-and-strength-training group was significantly larger than that in the calisthenics-and-breathing-exercises group (p=0.04) for: Maximum work load; One-Repetition Maximum Strength Tests (Table 3)</li> <li>- <b>Health-related quality of life and functional status</b> improved significantly in both groups.</li> <li>- functional status assessed with <ul style="list-style-type: none"> <li>&gt; London Chest Activity of Daily Living Scale total score: only the endurance-and-strength group showed significant improvement</li> <li>&gt; Pulmonary Functional Scale and Dyspnea Questionnaire: (dyspnea and fatigue domains) showed significant improvements only in the calisthenics-and-breathing group (Table 4)</li> </ul> </li> </ul> </li> <li>• <u>Subgruppenanalysen</u> <ul style="list-style-type: none"> <li>In both groups, the subgroups of patients who dropped-out were not significantly different from the subgroups that completed the exercise programs,</li> </ul> </li> </ul>



Zitat	Studiencharakteristika	Interventionen	Studienergebnisse
			<p>except in the 6-min walk test in the calisthenics-and-breathing group. 6-min walk distance was greater in the drop-out group (median 496 m, IQR 460–560 m, vs 420 m, IQR 351– 468 m, P = 0.006).</p> <p>• <b>Sicherheit:</b> No patients had hypoxemia at rest, but 10 patients used oxygen during exercise throughout the endurance-and strength program, due to desaturation during exertion, whereas no patients in the calisthenics-and-breathing group needed supplemental oxygen during the training.</p>
<p><b>Selection bias</b>                      Randomisierung: unklar                      Allocation concealment: unklar</p> <p><b>Performance bias</b>                      Verblindung von Teilnehmern und Personal: nicht anwendbar</p> <p><b>Detection bias</b>                      Verblindung der Ergebnisevaluation: unklar</p> <p><b>Attrition bias</b>                      Verlust von Studienteilnehmern/ fehlende Daten: gering                      ITT-Analyse: unklar</p> <p><b>Reporting bias</b>                      selektive Ergebnisdarstellung: unklar</p> <p><b>Andere Biasursachen</b>                      Baseline imbalance: gering                      Interessenkonflikte/ Sponsoring: CoI wurden beschrieben</p> <p>Setting: out-patient clinic</p>			

### Anhang 9.3 Telemedizin

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Hong Y. Effectiveness of tele-monitoring by patient severity and intervention type in chronic obstructive pulmonary disease patients: A systematic review and meta-analysis. Int J Nurs Stud 2019;</p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> to analyze the effect of tele-monitoring on chronic obstructive pulmonary disease patients and performed subgroup analysis by patient severity and intervention type.</li> <li>• <b>Suchzeitraum:</b> up to April 2017</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b></li> </ul>	<ul style="list-style-type: none"> <li>- 15 studies used tele-monitoring only</li> <li>- 4 studies used integrated tele-monitoring (pure control = exercise or education was not applied to control group)</li> <li>- 8 studies used integrated tele-monitoring (not pure control=received some degree of chronic obstructive pulmonary disease education or exercise additionally)</li> <li>• <b>Emergency room visits (n=11 studies)</b></li> </ul>	<p>AMSTAR-II:                      - critically low</p>	

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
92:1–15. <a href="https://www.ncbi.nlm.nih.gov/pubmed/30690162">https://www.ncbi.nlm.nih.gov/pubmed/30690162</a> .	<p>- COPD; RCT; Intervention: telemonitoring; outcome measures: QoL, hospitalization; emergency room visits, mortality, length of stay, readmission, exacerbations, outpatient visits</p> <p>- n=27 RCTs eingeschlossen</p> <p>• <b>Interventionen:</b> - tele-monitoring only - integrated tele-monitoring: such as the delivery of self-management education or teleconsultation by phone in addition to tele-monitoring of vital sign and systems</p> <p>• <b>Vergleich:</b> usual care</p>	<p>tele-monitoring (alle) reduced the emergency room visits (risk ratio 0.63, 95% confidence interval 0.55-0.72; I<sup>2</sup>=69%;)</p> <p>- subgroup analysis of patient severity showed that tele-monitoring more effectively reduced emergency room visits in patients with severe (risk ratio 0.48, 95% confidence interval 0.31-0.74) vs. moderate disease (risk ratio 1.28, 95% confidence interval 0.61-2.69)</p> <p>- Tele-monitoring only (p &lt; 0.01, RR=0.65, 95% CI 0.55- 0.76, I<sup>2</sup>=72%) and integrated tele-monitoring (p &lt; 0.01, RR =0.42, 95% CI 0.28-0.62, I<sup>2</sup>= 65%) significantly reduced emergency room visits.</p> <p>• <b>Hospitalization (n=12 studies)</b> tele-monitoring (alle) reduced hospitalizations (risk ratio 0.88, 95% confidence interval 0.80-0.97)</p> <p>- subgroup analysis of patient severity (severe vs. moderate) showed that tele-monitoring more effectively reduced hospitalizations (risk ratio 0.92, 95% confidence interval 0.82-1.02; risk ratio 1.24, 95% confidence interval 0.57-2.70, retrospectively)</p> <p>- Tele-monitoring only reduced hospitalizations but this was not statistically significant (p=0.13, RR=0.92, 95% CI 0.82-1.03, I<sup>2</sup>=36%). On the other hand, integrated tele-monitoring did significantly reduce hospitalizations (p=0.03, RR-0.79, 95% CI 0.64 to 0.98, I<sup>2</sup>=26%)</p> <p>• <b>QoI (n=4 studies)</b> The mental health quality of life score (mean difference 3.06, 95% confidence interval 2.15-3.98) showed more improved quality of life than the physical health quality of life score (mean difference -0.11, 95% confidence interval -0.83-0.61)</p> <p>• <b>Mortality (n=8 studies)</b> There was a slight reduction in mortality between the tele-monitoring group and the control group, but it was not statistically significant (p =0.25, RR = 0.85, 95% CI 0.64-1.13). No heterogeneity was found (p=0.66, I<sup>2</sup>=0)</p> <p>• Our results showed that tele-monitoring reduced emergency room visits, hospitalizations, and the mental health quality of life, while there were no differences in mortality, outpatient visits, or length of stay.</p> <p>• Tele-monitoring has proved to be more useful in reducing the number of Emergency room visits and hospitalization of patients</p>		

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
		with (very) severe chronic obstructive pulmonary disease than those with moderate diseases, • Active integrated tele-monitoring, which includes the act of delivering skills and education to cope with disease and online pulmonary rehabilitation, produced more improvement than tele-monitoring only intervention when it comes to emergency room visits and hospitalization.		
Lundell S. Telehealthcare in COPD: A systematic review and meta-analysis on physical outcomes and dyspnea. 2015 Jan.	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> to investigate the effects of telehealthcare on physical activity level, physical capacity and dyspnea in patients with COPD, and to describe the interventions used</li> <li>• <b>eingeschlossene Studien:</b> n=9 RCTs; 982 patients</li> <li>• <b>Suchzeitraum:</b> inception to August 30/ 2013</li> <li>• <b>Population:</b> Patienten mit COPD &gt; 40 Jahre alt</li> <li>• <b>Einschlusskriterien</b> (Auswahl)                             <ul style="list-style-type: none"> <li>- Interventions: The major part (in length of time or number of contacts) could be classified as home based telehealthcare. Some kind of feedback, motivational element, or counseling had to be provided to the patient through telehealthcare at least three times during the first three months.</li> </ul> </li> <li>• <b>Interventionen:</b> Telehealthcare (phone calls, websites or mobile phones, often combined with education and/or exercise training)</li> <li>• <b>Vergleich:</b> ordinary care, exercise training and/or education</li> <li>• telehealthcare = “the use of electronic information and communications technologies to provide and support health care when distance separates the participants”</li> <li>• telehealthcare criteria:                             <ul style="list-style-type: none"> <li>- information (delivery of health services) is transmitted electronically over a distance</li> <li>- information can be, for example, voice, sounds, video, pictures or text</li> <li>- transmission can be asynchronous (store-and</li> </ul> </li> </ul>	` - total of 982 patients (34% women) - moderate to severe COPD  For <b>physical activity level</b> , there was a significant effect favoring telehealthcare (MD, 64.7 min; 95% CI, 54.4-74.9). No difference between groups was found for <b>physical capacity</b> (MD, -1.3 m; 95% CI, -8.1-5.5) and <b>dyspnea</b> (SMD, 0.088; 95% CI, -0.056-0.233; n=7 studies). • <b>authors conclusion:</b> The use of telehealthcare may lead to improvements in physical activity level, <u>although the results should be interpreted with caution given the heterogeneity</u> in studies. This is an important area of research and further studies of the effect of telehealthcare for patients with COPD would be beneficial.	AMSTAR-II: - low	n=9 Studien RCTs eingeschlossen - Bourbeau, 2003 - Carrieri- Kohlman, 1996 - Garcia-Aymerich, 2007 - Maltais, 2008 - Nguyen, 2009 - Nguyen, 2013 - Nield, 2012 - Oh, 2003 - Waterhouse, 2010

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	forward applications) or synchronous (e.g. two-way video consultations)			

### Anhang 9.4 Selektiv eingebrachte Literatur

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
<p>Schultz K, Jelusic D, Wittmann M, et al. Inspiratory muscle training does not improve clinical outcomes in 3-week COPD rehabilitation: Results from a randomised controlled trial. Eur Respir J 2018; 51(1). DOI: 10.1183/13993003.02000-2017. <a href="http://www.ncbi.nlm.nih.gov/pub-med/29371382">http://www.ncbi.nlm.nih.gov/pub-med/29371382</a>.</p>	<p>RIMTCORE (Routine Inspiratory Muscle Training within COPD Rehabilitation)</p> <ul style="list-style-type: none"> <li>• <b>Studiendesign:</b> RCT, parallel-group</li> <li>• <b>Population:</b> patients with COPD (GOLD II - IV); n=602</li> <li>• <b>Intervention:</b> highly intensive IMT + 3-week inpatient pulmonary rehabilitation</li> <li>• <b>Vergleich:</b> sham IMT+3 -week inpatient pulmonary rehabilitation</li> </ul> <p><u>intensive pulmonary rehabilitation programme:</u></p> <ul style="list-style-type: none"> <li>- Obligatory components (mostly 30- to 60-min sessions): physical training (endurance training: four or five sessions per week; strength training: three sessions per week; whole-body vibration muscle training: seven sessions per week), patient education (seven or more sessions) and respiratory physiotherapy in groups (two to four sessions per week).</li> <li>- Optional components: smoking cessation (eight sessions), mucolytic physiotherapy, saline inhalation, psychological interventions, social counselling, nutritional counselling and occupational therapy.</li> </ul> <ul style="list-style-type: none"> <li>• <b>Studienzeitraum:</b> 02/2013 - 07/2014</li> <li>• <b>Ort:</b> Bad Reichenhall, Germany</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Patientencharakteristika:</b> 64.6% of the patients were male, mean±SD age was 57.8±7.4 years; most frequent comorbidities: Cardiovascular (63.5%), musculoskeletal (58.1%) and metabolic disorders (54.7%)</li> <li>- hinsichtlich Alter, Geschlecht, Erkrankungsstadium, Rauchstatus weitestgehend ausgeglichen</li> <li>• n=602 ITT; n=611 gesamt randomisiert</li> </ul> <ul style="list-style-type: none"> <li>• Outcomes were assessed pre- and post-pulmonary rehabilitation</li> <li>• <b>secondary outcomes:</b> 6-min walk distance, dyspnoea, quality of life and lung function --&gt; outcomes in both study groups improved significantly, but without further between-group differences. Sex and pulmonary rehabilitation admission shortly after hospitalisation modified quality of life effects.</li> </ul> <p><u>Change after 3 weeks rehabilitation</u></p> <p><b>6MWD (m)</b> Control: 83.99±65.74 Intervention: 85.30±62.80 aMD: 1.59 (-7.94–11.12)</p> <p><b>SGRQ-Total</b> Control: -10.50±13.22 Intervention: -9.42±13.44 aMD: 1.57 (-0.44–3.59)</p> <p><b>CAT</b> Control: -3.42±5.85 Intervention: -3.76±5.76 aMD: -0.09 (-0.94–0.76)</p> <p><b>CCQ-Total</b> Control: -0.58±0.90</p>	<p><b>Selection bias</b> Randomisierung: gering Allocation concealment: gering</p> <p><b>Performance bias</b> Verblindung von Teilnehmern und Personal: unklar</p> <p><b>Detection bias</b> Verblindung der Ergebnisevaluation: gering</p> <p><b>Attrition bias</b> Verlust von Studienteilnehmern/ fehlende Daten: gering</p> <p>ITT-Analyse: durchgeführt</p> <p><b>Reporting bias</b> selektive Ergebnisdarstellung: unklar</p> <p><b>Andere Biasursachen</b> Baseline imbalance: gering Interessenkonflikte/ Sponsoring: online verfügbar (für Autoren); This study was supported by Deutsche Rentenversicherung Bayern Süd.</p>	<p>selektiv eingebrachte Literatur</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	<ul style="list-style-type: none"> <li>• <b>Fragebögen QoL:</b> St George's Respiratory Questionnaire (SGRQ), COPD Assessment Test (CAT), Clinical COPD Questionnaire (CCQ)</li> <li>• <b>Erfassung Dyspnoe:</b> Baseline and transition dyspnoea indexes (BDI and TDI)</li> </ul>	<p>Intervention: <math>-0.63 \pm 0.98</math> aMD: <math>0.01 (-0.12-0.15)</math></p> <p><b>TDI</b> control (n=268): <math>4.60 \pm 3.01</math> Intervention (n=275): <math>4.57 \pm 3.17</math> aMD: <math>-0.09 (-0.61-0.42)</math></p> <ul style="list-style-type: none"> <li>• <b>authors conclusion:</b> IMT as an add-on to a 3-week pulmonary rehabilitation improves inspiratory muscle strength, but does not provide additional benefits in terms of exercise capacity, quality of life or dyspnoea. A general recommendation for COPD patients to add IMT to a 3-week pulmonary rehabilitation cannot be made.</li> </ul>		

## Anhang 10 Evidenztabellen Versorgungskoordination

### Anhang 10.1 Cochrane Reviews Versorgungskoordination

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Kruis AL. Integrated disease management interventions for patients with chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2013;(10).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009437.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009437.pub2/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To evaluate the effects of integrated disease management (IDM) programs or interventions in people with COPD on health-related QoL, exercise tolerance and number of exacerbations.</li> <li>• <b>Suchzeitraum:</b> 12 April 2012</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Interventionen:</b> <u>IDM programs for COPD</u> <ul style="list-style-type: none"> <li>- consisted of multidisciplinary (two or more health care providers) and</li> <li>- multi-treatment (two or more components) IDM programs with</li> <li>- duration of at least three months.</li> </ul> </li> <li>- <u>mögliche Komponenten:</u> <ol style="list-style-type: none"> <li><b>1. Education/self management:</b> i.e. education, selfmanagement, personal goals and/or action plan, exacerbation management</li> <li><b>2. Exercise:</b> i.e. (home) exercise training and/or strength and/ or endurance training</li> <li><b>3. Psychosocial:</b> cognitive behavioral therapy, stress management, other psychological assessment and/or treatment</li> <li><b>4. Smoking cessation</b></li> </ol> </li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika:</b> <ul style="list-style-type: none"> <li>- mean age: 68 years, 68% male; mean FEV1% predicted value was 44.3% (range 28% to 66%)</li> <li>- Participants were treated in all types of healthcare settings: primary (n = 8), secondary (n = 12), tertiary care (n = 1), and in both primary and secondary care (n = 5).</li> </ul> </li> <li>• <b>Quality of life measured on the CRQ (Chronic Respiratory Questionnaire) (GRADE: Moderate )</b> Compared with controls, IDM showed a statistically and clinically significant improvement in disease-specific QoL on all domains of the Chronic Respiratory Questionnaire after 12 months: <ul style="list-style-type: none"> <li>• dyspnea MD 1.02; 95% CI 0.67 to 1.36 (n=4 studies; 160 participants; GRADE moderate)</li> <li>• fatigue MD 0.82; 95% CI 0.46 to 1.17</li> <li>• emotional MD 0.61; 95% CI 0.26 to 0.95</li> <li>• mastery MD 0.75; 95% CI 0.38 to 1.12</li> </ul> </li> </ul>	<p>AMSTAR Score: 9/11</p> <p>y-y-y-y-y-y-y-n-n</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<p><b>5. Medication:</b> optimal medication/prescription of medication adherence</p> <p><b>6. Nutrition:</b> dietary intervention</p> <p><b>7. Follow-up and/or communication:</b> structural follow-up and/or communication, case management by nurses, optimal diagnosis</p> <p><b>8. Multidisciplinary team:</b> active participation and formation of teams of professional caregivers from different disciplines, revision of professional roles, integration of services, local team meetings</p> <p><b>9. Financial intervention:</b> fees/payment/grants for providing IDM.</p> <p>• <b>Vergleich:</b> <u>controls</u> (varying from usual care or no treatment to single interventions, mono-disciplinary interventions)</p> <p>• <b>eingeschlossene Studien:</b> 26 RCTs; involving 2997 people</p> <p>• <b>Follow-up:</b> from 3 to 24 months</p> <p>• Overall: studies were of high to moderate methodological quality</p>	<p><b>Quality of life measured on the SGRQ (St. George’s Respiratory Questionnaire) (GRADE: High)</b></p> <ul style="list-style-type: none"> <li>• <b>total score:</b> MD -3.71 (-5.83 to -1.59) (n=13 studies; 1425 participants; GRADE high)</li> <li>• <b>impact domain:</b> clinically relevant difference of four units: (MD -4.04; 95% CI -5.96 to -2.11, P &lt; 0.0001).</li> <li>• <b>activity domain:</b> significantly improved disease specific QoL (MD -2.70 (95% CI -4.84 to -0.55, P = 0.01)</li> <li>• <b>symptom domain:</b> no significant difference (MD -2.39 (95% CI -5.31 to 0.53, P = 0.11)</li> </ul> <p><b>Functional exercise capacity (6-minute Walking Distance) (GRADE: Moderate)</b></p> <ul style="list-style-type: none"> <li>• clinically relevant improvement: MD 43.86 meters compared with controls after 12months (95%CI 21.83 to 65.89; P &lt; 0.001, n=14 studies; 838 participants)</li> </ul> <p><b>Respiratory-related hospital admissions (GRADE: High)</b></p> <ul style="list-style-type: none"> <li>• reduction in the number of participants with one or more hospital admissions over three to 12 months from 27 per 100 participants in the control group to 20 (95% CI 15 to 27) per 100 participants in the IDM group</li> <li>• OR 0.68; 95% CI 0.47 to 0.99, P = 0.04; number needed to treat = 15; n=7 studies; 1470 participants)</li> </ul> <p><b>Hospital days per patient (all causes) (GRADE: High)</b></p> <ul style="list-style-type: none"> <li>• significantly lower in the IDM group compared with controls after 12 months</li> <li>• MD -3.78 days; 95% CI -5.90 to -1.67, P &lt; 0.001</li> </ul> <p><b>Adverse events</b></p> <p>No adverse effects were reported in the intervention group.</p> <p><b>Mortality</b></p> <p>No difference between groups was found on mortality (OR 0.96; 95%CI 0.52 to 1.74).</p> <p><b>Long term effects</b></p> <p>There was insufficient evidence to refute or confirm the long term effectiveness of IDM.</p>	

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>Gonçalves-Bradley DC. Early discharge hospital at home. Cochrane Database of Systematic Reviews 2017;(6).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000356.pub4/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000356.pub4/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To determine the effectiveness and cost of managing patients with early discharge hospital at home compared with inpatient hospital care.</li> <li>• <b>Suchzeitraum:</b> 9 January 2017</li> <li>• <b>Population:</b> 1 Subgruppe= Patient*innen mit COPD</li> <li>• <b>Ausschlusskriterien:</b> services providing long-term care, services provided in outpatient settings or post-discharge from hospital, end-of-life care at home and selfcare by the patient in their home, such as self-administration of an intravenous infusion.</li> <li>• <b>Interventionen:</b> <u>early discharge hospital at home</u> <ul style="list-style-type: none"> <li>- service that provides active treatment by healthcare professionals in the patient's home for a condition that otherwise would require acute hospital inpatient care, and always for a limited time period.</li> <li>- has to offer a specific service to patients in their home requiring healthcare professionals to take an active part in the patients' care</li> <li>- If not available then the patient would not be discharged early from hospital and would remain on an acute hospital ward</li> </ul> </li> <li>• <b>Vergleich:</b> <u>acute hospital inpatient care</u></li> <li>• <b>eingeschlossene Studien:</b> n=5 RCTs (für Patient*innen mit COPD)</li> </ul>	<ul style="list-style-type: none"> <li>• insgesamt 32 RCT (4746 participants)</li> <li>• <u>1 Subgruppe=COPD</u></li> <li><b>Mortality</b> <ul style="list-style-type: none"> <li>- In people with COPD there was insufficient information to determine the effect of early discharge hospital at home vs. acute hospital inpatient care on mortality</li> <li>- RR 0.53, 95% CI 0.25 to 1.12, N = 496, 5 trials, <b>GRADE: low certainty evidence</b></li> </ul> </li> <li><b>Hospital readmission</b> <ul style="list-style-type: none"> <li>- Early discharge hospital at home may decrease the risk of readmission for people with COPD</li> <li>- RR 0.86, 95% CI 0.66 to 1.13, N = 496, 5 trials; <b>GRADE: low-certainty evidence</b></li> </ul> </li> </ul>	<p>AMSTAR Score 8/11</p> <p>y-y-y-y-y-y-y-ca-n-n</p>
<p>Jeppesen E. Hospital at home for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2012;(5).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003573.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003573.pub2/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To evaluate the efficacy of hospital at home compared to hospital inpatient care in acute exacerbations of COPD.</li> <li>• <b>Suchzeitraum:</b> October 2010</li> <li>• <b>Population:</b> patients presented to the emergency department with an <u>exacerbation of COPD</u></li> <li>• <b>Einschlusskriterien:</b> Studies must not have recruited patients for whom treatment at home is usually not viewed as an responsible option (e.g. patients with an impaired level of consciousness, acute confusion, acute changes on the radiograph or electrocardiogram, arterial pH less than 7.35, concomitant medical conditions)</li> <li>• <b>Interventionen:</b> <u>hospital at home</u> <ul style="list-style-type: none"> <li>- under the care of a specialist respiratory nurse (under guidance of the hospital medical team)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li><b>Readmission to hospital (inpatient)</b> <ul style="list-style-type: none"> <li>- significant reduction in readmission rates for hospital at home compared with hospital inpatient care of acute exacerbations of COPD</li> <li>- RR 0.76; 95% CI from 0.59 to 0.99; P=0.04; n=8 studies; 870 participants; <b>GRADE: moderate</b></li> </ul> </li> <li><b>Mortality</b> <ul style="list-style-type: none"> <li>- trend towards lower mortality in the hospital at home group, but the pooled effect estimate did not reach statistical significance</li> <li>- RR 0.65, 95% CI 0.40 to 1.04, P = 0.07; n=7 studies; 845 participants; <b>GRADE: moderate</b></li> </ul> </li> <li><b>Patient satisfaction</b> (follow-up: 0 to 2 weeks after discharge)                     <ul style="list-style-type: none"> <li>- RR 1.06 (95% CI 0.96 to 1.17); n=2 studies; 158 participants; <b>GRADE: low</b></li> </ul> </li> </ul>	<p>AMSTAR Score: 8/11</p> <p>y-n-y-y-y-y-y-n-n</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
	<ul style="list-style-type: none"> <li>- provided with the treatment as deemed appropriate at the time of initial assessment on presentation to the emergency department</li> <li>- would have regular scheduled visits by the nurse as well as additional visits as requested by the patient or deemed appropriate by the nurse or the medical team</li> <li>- should be visited by the respiratory nurse until discharged from care</li> </ul> <ul style="list-style-type: none"> <li>• <b>Vergleich:</b> <u>hospital inpatient care</u> (treated as usual)</li> <li>• <b>eingeschlossene Studien:</b> 8 RCTs (870 participants)</li> </ul>	<p><b>Carer satisfaction</b> (follow-up: 2 weeks after discharge)</p> <ul style="list-style-type: none"> <li>- RR 0.97 (95% CI 0.79 to 1.19); n=1 study; 34 participants;</li> </ul> <p><b>GRADE: very low</b></p> <ul style="list-style-type: none"> <li>• For health-related quality of life, lung function (FEV1) and direct costs, the quality of the available evidence is in general too weak to make firm conclusions.</li> </ul> <p><b>Authors' conclusions</b> Selected patients presenting to hospital emergency departments with acute exacerbations of COPD can be safely and successfully treated at home <u>with support from respiratory nurses</u>.[...]</p>	
<p>Wong C, X. Home care by outreach nursing for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2012;(4).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000994.pub3/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000994.pub3/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Fragestellung:</b> To evaluate the effectiveness of outreach respiratory health care worker programmes for COPD patients in terms of improving lung function, exercise tolerance and health related quality of life (HRQL) of patient and carer, and reducing mortality and medical service utilisation.</li> <li>• <b>Suchzeitraum:</b> November 2011</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Ausschlusskriterien:</b> Studies in which the therapeutic intervention under test was physical training were not included.</li> <li>• <b>Interventionen:</b> <u>outreach nurse visiting patients in their homes</u> <ul style="list-style-type: none"> <li>- providing social support, education, monitoring health and liaising with physicians.</li> <li>- identify respiratory deteriorations promptly and reinforce correct technique with inhaler therapy</li> </ul> </li> <li>• <b>Vergleich:</b> <u>routine care</u> (without respiratory nurse/health worker input)</li> <li>• <b>eingeschlossene Studien:</b> 9 RCTs (1498 participants)</li> </ul>	<p><b>Mortality</b></p> <ul style="list-style-type: none"> <li>- OR 0.72, 95% CI 0.45 to 1.15, n=5 studies; 711 participants;</li> </ul> <p><b>GRADE: low</b></p> <p><b>Disease-specific health-related quality of life (SGRQ total)</b></p> <ul style="list-style-type: none"> <li>- statistically significant improvement in HRQL</li> <li>- MD -2.61, 95% CI -4.82 to -0.40; n=4 studies; 587 participants;</li> </ul> <p><b>GRADE: low</b></p> <p><b>Hospitalisation</b></p> <ul style="list-style-type: none"> <li>- no statistically significant difference in the number of hospitalisations</li> <li>- OR 1.01, 95%CI 0.71 to 1.44; n=5 studies; 686 participants;</li> </ul> <p><b>GRADE: low</b></p> <ul style="list-style-type: none"> <li>- there was significant heterogeneity</li> </ul> <p><b>Authors' conclusions</b> Outreach nursing programmes for COPD improved disease-specific HRQL. However the effect on hospitalisations was heterogeneous, reducing admissions in one study, but increasing them in others, therefore we could not draw firm conclusions for this outcome.</p>	<p>AMSTAR Score: 7/11</p> <p>y-n-y-y-y-y-y-ca-n-n</p>
<p>Lenferink A. Self-management interventions including action plans for</p>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=22 eingeschlossene RCTs für Metaanalyse (n=3854 eingeschlossene Patienten)</li> </ul>	<p><u>Health-related quality of life (HRQoL)</u> assessed with: SGRQ: n=1582 (10 RCTs), <b>GRADE: High</b></p> <ul style="list-style-type: none"> <li>- usual care: mean HRQoL ranged from 37.7 to 70. 4 points</li> </ul>	<p>AMSTAR Score 10/11</p>



Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>exacerbations versus usual care in patients with chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2017;(8).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011682.pub2/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011682.pub2/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Suchzeitraum:</b> 1995-05/2016</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b> self-management intervention included a written action plan for AECOPD and an iterative process between participant and healthcare provider(s) in which feedback was provided</li> <li>• <b>Ausschlusskriterien:</b> disease management programmes classified as pulmonary rehabilitation or exercise classes offered in a hospital, at a rehabilitation centre, or in a community-based setting; Participants with primary diagnoses of asthma</li> <li>• <b>Interventionen:</b> self-management interventions that included a written action plan for acute exacerbations of COPD(AECOPD) vs. Usual care</li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Health-related quality of life (HRQoL)</li> <li>- Respiratory-related hospital admissions</li> </ul> </li> </ul>	<p>- self-management interventions including action plans for exacerbations: MD <b>2.69 points lower</b> (4.49 lower to 0.9 lower) (Lower score indicates better health-related quality of life.)</p> <p><u>Respiratory-related hospital admissions</u> assessed with: number of patients with at least one respiratory-related hospital admission, n=3157 (14 RCTs), <b>GRADE: Moderate</b></p> <ul style="list-style-type: none"> <li>- usual care: 312 per 1,000</li> <li>- self-management interventions including action plans for exacerbations: 238 per 1,000 (188 to 298)</li> <li>- OR 0.69 (0.51 to 0.94)</li> </ul> <p><u>Respiratory-related mortality</u> assessed with: number of respiratory-related deaths, n=1219 (7 RCTs), <b>GRADE: Very low</b></p> <ul style="list-style-type: none"> <li>- usual care: 48 per 1000</li> <li>- self-management interventions including action plans for exacerbations: 89 per 1,000 (57 to 136)</li> <li>- OR 1.94 (1.20 to 3.13)</li> </ul> <p><u>Dyspnoea</u> assessed with: (modified) Medical Research Council Dyspnoea Scale, n=217 (3 RCTs), <b>GRADE: Low</b></p> <ul style="list-style-type: none"> <li>- usual care: mean dyspnoea ranged from 2.4 to 2.6</li> <li>- self-management interventions including action plans for exacerbations: MD <b>0.63 lower</b> (1.44 lower to 0.18 higher)</li> </ul> <p><u>COPD exacerbations</u> assessed with: number of COPD exacerbations per patient, n=740 (4 RCTs), <b>GRADE: Moderate</b></p> <ul style="list-style-type: none"> <li>- usual care: mean COPD exacerbations ranged from 1.13 to 4.3</li> <li>- self-management interventions including action plans for exacerbations: MD 0.01 higher (0.28 lower to 0.29 higher)</li> </ul> <p>- usual care: - self-management interventions including action plans for exacerbations:</p> <p>&gt;&gt; Self-management interventions including an action plan for worsening COPD symptoms improved health-related quality of life compared with usual care (high-quality evidence). The number of people who had at least one hospital admission related to lung disease was reduced among those who participated in a self-management intervention (moderate-quality evidence). There was a very small but significant increase in respiratory-related deaths for</p>	<p>y-y-y-y-y-y-y-y-n</p>

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
		self-management interventions (very low-quality evidence). [...] Although we were unable to identify the most effective components, we found that including a smoking cessation programme seemed to be effective to further improve health-related quality of life.	
Zwerink M. Self management for patients with chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2014;(3).  <a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002990.pub3/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002990.pub3/abstract</a>	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=23 eingeschlossene Controlled trials (randomised and non-randomised) für Metaanalyse</li> <li>• <b>Suchzeitraum:</b> 1994 - 11/2011</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b> interventions required at least an iterative process of interaction between participant and healthcare provider, and ideally also included formulation of goals and provision of feedback</li> <li>• <b>Ausschlusskriterien:</b> interventions with fewer than two contact moments between study participants and healthcare providers; Education only</li> <li>• <b>Interventionen:</b> Self management interventions (structured) vs. Usual care</li> <li>• <b>Primäre Endpunkte:</b> <ol style="list-style-type: none"> <li>1. Health-related quality of life (HRQoL) scores.</li> <li>2. Number of hospital admissions.</li> </ol> </li> </ul>	<p><b>HRQoL:</b> SGRQ total score, n=1413 (10 studies); <b>GRADE: Moderate</b></p> <ul style="list-style-type: none"> <li>- Control: mean SGRQ total scores from 34.7 to 65.3 points</li> <li>- Self management: Mean SGRQ total score was <b>3.51 lower</b> (5.37 to 1.65 lower)</li> </ul> <p><b>Respiratory-related hospital admissions:</b> n=1749 (9 studies), <b>GRADE: Moderate</b></p> <ul style="list-style-type: none"> <li>- Control: 293 per 1000</li> <li>- Self management: 190 per 1000 (151 to 237)</li> <li>- OR 0.57 (0.43 to 0.75 )</li> </ul> <p><b>Dyspnoea:</b> (m)MRC score, n= 119 (3 studies), <b>GRADE: Low</b></p> <ul style="list-style-type: none"> <li>- Control: mean (m)MRC scores varied from 2.4 to 3.6 points</li> <li>- Self management: Mean (m)MRC total score was <b>0.83 lower</b> (1.36 to 0.3 lower)</li> </ul> <p><b>Exercise capacity:</b> 6MWD, n= 570 (6 studies), <b>GRADE: Low</b></p> <ul style="list-style-type: none"> <li>- Control: Range of mean 6MWD varied from 68.6 to 440.9 m</li> <li>- Self management: Mean 6MWD was <b>33.69 higher</b> (9.12 lower to 76.50 higher)</li> </ul> <p><b>Mortality:</b> n=2134 (8 studies), <b>GRADE: Very low</b></p> <ul style="list-style-type: none"> <li>- Control: 97 per 1000</li> <li>- Self management: 79 per 1000 (59 to 103)</li> <li>- OR 0.79 (0.58 to 1.07 )</li> </ul> <p>&gt;&gt; The studies assessed in this review were diverse. Self management programmes differed in content and duration. Also, types of participants differed across studies. Therefore, no clear recommendations on the most effective content of self management training can be made at this time.</p>	AMSTAR Score 8/11  ca-n-y-y-y-y-n-y-y-y
Howcroft M. Action plans with brief patient education for exacerbations in	<ul style="list-style-type: none"> <li>• <b>Body of Evidence:</b> n=7 eingeschlossene parallel-group RCTs für Metaanalyse ( n= 1550 eingeschlossene Patient*innen)</li> </ul>	<ul style="list-style-type: none"> <li>• <b>Baseline-Charakteristika</b></li> <li>- mean age: 68 years</li> <li>- men=66%</li> </ul>	AMSTAR Score 11/11

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität
<p>chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2016;(12).</p> <p><a href="http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005074.pub4/abstract">http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005074.pub4/abstract</a></p>	<ul style="list-style-type: none"> <li>• <b>Suchzeitraum:</b> current to 11/2015</li> <li>• <b>Population:</b> Patient*innen mit COPD</li> <li>• <b>Einschlusskriterien:</b> Participants with a clinical diagnosis of COPD based on spirometric criteria</li> <li>• <b>Ausschlusskriterien:</b> participants who had received a primary diagnosis of asthma; cross-over trials</li> <li>• <b>Interventionen:</b> action plan for COPD exacerbations provided with a single short patient education component and without a comprehensive self-management programme vs. usual care</li> <li>• <b>Primäre Endpunkte:</b> <ul style="list-style-type: none"> <li>- Healthcare utilisation, including respiratory-related hospital admission, treatment in an emergency department (ED) and GP visits for COPD</li> <li>- Mortality: respiratory-related and all-cause</li> <li>- Use of medication: time to initiation of therapy after symptom onset; courses/duration of antibiotic or corticosteroid use, or both; participant initiation of antibiotic or steroid use, or both</li> </ul> </li> </ul>	<p><u>Hospitalisations for COPD/ 100 patient- years (action plan + phone follow-up), n=743 (1 RCT), GRADE: Moderate</u> - Rate ratio 0.69 (0.47 to 1.01)</p> <p><u>Hospitalisations and emergency visits for COPD/ 100 patient-years (action plan + phone follow-up), n= 743 (1 RCT), GRADE: High</u> - Rate ratio 0.59 (0.44 to 0.79)</p> <p><u>At least 1 hospital admission, n=897 ( 2 RCTs), GRADE: Moderate</u> - Usual care: 209 per 1000 - Action plan: 154 per 1000 (114 to 204) - Odds ratio 0.69 (0.49 to 0.97)</p> <p><u>Mortality (all-cause), n= 1134 (4 RCTs), GRADE: Moderate</u> - Usual care: 103 per 1000 - Action plan: 91 per 1000 (63 to 130) - Odds ratio 0.88 (0.59 to 1.31)</p> <p><u>Respiratory- related quality of life: SGRQ, n=1009 (3RCTs), GRADE: Moderate</u> - Usual care: Mean SGRQ overall score ranged from -2 to +6 units - Action plan: Mean SGRQ overall score in the intervention group was <b>2.82 units lower</b> (0. 83 lower to 4.81 lower)</p> <p><u>Depression score assessed with HADS Scale from 0 to 21 (worst), n=154 (1 RCT), GRADE: Low</u> - Usual care: Mean depression score was -0.04 - Action plan: Mean depression score was <b>0.25 lower</b> (1.14 lower to 0.64 higher)</p> <p>&gt;&gt; People with COPD should be given an individualised action plan with a short educational component so they can benefit from fewer and shorter hospital stays, better understanding of the need to self-start treatment and appropriate use of medication for exacerbations.</p>	<p>y-y-y-y-y-y-y-y-y-y</p>

Anhang 10.2 Auswirkungen des Wechsels von Inhalationssystemen ohne erneute Instruktion (NVL Asthma)

Zitat	Studiencharakteristika	Ergebnisse	Methodische Bewertung
<p>26961</p> <p>Thomas M. Inhaled corticosteroids for asthma: impact of practice level device switching on asthma control. BMC Pulm Med 2009;9:1.</p> <p><a href="http://www.ncbi.nlm.nih.gov/pub-med/19121204">http://www.ncbi.nlm.nih.gov/pub-med/19121204</a></p>	<p><b>Retrospektive Kohortenstudie,</b></p> <ul style="list-style-type: none"> <li>- 2 Jahre, Registerdaten</li> <li>- Indexdatum: Wechsel des Inhalationssystems ohne Konsultation, 1 Jahr Vor- u. Nachbetrachtung</li> <li>n= 1648 (1:1)</li> </ul> <p><b>Fragestellung:</b></p> <ul style="list-style-type: none"> <li>- evaluate the impact on asthma control of inhaler device switching without an accompanying consultation in general practice in the United Kingdom</li> </ul> <p><b>Einschlusskriterien:</b></p> <ul style="list-style-type: none"> <li>- Alter: 6-65 J., dokumentierte Diagnose Asthma</li> <li>- switches to inhaler devices that require training to use</li> </ul> <p><b>Ausschlusskriterien:</b></p> <ul style="list-style-type: none"> <li>- COPD</li> <li>- changed to a device recorded as 'generic'</li> </ul> <p><b>Definition des primären EP:</b></p> <p>Successful treatment: ≤0.5 dose/day SABA, keine OCS, unveränderte Langzeittherapie, keine Hospitalisierung</p> <p>Partially successful treatment: 0.5 bis ≤2 dose/day SABA, ≤2 OCS, unveränderte Langzeittherapie, keine Hospitalisierung</p> <p>Unsuccessful treatment: &gt; 2 dose/day SABA, ≥3 OCS, veränderte Langzeittherapie, ≥1 Hospitalisierung</p> <p><b>Statistik:</b></p> <ul style="list-style-type: none"> <li>- logistische Regression für Korrektur von Baseline-Confoundern</li> </ul>	<p><b>Baseline-Charakteristika:</b></p> <p>ausgeglichen bis auf Sozioökonomischer Status, tägliche SABA-Dosis, Konsultationshäufigkeit</p> <p><u>häufigster Wechsel:</u> DPI to MDI (53%)</p> <p><b>Primärer EP:</b> Asthmakontrolle (Composit-Endpunkt):</p> <ul style="list-style-type: none"> <li>- switched having significantly lower odds of success than control patients (OR, 0.30; 95% CI, 0.20 to 0.45; p &lt; 0.001)</li> <li>- likelihood of unsuccessful treatment among switched patients (50,7%) and control patients (37,9%)</li> <li>- not substantially different when the ICS dose was included in the analysis (OR, 1.89; 95% CI, 1.48 to 2.40; p &lt; 0.001)</li> </ul> <p><b>Sekundäre EP</b></p> <ul style="list-style-type: none"> <li>- <u>number of patient per year analyzed for inhaled SABA:</u> switched cohort used 0.38 extra doses/day of SABA, compared with baseline use, than the control cohort (95% CI, 0.22 to 0.53; p &lt; 0.001)</li> <li>- <u>number of patient per year analyzed for inhaled OCS:</u> no significant differences</li> <li>- <u>number of general practice consultations for asthma:</u> no significant difference</li> <li>- <u>number of hospital admissions for asthma:</u> k.A.</li> <li>- <u>number of hospital admissions for possible asthma</u> (defined as non-specific hospitalization code and asthma-related code within a 1-week window): no significant difference</li> </ul>	<p>(In Anlehnung an NOS)</p> <p><u>I. Selektion der Studienteilnehmer</u></p> <ol style="list-style-type: none"> <li>1. exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition: ja</li> <li>2. nicht-exponierte Kohorte repräsentativ, adäquat ausgewählt: ja</li> <li>3. valide Erfassung der Exposition: ja (Registerdaten)</li> <li>4. wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war: ja (1 Jahr Vorbeobachtung)</li> </ol> <p><u>II. Vergleichbarkeit</u></p> <ol style="list-style-type: none"> <li>1. Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben: ja</li> </ol> <p><u>III. Endpunkterfassung</u></p> <ol style="list-style-type: none"> <li>1. valide Erfassung der Endpunkte: ja</li> <li>2. Konnte in der Beobachtungszeit der Endpunkt auftreten: ja</li> <li>3. fehlende Daten adäquat berücksichtigt: ja (Ausschluss)</li> </ol> <p><u>IV. Col/ Funding</u></p> <ul style="list-style-type: none"> <li>- unrestricted grant from GlaxoSmithKline, from Schering-Plough</li> </ul>
<p>26959</p> <p>Doyle S. What happens to patients who have their asthma device switched without their consent? Prim</p>	<p><b>Qualitative Studie</b></p> <p>n = 19</p> <p><b>Fragestellung:</b></p> <ul style="list-style-type: none"> <li>- describe patients' experiences of non-consented switching of medication</li> </ul>	<p><b>Baseline-Charakteristika:</b></p> <ul style="list-style-type: none"> <li>- Weiblich: n=14</li> <li>- Raucher*innen: ja:3, nein: 10, ehemals: 6</li> <li>- Ergebnisse des ACT: well controlled: n=12 (63%)</li> </ul> <p><b>Ergebnisse:</b></p> <p><u>Patient views on the circumstances of the NCS:</u></p>	<p>(In Anlehnung an McMaster)</p> <ol style="list-style-type: none"> <li>1. <b>Ziel/ Fragestellung:</b> ja</li> <li>2. <b>Literatur:</b></li> <li>2.1 relevante Literatur gesichtet: ja</li> <li>3. <b>study design</b></li> <li>3.1. Studiendesign: dargestellt: ja</li> </ol>

Zitat	Studiencharakteristika	Ergebnisse	Methodische Bewertung
<p>Care Respir J 2010;19(2):131-9.  <a href="http://www.ncbi.nlm.nih.gov/pub-med/20174771">http://www.ncbi.nlm.nih.gov/pub-med/20174771</a></p>	<ul style="list-style-type: none"> <li>- investigate the potential range of circumstances in which switches happened</li> <li>- investigate the perception of the impact of the switch</li> </ul> <p><b>Einschlusskriterien:</b></p> <ul style="list-style-type: none"> <li>- reported diagnosis of asthma and currently using an inhaler device</li> <li>- experience of having an asthma inhaler device changed/switched without their knowledge or consent</li> <li>- ≥ 18 J</li> </ul> <p><b>Ausschlusskriterien:</b></p> <ul style="list-style-type: none"> <li>- no inhaler device or no switch in inhaler device</li> <li>- presence of acute illness or other impairment</li> </ul> <p><b>Studiendesign:</b></p> <ul style="list-style-type: none"> <li>- Rekrutierung: Normalbevölkerung (lokale Medien)</li> <li>- in-depth exploratory interviews</li> <li>- Semi-structured face-to-face interviews</li> <li>- demographic questionnaire, a clinical questionnaire, and ACT</li> </ul>	<ul style="list-style-type: none"> <li>- Most participants: identified doctor being responsible for instigating the switch, a couple identified the pharmacist.</li> <li>- one case: pharmacist identified as source of the nonconsented switch (NCS), doctor unaware of switch</li> <li>- two cases, source of the NCS unclear</li> <li>- vermutete Gründe der Patienten für Wechsel: cost issues, many believed the decision was not made in their best interests</li> </ul> <p><u>Device use post-switch:</u></p> <ul style="list-style-type: none"> <li>- nine preventer, nine rescue inhalers, one both</li> <li>- most: not shown how to operate new device.</li> <li>- Many: struggled to actuate new device as effectively as their previous</li> <li>- some: admitted not using the new device; unable to operate.</li> </ul> <p>- Lösungsansätze: resorted to use of old inhalers, returned to their doctor, went without asthma therapy until someone explained how to use device.</p> <ul style="list-style-type: none"> <li>- p. indicated overuse of medication due to lack of confidence in new medication or inability to actuate new device effectively</li> </ul> <p><u>Changes in perception of asthma control:</u></p> <ul style="list-style-type: none"> <li>- most: more asthma symptoms and worse asthma control</li> <li>- some: no change in their asthma</li> <li>- two: reported improvements in symptom relief.</li> </ul> <p><u>Relationship with health professionals:</u></p> <ul style="list-style-type: none"> <li>- levels of relationship with doctors, ranging from, "I am completely satisfied", to, "I don't think they know who I am".</li> <li>- inhaler switches had a clear impact on the doctor-patient relationship</li> <li>- Almost all said: switch impacted on their relationship with doctor, irrespective of whether their previous relationship had been good or not. Participants talked of being 'angry' and 'upset' or 'shocked' that they had not been told anything about the NCS.</li> <li>- while participants mainly experienced a deterioration in their physical functioning (though not always), the participants indicated that the surreptitious nature of the switch was to blame for the impairment in their doctor-patient relationship, not the decline in symptom control</li> </ul>	<p>3.2. theoretische Perspektive dargestellt: ja</p> <p>3.3. Methoden dargestellt: ja</p> <p><b>4. Sampling</b></p> <p>4.1. Selektion beschrieben: ja</p> <p>4.2. Auswahl durchgeführt bis Redundanz erreicht: unklar</p> <p>4.3. informed consent: ja</p> <p><b>5. Data collection</b></p> <p>5.1. Beschreibung von Teilnehmern und Situation: ja</p> <p>5.2. Beschreibung der Rolle des Forschers: unklar</p> <p>5.3. Annahmen der Forscher und Biasrisiko beschrieben:</p> <p><b>6. Procedural Rigour:</b> ja</p> <p><b>7. Datenanalyse:</b></p> <p>7.1. analytische Stringenz: ja</p> <p><b>8. Nachvollziehbarkeit:</b> ja</p> <p><b>9. Theoretische Zusammenhänge:</b> ja</p> <p><b>10. Gesamtstringenz:</b> unklar</p> <p><b>11. Zusammenfassung:</b> ja</p> <p><b>Funding:</b> unrestricted grant from GlaxoSmithKline</p>

Zitat	Studiencharakteristika	Ergebnisse	Methodische Bewertung
<p><b>26956</b>                      Ekberg-Jansson A. Budesonide inhaler device switch patterns in an asthma population in Swedish clinical practice (ASSURE). Int J Clin Pract 2015;69(10):1171-8.  <a href="http://www.ncbi.nlm.nih.gov/pub-med/26234385">http://www.ncbi.nlm.nih.gov/pub-med/26234385</a></p>	<p><b>Retrospektive Kohortenstudie</b>                      - 2005-2013, Registerdaten, Schweden                      - Indexdatum: Erste Verschreibung BDP DPI                      - Ursache für Wechsel nicht ermittelbar</p> <p><b>Untersuchte Populationen:</b>                      - switch population: P. mit erfasstem Wechsel des Systems                      - non-switch population: P. ohne Wechsel des Systems                      - valid switch population: P. mit verfügbaren Daten 12 Monate vor und nach Wechsel: n= 463                      - nested case-control population: P. mit verfügbaren Daten 12 Monate vor Wechsel: n = 960                      &gt;&gt; Subgruppenanalysen stratifiziert nach MPR (Medication possession ratio = prozentualer Anteil der Tage im Jahr, an denen Medikation vorliegt)</p> <p><b>Fragestellung:</b>                      - provide scientific insights on inhaler device switching on asthmatic patients treated with BUD DPI</p> <p><b>Einschlusskriterien:</b>                      - ≥ 6 Jahre,                      - Diagnose: Asthma</p> <p><b>Ausschlusskriterien:</b>                      - COPD                      - Ipratropium, Tiotropium</p> <p><b>Definition der Asthmakontrolle (bezogen auf das letzte Jahr):</b>                      - kontrolliert: keine OCS, ≤ 1 SABA-Verschreibung                      - teilweise kontrolliert: 1 OCS- und/ oder 1 SABA-Verschreibung                      - unkontrolliert: &gt; 1 OCS- und/ oder &gt; 1 SABA-Verschreibung</p>	<p><b>Baseline-Charakteristika:</b> ausgeglichen</p> <p><b>Ergebnisse der valid-switch-population [n= 926 (1:1)]</b>                      Events pro Patient und Jahr [switch vs. non-switch]                      - Exazerbationsrate: 0,4 vs. 0,32                      - Konsultationsrate: 2,57 vs. 2,26                      - SABA-Verschreibung: 1,32 vs. 1,21                      - LABA-Verschreibung: 0,56 vs. 0,60</p> <p><b>Ergebnisse der nested case-control population [n = 1920 (1:1)]</b>                      - Evaluation möglicher prädiktiver Faktoren für Wechsel                      - switch-Population: 4,5 Jahre jünger, niedrigere MPR, LABA-Nutzung seltener</p> <p><b>Relevante Subgruppenanalyse:</b>  <b>Endpunkt in Abhängigkeit von Kontakt zum Gesundheitswesen am Tag des Wechsels</b>                      Wechsler mit Arzt- oder Pflegepersonalkontakt (n=214) Wechsler ohne Kontakt (n= 116):                      - ambulanter Krankenhauskontakt: 0,81 vs. 2,01 (p&lt;0,001)                      - Konsultationen: 4,29 vs. 4,96                      - Exazerbationen: 0,77 vs. 0,90</p>	<p>(In Anlehnung an NOS)</p> <p><b>I. Selektion der Studienteilnehmer</b>                      1. exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition: ja                      2. nicht-exponierte Kohorte repräsentativ, adäquat ausgewählt: ja                      3. valide Erfassung der Exposition: ja (Registerdaten)                      4. wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war: ja</p> <p><b>II. Vergleichbarkeit</b>                      1. Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben: ja</p> <p><b>III. Endpunkterfassung</b>                      1. valide Erfassung der Endpunkte: ja                      2. Konnte in der Beobachtungszeit der Endpunkt auftreten: ja                      3. fehlende Daten adäquat berücksichtigt: k.A.</p> <p><b>IV. Col/ Funding</b>                      - study sponsor: AstraZeneca</p>

## Anhang 11 Kommentare aus der öffentlichen Konsultation

### Anhang 11.1 Inhaltliche Kommentare

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
2	<b>Diagnostik und Monitoring</b> Abbildung 1; S. 14	Rö Thorax nicht als obligate Untersuchung abbilden	Im Algorithmus werden sowohl Spirometrie als auch Rö Thorax als obligate Untersuchungen abgebildet. Die begründende Evidenz würde mich interessieren. Aus Screening-Untersuchungen an rauchenden Menschen weiß man, dass ein generelles Röntgen eher zu vermehrten Krebserkrankungen führt, als durch Früherkennung Leben zu retten. Warum soll es im Einzelfall nicht möglich sein, bei spirometrischer Diagnose einer COPD symptomorientiert zu behandeln und nur bei ausbleibender Symptomkontrolle zu röntgen?	Algorithmus so belassen.  Keine Änderung.
4 (vorab)	<b>Diagnostik und Monitoring</b> Tabelle 5 Risikofaktoren; S. 17	E-Zigaretten aufnehmen?	[...] Eigentlich müssten wir daher E-Zigaretten in die Tabelle schreiben. Langzeitdaten haben wir natürlich nicht, sondern nur Tier-Daten. Als Kompromiss können Sie „Gasen und Partikel / Feinstaub“ schreiben. Unten im Text können Sie dann bei den EZ auf die Tabelle Bezug nehmen und darstellen das bei Rauchen von EZ Gase und... freigesetzt werden.	Der Punkt: • „Inhalativer Konsum alternativer Tabakprodukte (wie Wasserpfeife, Tabakerhitze, E-Zigaretten)“  wird in die Tabelle 5 Risikofaktoren aufgenommen. Im Hintergrundtext wird ein Analogismus zu den breiter vorhandenen Daten zu Gasen und Feinstaub hergestellt.
5	<b>Diagnostik und Monitoring</b> 2.4.2 Spirometrie  Empfehlung 2-3; S. 18 Bei Patient*innen mit nachgewiesener Atemwegsobstruktion soll zur Bestätigung der Diagnose zunächst ein Reversibilitätstest mit kurzwirkenden Beta-2-Sympathomimetika (SABA) durchgeführt werden.	Eine COPD ist aber nur bei einer Normalisierung der Obstruktion ausgeschlossen. Auch ein negativer Reversibilitätstest schließt ein Asthma bronchiale nicht sicher aus.	Leitlinie 020-017, Spirometrie, Seite 24	Die Empfehlung zum Reversibilitätstest wird angepasst; der Grund für einen Reversibilitätstest wird gestrichen (zur Bestätigung der Diagnose).  Somit lautet die Empfehlung 2-3: <i>Bei Patient*innen mit nachgewiesener Atemwegsobstruktion soll zunächst ein Reversibilitätstest mit kurzwirkenden Beta-2-Sympathomimetika (SABA) durchgeführt werden.</i>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
				Der Hintergrundtext wird dahingehend angepasst und der Sachverhalt näher erläutert.
6	<p><b>Diagnostik und Monitoring</b> 2.4.3 Ganzkörperplethysmographie; S. 20</p> <p>Die Ganzkörperplethysmographie ist eine in Deutschland flächendeckend verfügbare Untersuchungsmethode und fester Bestandteil der ambulanten Versorgung. Sie stellt eine annähernd mitarbeitsunabhängige objektive Messmethode der Obstruktion dar und ist sinnvoll bei Patient*innen, die nicht in der Lage sind, auswertbare maximale und/oder forcierte Atemmanöver zusätzlich zur Spirometrie durchzuführen [11]. Die Druckflusskurve gibt Informationen über den Elastizitätsverlust der Lunge (expiratorische Keule) und kann zur Abschätzung der Überblähung herangezogen werden.</p>	<p>Die Ganzkörperplethysmographie ist eine in Deutschland flächendeckend verfügbare Untersuchungsmethode und fester Bestandteil der ambulanten Versorgung. Sie stellt eine annähernd mitarbeitsunabhängige objektive Messmethode der Obstruktion dar und misst im Gegensatz zur Spirometrie sämtliche Volumina; gibt somit wichtige Informationen über eine Überblähung der Lunge und ist auch sinnvoll bei Patient*innen, die nicht in der Lage sind, auswertbare maximale und/oder forcierte Atemmanöver zusätzlich zur Spirometrie durchzuführen [11]. Die Druckflusskurve gibt Informationen über den Elastizitätsverlust der Lunge (expiratorische Keule) und kann zur Abschätzung der Überblähung herangezogen werden.</p>	<p>Nähere Erläuterungen zu Methode auch in Abgrenzung zur Spirometrie</p> <p>Crieé et al. Body plethysmography e Its principles and clinical use. Respir Med. 2011 Jul;105(7):959-71. doi: 10.1016/j.rmed.2011.02.006.</p>	<p>Der ergänzende Textvorschlag wird eingefügt.</p> <p>Um den Stellenwert der Bodyplethysmographie nicht über den der Spirometrie zu stellen, wird die Formulierung „im Gegensatz zur“ geändert in „ergänzend zur“. Somit lautet der Textabschnitt:</p> <p><i>Die Ganzkörperplethysmographie ist eine in Deutschland flächendeckend verfügbare Untersuchungsmethode und fester Bestandteil der ambulanten Versorgung. Sie stellt eine annähernd mitarbeitsunabhängige objektive Messmethode der Obstruktion dar und misst ergänzend zur Spirometrie sämtliche Volumina; gibt somit wichtige Informationen über eine Überblähung der Lunge und ist auch sinnvoll bei Patient*innen, die nicht in der Lage sind, auswertbare maximale und/oder forcierte Atemmanöver zusätzlich zur Spirometrie durchzuführen [11]. Die Druckflusskurve gibt Informationen über den Elastizitätsverlust der Lunge (expiratorische Keule) und kann zur Abschätzung der Überblähung herangezogen werden.</i></p>
7	<p><b>Diagnostik und Monitoring</b> 2.5 Diagnostik von Komorbiditäten; S. 22</p>	<p>Neuer Abschnitt 2.5.3, einzufügen nach 2.5.2 (Angst und Depression)</p> <p>Vorgeschlagene Ergänzung: Patienten, die die Einschlusskriterien für ein Screening auf Lungenkrebs erfüllen (Siehe S3-Leitlinie „Prävention, Diagnostik, Therapie und Nachsorge des Lungenkarzinoms), sollte die Teilnahme an einem entsprechenden, qualitätsgesicherten Screeningprogramm angeboten werden. Da-</p>	<p>Lungenkarzinom und COPD haben ähnliche Risikofaktoren, die Risikopopulation ist größtenteils identisch, zudem ist das Lungenemphysem ein unabhängiger Risikofaktor für Lungenkrebs (de Torres, J. P., et al. (2007). "Assessing the relationship between lung cancer risk and emphysema detected on low-dose CT of the chest." Chest 132(6): 1932-1938.). Lungenkrebscreening ist eine geeignete Maßnahme, die Mortalität von Lungenkrebs in der Risikogruppe zu senken –</p>	<p>Die Schritte des G-BA werden abgewartet (IqWiG-Bericht zum Thema wurde 10/2020 fertiggestellt).</p> <p>Nach der Definition der Risikogruppe (G-BA) wird die Leitliniengruppe abschätzen, ob auch Patient*innen mit COPD entsprechend abgebildet wurden - oder ob eine zusätzliche systematische Recherche notwendig wird.</p>



Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
		bei sollte der Schweregrad der COPD und die individuelle Möglichkeit für den Patienten, von einer frühen Therapie eines Lungenkarzinoms zu profitieren, berücksichtigt werden.	dies wurde in zahlreichen Studien und Pilotprojekten nachgewiesen (Beispiele für Studien: The National Lung Screening Trial Research Team (2011). "Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening." New England Journal of Medicine 365(5): 395-409.; de Koning, H. J., et al. (2020). "Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial." New England Journal of Medicine.) und auch in der Bewertung des IQWiG für Deutschland bestätigt (Projekt S19-02). Da beim Lungenkarzinom in frühen Stadien zunehmend minimal-invasive Therapien möglich sind, die auch bei Patienten mit eingeschränkter Lungenfunktion sehr gute Ergebnisse zeigen, sollte die Chance genutzt werden, diese Patienten in Screeningprogramme aufzunehmen. Dabei sollte natürlich der individuelle Gesundheitszustand und die Lebenserwartung des Patienten sowie seine Möglichkeiten, von möglichen kurativen Therapien eines frühen Lungenkarzinoms zu profitieren, Berücksichtigung finden.	Das Thema wird in der 3. Auflage der NVL COPD thematisiert.
8	<b>Diagnostik und Monitoring</b> 2.5.1 Tabakabhängigkeit  Empfehlung 2-7; S. 22  Bei rauchenden Patient*innen mit COPD soll der Fagerströmtest (FTCD) zur weiterführenden Diagnostik eingesetzt werden, um die Stärke der Zigarettenabhängigkeit einzuschätzen.	Bei rauchenden Patient*innen mit COPD soll der Fagerströmtest (FTCD) eingesetzt werden, wenn es für die Therapie relevant ist, die Stärke der Zigarettenabhängigkeit einzuschätzen.	Die Empfehlung in der ursprünglichen Variante ignoriert die Empfehlungen des motivational interviewing: nur wenn die entsprechende Veränderungsbereitschaft vorhanden ist, hat es Sinn, das Ausmaß des Rauchens zu quantifizieren. Gerade in der Hausarztpraxis kann das „Überziehen der Patient*innen“ mit Fragebogen-Instrumenten die therapeutische Beziehung empfindlich stören, wenn sie nicht als angemessen empfunden werden. Die Empfehlung würde mit Sicherheit auch in 99% der Fälle nicht befolgt werden.	Zustimmung zur neuen Formulierung.  Es wird darauf hingewiesen, dass die neue Formulierung somit etwas von der S3-Leitlinie „Screening, Diagnostik und Behandlung des schädlichen und abhängigen Tabakkonsums“ abweicht.  Empfehlung 2-7: <i>Bei rauchenden Patient*innen mit COPD soll der Fagerströmtest (FTCD) eingesetzt werden, wenn es für die Therapie relevant ist, die Stärke der Zigarettenabhängigkeit einzuschätzen.</i>
9	<b>Diagnostik und Monitoring</b> 2.5.1 Tabakabhängigkeit	"Wenn die Stärke der Zigarettenabhängigkeit abgeschätzt werden soll, soll der Fagerström-Test zur Zigarettenabhängigkeit verwendet werden."	Die generelle SOLL-Empfehlung erscheint uns für die Umsetzung in der Hausarztpraxis nicht realistisch zu sein. Außerdem leitet sich kein direktes	siehe Nr. 8

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	Empfehlung 2-7; S. 22: Bei rauchenden Patient*innen mit COPD soll der Fagerströmtest (FTCD) zur weiterführenden Diagnostik eingesetzt werden, um die Stärke der Zigarettenabhängigkeit einzuschätzen		Patientenmanagement daraus ab. Wir befürworten daher an dieser Stelle einen KANN-Hinweis.  Die Empfehlung orientiert sich allerdings an der S3-Leitlinie Screening, Diagnostik und Behandlung des schädlichen und Abhängigen Tabakkonsums“ (die an dieser Stelle auf einem Expert*innenkonsens beruht). Insofern muss die NVL COPD an dieser Stelle wohl mitgehen.	
10	<b>Diagnostik und Monitoring</b> 2.5.1.1 Objektive Messung des Tabakkonsums; S. 23  Objektive Messverfahren stellen eine Handlungsoption dar, wenn Zweifel an den Selbstauskünften des/der Patient*in hinsichtlich des Rauchverhaltens bzw. einer Tabakabstinenz nach Tabakentwöhnungsversuch bestehen. Jegliche Tests bedürfen der aktiven Zustimmung der Patienten*innen.	Zusatz: Die CO Bestimmung zusammen mit der kapillären BGA kann ohne Aufklärung durchgeführt werden.	Die Forderung ist im Alltag einer Praxis, bei der bei sehr vielen Patienten vor Arztkontakt eine kapilläre BGA durchgeführt wird, nicht umzusetzen.  Die Forderung wird dazu führen, dass dieser wichtige Wert nicht mehr erhoben wird.	Anpassung im Hintergrundtext: <i>Objektive Messverfahren stellen eine Handlungsoption dar, wenn Zweifel an den Selbstauskünften des/der Patient*in hinsichtlich des Rauchverhaltens bzw. einer Tabakabstinenz nach Tabakentwöhnungsversuch bestehen. Entsprechende Tests bedürfen der aktiven Zustimmung der Patienten*innen.</i>
11 (vorab)	<b>Diagnostik und Monitoring</b> 2.5.1.1 Objektive Messung des Tabakkonsums; S. 23  Objektive Messverfahren stellen eine Handlungsoption dar, wenn Zweifel an den Selbstauskünften des/der Patient*in hinsichtlich des Rauchverhaltens bzw. einer Tabakabstinenz nach Tabakentwöhnungsversuch bestehen. Jegliche Tests bedürfen der aktiven Zustimmung der Patienten*innen.		Eine aktive Zustimmung bei der Bestimmung der BGA ist im Alltag schwer umzusetzen. Ich hatte dies bei einer vorigen Version in einer E-Mail mitgeteilt und hierbei auf andere Verfahren in der Medizin verwiesen, die ebenfalls relevante Befunde abklären ohne dass eine aktive Zustimmung eingeholt wird. Z:B Ultraschall Abdomen etc.	Siehe Nr. 10
12	<b>Diagnostik und Monitoring</b> 2.7 Strukturierte Symptomerfassung  Tabelle 10; S. 25		Mir ist es nicht ersichtlich, warum hier nicht der CAT zum Abfragen der Symptome abgebildet ist. Seine einzelnen Items werden Punkt für Punkt im DMP abgefragt	Keine Änderung.  Die Gruppe hat sich bewusst für ein eigenes kürzeres Instrument entschieden. Zudem würde die Verwendung des CAT zu

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
				einer anderen (strengeren) Symptomeinschätzung führen im Vergleich zum mMRC.
13	<p><b>Diagnostik und Monitoring</b> 2.7.1 Erfassung von Exazerbationen</p> <p>Tabelle 11; S. 27</p> <p>Hatten Sie wegen Ihrer COPD seit dem letzten Besuch in der Praxis einen stationären Krankenhausaufenthalt?</p>		Exazerbationen sind im allgemeinen der Grund für einen Krankenhausaufenthalt wegen COPD. Warum muss ein weiteres Kriterium erfüllt sein, um auf eine Exazerbation zu schließen?	Keine Änderung.  Abbildung der Fragen entsprechend dem systematisch entwickelten Patient*innen-Questionnaire „Monitoring of Exacerbation Probability (MEP)“.
14	<p><b>Diagnostik und Monitoring</b> 2.2.1 Zusätzliche Anamnese für rauchende Patient*innen mit COPD</p> <p>- Abb. 2: Raucheranamnesebogen („Vorschlag“ für ausführliche Anamnese zum aktuellen Rauchverhalten, zur Empf. 2-1 und Abb. 1, Diagnostik-Algorithmus), S. 14, S. 16</p> <p>Empfehlung 2-1 Bei der Diagnose der COPD soll entsprechend dem Algorithmus (siehe Abbildung 1) vorgegangen werden.</p>	<p>In der aktuellen Fassung werden für COPD-Patienten insgesamt vier (!) Fragebögen empfohlen. Das erscheint uns für die Gesamtheit der COPD-Patienten in Hausarztpraxen nicht realisierbar zu sein. [ÄZQ: Kommentar gilt für Nr. 14-17 zusammen]</p> <p>Für eine strukturierte Erfassung von Tabakabhängigkeit, Symptomschwere und Exazerbationen wird die Verwendung von Fragebögen allerdings lediglich empfohlen (KANN) und nur die konkreten Fragebögen sind dann mit einer SOLLTE-Empfehlung versehen. [ÄZQ: Kommentar gilt für Nr. 14-17 zusammen]</p>		Keine Änderung.  Kein konkreter Änderungsvorschlag, durch den Hinweis auf den offenen Empfehlungsgrad („KANN“).
15	<p><b>Diagnostik und Monitoring</b> 2.5.1 Tabakabhängigkeit</p> <p>Empf. 2-7: Fagerströmtest (Objektivierung der Tabakabhängigkeit); S. 22</p> <p>Empfehlung 2-7 Bei rauchenden Patient*innen mit COPD soll der Fagerströmtest</p>			Siehe weiteres Vorgehen Nr. 8

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	(FTCD) zur weiterführenden Diagnostik eingesetzt werden, um die Stärke der Zigarettenabhängigkeit einzuschätzen.			
16	<p><b>Diagnostik und Monitoring</b></p> <p>2.7 Strukturierte Symptomerfassung</p> <p>- Empf. 2-8/2-9: Strukturierte Dokumentation, z.B. anhand Tab. 10 (neues Instrument anstelle CAT-/MRC-Fragebogen); S. 24</p> <p>Empfehlung 2-8 Die Schwere der Symptomatik einer COPD soll strukturiert erfasst und beurteilt werden.</p> <p>Empfehlung 2-9 Für die strukturierte Erfassung und Beurteilung kann Tabelle 10 genutzt werden.</p>			Keine Änderung.
17	<p><b>Diagnostik und Monitoring</b></p> <p>2.7.1 Erfassung von Exazerbationen</p> <p>Empfehlung 2-10; S. 26 Die Exazerbationen sollen strukturiert erfasst und dokumentiert werden.</p> <p>Empfehlung 2-11 Für die Erfassung der Exazerbationen kann der (validierte) MEP-Fragebogen (Monitoring of Exacerbation Probability) genutzt werden.</p>			Keine Änderung.
18	<p><b>Tabakentwöhnung</b></p> <p>Empfehlung 3-4; S. 31</p>	Bei entwöhnungsbereiten Patient*innen mit COPD soll eine Verhaltenstherapie und bei entsprechendem Bedarf eine medikamentöse Entzugssyndrombehandlung nachdrücklich empfohlen und angeboten werden	Keineswegs alle benötigen oder wünschen eine Entzugssyndrombehandlung. In den Studien zur medikamentösen Begleittherapie waren nur Patienten eingeschlossen, die nach entsprechender	Empfehlung nicht ändern.  Diese wurde ausführlich in der Arbeitsgruppe diskutiert und auch aufgrund der

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	Bei entwöhnungsbereiten Patient*innen mit COPD soll eine kombinierte Therapie mit Verhaltenstherapie und medikamentöser Entzugssyndrombehandlung nachdrücklich empfohlen und angeboten werden.		intensiver Aufklärung einer potentiellen Behandlung mit Psychopharmaka zugestimmt haben- meist solche mit vorherigen frustranen Absetzversuchen	vorhandenen Evidenz so formuliert. Der identifizierte Cochrane Review (van Eerd 2016) zeigt deutlich den Vorteil einer Kombinationsbehandlung (bzw. einer pharmakologischen Behandlung als Add on zur Verhaltenstherapie) auf (siehe S. 31).  Zudem wurde im Cochrane Review kein direkter Vergleich zwischen Verhaltenstherapie und medikamentöser Therapie (entweder/oder) durchgeführt - somit kann entsprechend der vorliegenden Evidenz die Verhaltenstherapie nicht direkt über die medikamentöse Therapie gestellt werden. Auch wird im Hintergrundtext die medikamentöse Therapie nicht konkretisiert; bezieht sich also nicht zwangsläufig nur auf Psychopharmaka.(S. 32)
20 (vorab)	<b>Tabakentwöhnung</b>  Empfehlung 3-7; S. 34 Als Möglichkeit des Biomonitorings kann eine CO-Messung durchgeführt werden.	Was soll gemessen werden? Hb-CO?		Kurze Erläuterung im Hintergrundtext.  Im Kapitel 2.5.1.1 wird bereits auf die verschiedenen Möglichkeiten der CO-Messung eingegangen: Verlinkung darauf wird eingefügt
21	<b>Tabakentwöhnung</b> 3.4 Strukturierte Entwöhnung im Akutkrankenhaus/im Rahmen der Rehabilitation  Empfehlung 3-8; S. 36 Bei rauchenden Patient*innen mit COPD soll bereits während eines (akut)stationären Aufenthaltes im Krankenhaus eine Tabakentwöhnung	Bei entwöhnungsbereiten Patient*innen mit COPD soll eine Verhaltenstherapie und bei entsprechendem Bedarf eine medikamentöse Entzugssyndrombehandlung nachdrücklich empfohlen und angeboten werden.	Die Empfehlung könnte etwas zurückhaltender formuliert werden. Keineswegs benötigen oder wünschen alle eine Entzugssyndrombehandlung. In den Studien zur medikamentösen Begleittherapie waren nur Patienten eingeschlossen, die nach entsprechender intensiver Aufklärung einer potentiellen Behandlung mit Psychopharmaka zugestimmt haben- meist solche mit vorherigen frustranen Absetzversuchen	Empfehlung nicht ändern.  Siehe Nr. 18

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	initiiert und eine anschließende ambulante Entwöhnungsbehandlung organisiert werden.			
22	<b>Tabakentwöhnung</b>  Empfehlung 3-9; S. 36 Rauchenden Patient*innen mit COPD, die eine Rehabilitationsmaßnahme wahrnehmen, soll im Rahmen der Rehabilitation ein strukturiertes Entwöhnungsprogramm (kognitive Verhaltenstherapie und medikamentöse Therapie) angeboten werden.	Rauchenden Patient*innen mit COPD, die eine Rehabilitationsmaßnahme wahrnehmen, soll im Rahmen der Rehabilitation ein strukturiertes Entwöhnungsprogramm (kognitive Verhaltenstherapie und bei entsprechendem Bedarf medikamentöse Therapie) angeboten werden.	Analog zu 3-4 [Keineswegs alle benötigen oder wünschen eine Entzugssyndrombehandlung. In den Studien zur medikamentösen Begleittherapie waren nur Patienten eingeschlossen, die nach entsprechender intensiver Aufklärung einer potentiellen Behandlung mit Psychopharmaka zugestimmt haben- meist solche mit vorherigen frustrierten Absetzversuchen]	Empfehlung nicht ändern.  Siehe Nr. 18
69	<b>Tabakentwöhnung</b>  Empfehlung 3-9; S. 36 Rauchenden Patient*innen mit COPD, die eine Rehabilitationsmaßnahme wahrnehmen, soll im Rahmen der Rehabilitation ein strukturiertes Entwöhnungsprogramm (kognitive Verhaltenstherapie und medikamentöse Therapie) angeboten werden.	Rauchenden Patient*innen mit COPD, die eine Rehabilitationsmaßnahme wahrnehmen, soll im Rahmen der Rehabilitation ein strukturiertes Entwöhnungsprogramm (kognitive Verhaltenstherapie und bei entsprechendem Bedarf medikamentöse Therapie) angeboten werden.	Keineswegs benötigen oder wünschen alle eine Entzugssyndrombehandlung.  In den Studien zur medikamentösen Begleittherapie waren nur Patienten eingeschlossen, die nach entsprechender intensiver Aufklärung einer potentiellen Behandlung mit Psychopharmaka zugestimmt haben- meist solche mit vorherigen frustrierten Absetzversuchen	Dopplung. Umgang siehe Nr. 22
24	<b>Tabakentwöhnung</b> 3.3. E-Zigaretten; S. 35  Stellenwert [...]. Andererseits hält sie mögliche Vorzüge einer harm reduction Therapie mittels E-Zigarette bei solchen Patient*innen für plausibel, die entweder trotz mehrerer Entwöhnungsversuche weiterhin rauchen oder die eine Therapie der Tabakabhängigkeit kategorisch ablehnen. Idealerweise bedarf die Therapie mittels E-Zigarette einer verhaltenstherapeutischen Beratung	Der Passus sollte gestrichen werden. Alternativ: Stattdessen in Anlehnung an die S3 LL Tabak: Gleichwohl ist der Leitliniengruppe bewusst, dass manche Raucher dieses Produkt nutzen, um ihren Tabakkonsum zu beenden. Sollte der Einsatz der E-Zigarette zur Unterstützung der Tabakabstinenz erwogen werden, dann nur nach dokumentierten Versagen oder Ablehnung anderer evidenzbasierter Maßnahmen sowie Aufklärung über bekannte Risiken bei gleichzeitiger Beendigung des Tabakkonsums und abgestimmter Folgetermine.	Wegen der hohen Wahrscheinlichkeit von dual use mit hohem Schädigungspotential ist eine harm reduction hier nicht plausibel.  Anfang September wurde dem ÄZQ bereits die Argumentation der DGP und das ERS Positionspapier sowie weitere Dokumente zugeleitet.  Die DGP vertritt mit allen bekannten pneumologischen Gesellschaften diese Meinung. Die DGP hat hierzu klar Stellung bezogen und dies zB auf der Homepage deutlich gemacht. <a href="https://pneumologie.de/fileadmin/user_upload/Aktuelles/2020-11-02_DGP_Stellungnahme_Tabakentwoehnung_mit_E-Zigarette.pdf">https://pneumologie.de/fileadmin/user_upload/Aktuelles/2020-11-02_DGP_Stellungnahme_Tabakentwoehnung_mit_E-Zigarette.pdf</a>	Der vorgeschlagene Text aus der öffentlichen Konsultation wird übernommen; der ursprüngliche Passus zur harm reduction (siehe 2. Spalte NVL) wird damit ersetzt: <i>Gleichwohl ist der Leitliniengruppe bewusst, dass manche Raucher dieses Produkt nutzen, um ihren Tabakkonsum zu beenden. Sollte der Einsatz der E-Zigarette zur Unterstützung der Tabakabstinenz erwogen werden, dann nur nach dokumentierten Versagen oder Ablehnung anderer evidenzbasierter Maßnahmen sowie Aufklärung über bekannte Risiken bei gleichzeitiger Beendigung des Tabakkonsums und abgestimmter Folgetermine.</i>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
				<ul style="list-style-type: none"> <li>- Der Hinweis über die verhaltenstherapeutische Beratung aus der ursprünglichen Textversion wird aufgenommen.</li> <li>- Die Formulierung „und abgestimmter Folgetermine“ wird redaktionell angepasst.</li> </ul>
25	<p><b>Tabakentwöhnung</b> 3.3. E-Zigaretten; S. 35</p> <p>„Aufgrund der aktuell unzureichenden Datenlage, und auch wegen der noch nicht abschätzbaren gesundheitlichen Langzeitfolgen für Patient*innen mit COPD, sieht die Leitliniengruppe in der E-Zigarette keine Option für einen primären Entwöhnungsversuch. Andererseits hält sie mögliche Vorzüge einer harm reduction Therapie mittels E-Zigarette bei solchen Patient*innen für plausibel, die entweder trotz mehrerer Entwöhnungsversuche weiterhin rauchen oder die eine Therapie der Tabakabhängigkeit kategorisch ablehnen.“</p>	Neue Empfehlung	Evtl. könnte hier eine zusätzliche Empfehlung eingefügt werden	<p>Nicht berücksichtigen.</p> <p>In den Diskussionen: bewusste Entscheidung der Gruppe, keine Empfehlung zu formulieren.</p>
26	<p><b>Tabakentwöhnung</b> 3.3. E-Zigaretten; S. 35</p> <p>„Aufgrund der aktuell unzureichenden Datenlage, und auch wegen der noch nicht abschätzbaren gesundheitlichen Langzeitfolgen für Patient*innen mit COPD, sieht die Leitliniengruppe in der E-Zigarette keine Option für einen primären Entwöhnungsversuch. Andererseits hält sie mögliche Vorzüge einer harm reduction Therapie mittels E-Zigarette bei solchen Patient*innen für plausibel, die entweder trotz mehrerer Entwöhnungsversuche weiterhin rauchen oder die eine Therapie der</p>	Die Befundlage hinsichtlich Wirkung und Risiken der E-Zigarette in der Tabakentwöhnung ist uneinheitlich mit Hinweisen auf ein Entwöhnungspotential und auf langfristige Risiken dieser neuen Produkte. E-Zigaretten sollten zur Reduktion des Zigarettenkonsums nicht angeboten werden.	[...] sind die pneumologischen Fachgesellschaften sich einig, dass die E-Zigarette nicht empfohlen wird. In der Anlage ein Dokument der Deutschen Gesellschaft für Pneumologie, welches eine Übersetzung der europäischen Fachgesellschaften ist. Weiter eine Empfehlung aus Australien. Positive Empfehlungen pneumologischer Fachgesellschaften zur EC sind nicht bekannt. Aus Sicht der DGP, mit der ich das Vorgehen abgestimmt habe, sollte daher der letzte Satz geändert werden. Wir würden vorschlagen „Die Befundlage hinsichtlich Wirkung und Risiken der E-Zigarette in der Tabakentwöhnung ist uneinheitlich mit Hinweisen auf ein Entwöhnungspotential und auf langfristige Risiken dieser neuen Produkte“. Und „E-Zigaretten sollten zur Reduktion des Zigarettenkonsums nicht	<p>Siehe Umgang zu Nr. 24.</p> <p>Nach Einarbeitung des neuen Passus wird der Textabschnitt nochmals in Gänze auf Plausibilität geprüft.</p> <p>Es wird darauf geachtet, dass eine eventuelle „sprachliche Verwirrung von harm reduction und Reduktion des Tabakkonsums“ vermieden wird.</p>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	Tabakabhängigkeit kategorisch ablehnen.“		angeboten werden“. Dies entspricht der bisher konsentierten Fassung der Tabakleitlinie, die allerdings nicht COPD-spezifisch ist.	
27	<b>Nicht-medikamentöse Therapie</b>  Tabelle 12, S. 38	Ergänzungspunkt für Barrieren. Neu aufnehmen: Ansteckungsgefahr	Wichtiger Punkt in Pandemiezeiten	Zusätzlichen Punkt in Tabelle 12 aufnehmen: • Angst vor Ansteckung
70	<b>Nicht-medikamentöse Therapie</b>  Tabelle 12, S. 38	Ergänzungspunkt für Barrieren. Neu aufnehmen: Ansteckungsgefahr	Wichtiger Punkt in Pandemiezeiten	Doppelt eingegangenes Kommentar. Umgang siehe Nr. 27
28	<b>Nicht-medikamentöse Therapie</b>  Empfehlung 4-11; S. 48 Nachschulungen sollen nach spätestens zwei Jahren angeboten werden	Nachschulungen sollten nach spätestens zwei Jahren angeboten werden	Aufgrund fehlender solider Evidenz nur sollte, zumal dies mit erheblichem Ressourcenverbrauch verbunden ist	Nach Diskussion der aktuellen Datenlage zum Thema wird beschlossen, die Empfehlungsformulierung der NVL Asthma anstelle der ursprünglichen Empfehlung zu übernehmen. Somit lautet die Empfehlung: <i>Nachschulungen sollen bei Bedarf angeboten werden.</i>  Im Hintergrundtext wird der Begriff Nachschulung entsprechend dem jeweiligen Bedarf der Patient*innen spezifizierter dargestellt (wann komplette Schulungen bzw. Teile wiederholt werden; Gruppensetting oder individuell; regelmäßige Erhebung des Bedarfes).  Ein Patientenblatt zum Thema wird erstellt.
71	<b>Nicht-medikamentöse Therapie</b>  Empfehlung 4-11; S. 48 Nachschulungen sollen nach spätestens zwei Jahren angeboten werden	Nachschulungen sollten nach spätestens zwei Jahren angeboten werden	Aufgrund fehlender solider Evidenz nur sollte, zumal dies mit erheblichem Ressourcenverbrauch verbunden ist	Doppelt eingegangenes Kommentar. Umgang siehe Nr. 28



Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
29	<b>Nicht-medikamentöse Therapie</b> 4.2. Atemphysiotherapie; ab S. 41	Bitte eingehen auf Hustentechniken.	Bei ca. 30% ist Husten das dominante Symptom. Es wird aber dominant auf Techniken zur Linderung der Dyspnoe bzw. der Sekretelimination eingegangen.	Nicht berücksichtigen.  - Verweis wird eingefügt: S. Weise, Peter Kardos, D. Pfeiffer-Kascha, H. Worth. Empfehlungen zur Atemphysiotherapie. Dustri Verlag, 3. Auflage, 2019  - Hustentechniken sind auf Seite 47 erwähnt (Vertiefende Informationen, Punkt 4). Die Sekretretention ist meist die Ursache des Hustens bei COPD. Eine besonders häufige Reizhustenproblematik, die noch gemeint sein könnte, wird für Patient*innen mit COPD nicht gesehen.
72	<b>Nicht-medikamentöse Therapie</b> 4.2. Atemphysiotherapie; ab S. 41	Bitte eingehen auf Hustentechniken.	Bei ca. 30% ist Husten das dominante Symptom. Es wird aber dominant auf Techniken zur Linderung der Dyspnoe bzw. der Sekretelimination eingegangen.	Doppelt eingegangenes Kommentar. Umgang siehe Nr. 29
30 (vorab)	<b>Nicht-medikamentöse Therapie</b> 4.2 Atemphysiotherapie  Tabelle 14; S. 45/46 • Hypertonus und Druckdolenz der Atemmuskeln	Wo und für welche Muskeln soll man eine Druckdolenz verspüren?		Muskelgruppen im Text benennen. <i>Erfahrungsgemäß häufig betroffen und leicht zu palpieren sind der z. B. M. trapezius, die autochtonen Rückenmuskeln, die Mm. pectorales, die Mm. scaleni und der M. sternocleidomastoideus. Der Hypertonus wird durch Druck im Bereich des Muskelbauches erfasst. Die Druckdolenzen finden sich in Muskelbauch oder -ansätzen.</i>
31	<b>Nicht-medikamentöse Therapie</b> 4.3 4.3 Patientenschulung und Selbstmanagement; S. 49  „Die Schulung wird in 6x60 Minuten durchgeführt und kann in der Praxis sowohl durch die behandelnden	Die Schulung kann von in einem Trainerseminar qualifizierten Team aus Ärztin und Helferin in der Praxis durchgeführt werden	Missverständlicher Text, da beide Personen in der Schulung notwendig sind.	Hintergrundtext wird angepasst:  <i>Vertiefende Informationen Auch COBRA (Chronisch obstruktive Bronchitis mit und ohne Emphysem) ist eines der ambulanten Schulungsprogramme für Patient*innen mit COPD und zählt zu den evaluierten und strukturierten Maßnahmen in diesem Kontext [130].</i>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	Ärzt*innen, als auch durch qualifizierte Mitarbeiter*innen vermittelt werden.“			<i>Wichtige Inhalte sind u.a. die Selbstkontrolle der Erkrankung sowie das Erlernen geeigneter Selbsthilfemaßnahmen. Die Schulung wird in 6x60 Minuten durchgeführt und kann in der Praxis durch ein qualifiziertes Team aus einem Arzt/ einer Ärztin und einem/r Mitarbeiter*in vermittelt werden. Voraussetzung für die Durchführung ist das erfolgreiche Absolvieren eines zertifizierten Trainer-Seminars.</i>
73	<b>Nicht-medikamentöse Therapie</b> 4.3 4.3 Patientenschulung und Selbstmanagement; S. 49  „Die Schulung wird in 6x60 Minuten durchgeführt und kann in der Praxis sowohl durch die behandelnden Ärzt*innen, als auch durch qualifizierte Mitarbeiter*innen vermittelt werden.“	Die Schulung kann von in einem Trainerseminar qualifizierten Team aus Ärztin und HelferIn in der Praxis durchgeführt werden	Missverständlicher Text, da beide Personen in der Schulung notwendig sind.	Doppelt eingegangenes Kommentar. Umgang siehe Nr. 31
32	<b>Nicht-medikamentöse Therapie</b> 4.4 Ernährung  Empfehlung 4-13; S. 49 Untergewichtige oder adipöse Patient*innen mit COPD sollen eine Ernährungsberatung erhalten.	Untergewichtige oder adipöse Patient*innen mit COPD sollen eine Ernährungsberatung angeboten bekommen.	Auch hier: die Empfehlung muss zu den Bedürfnissen der Patient*innen passen. Eine starke Empfehlung zur Gewichtsreduktion bei Adipösen ignoriert die Tatsache, dass die meisten Betroffenen sich mit ihrem Gewicht in irgendeiner Weise arrangiert haben. Zudem ist – zumindest bei Adipositas – die Evidenz für die Effizienz solcher Beratungen sehr relativ.	Redaktionelle Änderung Empfehlung 4-13 (entspricht Empfehlungsduktus der NVL): <i>Untergewichtigen oder adipösen Patient*innen mit COPD soll eine Ernährungsberatung angeboten werden.</i>
33	<b>Nicht-medikamentöse Therapie</b> 4.4 Ernährung  Empfehlung 4-12; S. 49 Krankheitsbedingt untergewichtigen Patient*innen mit COPD soll eine ausgewogene hochkalorische Nahrungsergänzung zur Erhöhung des Körpergewichtes empfohlen werden.	Krankheitsbedingt untergewichtigen Patient*innen mit COPD und normalgewichtigen Patient*innen mit COPD und krankheitsbedingter (Risiko für) Mangelernährung/Sarkopenie soll – im Rahmen einer individuellen, bedarfsgerechten Ernährungstherapie durch den dafür qualifizierten Gesundheitsfachberuf (Diätassistenten) – eine supportive, ggf. krankheitsspezifische, orale bilanzierte Ergänzungsnahrung wie Trinknahrung zur Erhöhung bzw. zum Erhalt des Körpergewichtes empfohlen werden.	Neben krankheitsbedingt untergewichtigen Patient*innen mit COPD sollen auch normalgewichtigen Patient*innen mit COPD und krankheitsbedingter (Risiko für) Mangelernährung/Sarkopenie [1-6], möglichst im Rahmen einer individuellen, bedarfsgerechten Ernährungstherapie [3,7-11], eine supportive, ggf. krankheitsspezifische, orale bilanzierte Ergänzungsnahrung wie Trinknahrung zur Erhöhung bzw. zum Erhalt des Körpergewichtes empfohlen werden [3,5-6,8-16]. Im Sinne einer patientensicheren, prozessgeleiteten Durchführung von Ernährungstherapie muss der dafür per	Empfehlung nicht ändern.  Die Empfehlung beruht auf einer systematisch durchgeführten Recherche zum Thema. Es konnte 1 Cochrane Review identifiziert werden (Ferreira 2012; siehe Hintergrundtext S. 50). Hier zeigten die gepoolten Daten aus 11 RCTs mit insgesamt 325 unterernährten Patient*innen eine statistisch signifikante Gewichtszunahme (MD 1.65 kg (95% KI 0,14; 3,16); I <sup>2</sup> = 17%, 11 RCTs, n = 325; Datenqualität

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
			<p>Berufsgesetz (DiätAssG §3) [17] qualifizierte Gesundheitsfachberuf der Diätassistenten ausdrücklich genannt werden. Zur Initiierung der Ernährungstherapie bedarf es der ärztlichen An- oder Verordnung. Ärzte selbst (Approbationsordnung für Ärzte § 27 ) [18] oder gar Medizinische Fachangestellte (Verordnung über die Berufsausbildung zum Medizinischen Fachangestellten / zur Medizinischen Fachangestellten vom 26. April 2006) [19] sind per Approbationsordnung bzw. per Berufsausbildung in diesem Arbeitsgebiet nicht ausgebildet und könnten im Arbeitsalltag einen solch aufwendigen Prozess nicht durchführen. Wenn eine orale bilanzierte Ergänzungsnahrung, die es in verschiedenen Zusammensetzungen, Konsistenzen, Energiedichten und ml-Mengen pro Packungseinheit gibt [6,13], verschrieben wird, sollte sie, unter Berücksichtigung möglicher vorliegender Komorbidität, optimal im personbezogenen Ernährungs- [7-11] und Gesamtrehabilitationskonzept passen [14-16], eine zu hohe zusätzliche Energiezufuhr durch Trinknahrung kann sich nachteilig auswirken [20].</p> <ol style="list-style-type: none"> <li>1. Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, et al. GLIM criteria for the diagnosis of malnutrition - A consensus report from the global clinical nutrition community. Clin Nutr 2019;38(1):1-9. DOI: 10.1016/j.clnu.2018.08.002</li> <li>2. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyere O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 2019;48(1):16-31. DOI: 10.1093/ageing/afy169</li> <li>3. Hauner H, Beyer-Reiners E, Bischoff G, Breidenassel C, Ferschke M, Gebhardt A, et al. Leitfaden Ernährungstherapie in Klinik und Praxis (LEKuP). Manual of Nutritional Therapy in Patient Care. Aktuel Ernährungsmed 2019;44(6):384-419. DOI: 10.1055/a-1030-5207</li> <li>4. Jensen GL, Cederholm T. The malnutrition overlap syndromes of cachexia and sarcopenia: a malnutrition conundrum. Am J Clin Nutr</li> </ol>	<p>moderat) zugunsten der Nahrungsergänzung. Wurden RCTs gepoolt, welche sowohl normalgewichtige, als auch untergewichtige Patient*innen mit COPD untersuchten, so konnte jedoch kein signifikanter Unterschied zwischen den Gruppen identifiziert werden (MD-1.28 kg (95% KI - 6,27; 3,72); I<sup>2</sup> = 56%, 3 RCTs, n=116).</p> <p>Die selektiv eingebrachte Literatur wurde gesichtet. Eine systematische Übersichtsarbeit (Nr. 15: Aldahir AM) konnte hierbei identifiziert werden. Es gab keinen Hinweis auf relevante klinische Verbesserungen. Da Aussagen zur Wirksamkeit möglichst auf RCT-Basis getroffen werden, wurden die angeführten Kohortenstudien nicht betrachtet.</p> <p>Es ist nicht definiert, was unter einem Risiko für Mangelernährung oder Sarkopenie zu verstehen ist. Die erweiterte Formulierung kann zu einer Ausweitung der Indikation führen.</p> <p>Zudem war die Formulierung eine bewusste Entscheidung der Gruppe, die Empfehlung nicht weiter zu spezifizieren.</p>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
			<p>2018;108(6):1157-8. DOI: 10.1093/ajcn/nqy314</p> <p>5. Barazzoni R, Bischoff SC, Breda J, Wickramasinghe K, Krznaric Z, Nitzan D, et al. ESPEN expert statements and practical guidance for nutritional management of individuals with SARS-CoV-2 infection. Clin Nutr 2020;39(6):1631-8. DOI: 10.1016/j.clnu.2020.03.022.</p> <p>6. Volkert D, Beck AM, Cederholm T, Cruz-Jentoft A, Goisser S, Hooper L, et al. ESPEN guideline on clinical nutrition and hydration in geriatrics. Clin Nutr 2019;38(1):10-47. DOI: 10.1016/j.clnu.2018.05.024</p> <p>7. Rondanelli M, Faliva MA, Peroni G, Infantino V, Gasparri C, Iannello G, et al. Food Pyramid for Subjects with Chronic Obstructive Pulmonary Diseases. Int J Chron Obstruct Pulmon Dis 2020;15:1435-48. DOI: 10.2147/COPD.S240561. assessment and therapy in COPD: a European Respiratory Society statement. Eur Respir J 2014;44(6):1504-20. DOI: 10.1183/09031936.00070914.</p> <p>8. Schols AM, Ferreira IM, Franssen FM, Gosker HR, Janssens W, Muscaritoli M, et al. Nutritional</p> <p>9. Schäfer C. Ernährungstherapie bei COPD. Ernährung im Fokus 2013;13(03-04):128-33.</p> <p>10. Collins PF, Yang IA, Chang YC, Vaughan A. Nutritional support in chronic obstructive pulmonary disease (COPD): an evidence update. J Thorac Dis 2019;11(Suppl 17):S2230-S7. DOI: 10.21037/jtd.2019.10.41.</p> <p>11. Meteling-Eeken M, Schilling-Maßmann B. Die Bestimmung des Energie- und Eiweißbedarfs in der Ernährungstherapie. Beispiel COPD: Maßarbeit ist gefragt. Ernährungs Umschau 2012;59(12):690-4.</p> <p>12. Ferreira IM, Brooks D, White J, Goldstein R. Nutritional supplementation for stable chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2012;12:CD000998. DOI: 10.1002/14651858.</p> <p>13. Kalde S. E&amp;P: Orale Supplemente im klinischen Alltag. Ernährungs Umschau 2015;62(11):S43-S6.</p>	

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
			<p>14. Korkmaz C, Demirbas S, Vatansev H, Yildirim E, Teke T, Zamani A. Effects of comprehensive and intensive pulmonary rehabilitation and nutritional support on quality of life and functional status in patients with chronic obstructive pulmonary disease. J Int Med Res 2020;48(4):300060520919567. DOI: 10.1177/0300060520919567.</p> <p>15. Aldhahir AM, Rajeh AMA, Aldabayan YS, Drammeh S, Subbu V, Alqahtani JS, et al. Nutritional supplementation during pulmonary rehabilitation in COPD: A systematic review. Chron Respir Dis 2020;17:1479973120904953. DOI: 10.1177/1479973120904953, with Editorial:</p> <p>16. van den Borst B. Nutritional supplementation during pulmonary rehabilitation in COPD: Do not expect an elixir of life but keep the hunger for more robust evidence. Chron Respir Dis 2020;17:1479973120904954. DOI: 10.1177/1479973120904954.</p> <p>17. Bundestag, Bundesrat. Gesetz über den Beruf der Diätassistentin und des Diätassistenten (Artikel 1 des Gesetzes über den Beruf der Diätassistentin und des Diätassistenten und zur Änderung verschiedener Gesetze über den Zugang zu anderen Heilberufen) (Diätassistentengesetz - Diät-AssG). Diätassistentengesetz vom 8. März 1994 (BGBl. I S. 446), das zuletzt durch Artikel 38 des Gesetzes vom 15. August 2019 (BGBl. I S. 1307) geändert worden ist. 2019. <a href="http://www.gesetze-im-internet.de/di_tassg_1994/DiätAssG.pdf">http://www.gesetze-im-internet.de/di_tassg_1994/DiätAssG.pdf</a></p> <p>18. Bundesministerium für Gesundheit. Approbationsordnung für Ärzte (ÄApprO 2002) Approbationsordnung für Ärzte vom 27. Juni 2002 (BGBl. I S. 2405), die zuletzt durch Artikel 3 des Gesetzes vom 16. März 2020 (BGBl. I S. 497) geändert worden ist. Berlin: Bundesministerium für Gesundheit; 2020.</p> <p>19. Bundesministerium für Gesundheit. Verordnung über die Berufsausbildung zum Medizinischen Fachangestellten/zur Medizinischen Fachangestellten vom 26. April 2006. Bundesgesetzblatt 2006;2006(22):1097-108.</p>	

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
34	<p><b>Nicht-medikamentöse Therapie</b> 4.4 Ernährung</p> <p>Empfehlung 4-13; S. 49 Untergewichtige oder adipöse Patient*innen mit COPD sollen eine Ernährungsberatung erhalten.</p>	<p>Untergewichtige oder adipöse Patient*innen mit COPD sowie normal- oder übergewichtigen Patient*innen mit COPD und einer krankheitsbedingten (Risiko für) Mangelernährung/ Sarkopenie sollen eine Ernährungstherapie zur Ernährungsoptimierung und Verbesserung des Ernährungszustandes durch den dafür qualifizierten Gesundheitsfachberuf (Diätassistenten) erhalten.</p>	<p>20. Broekhuizen R, Creutzberg EC, Weling-Scheepers CA, Wouters EF, Schols AM. Optimizing oral nutritional drink supplementation in patients with chronic obstructive pulmonary disease. Br J Nutr 2005;93(6):965-71.</p> <p>Neben untergewichtigen und adipösen Patient*innen mit COPD sollen auch normal- und übergewichtigen Patient*innen mit COPD und einer krankheitsbedingten (Risiko für) Mangelernährung/Sarkopenie eine Ernährungstherapie zur Ernährungsoptimierung [21] und Verbesserung des Ernährungszustandes erhalten [1-11,14]. Im Sinne einer patientensicheren, prozessgeleiteten Durchführung von Ernährungstherapie muss der dafür per Berufsgesetz (DiätAssG §3) [17] qualifizierte Gesundheitsfachberuf der Diätassistenten ausdrücklich genannt werden. Zur Initiierung der Ernährungstherapie bedarf es der ärztlichen An- oder Verordnung. Ärzte selbst (Approbationsordnung für Ärzte § 27) [18] oder gar Medizinische Fachangestellte (Verordnung über die Berufsausbildung zum Medizinischen Fachangestellten / zur Medizinischen Fachangestellten vom 26. April 2006) [19] sind per Approbationsordnung bzw. per Berufsausbildung in diesem Arbeitsgebiet nicht ausgebildet und könnten im Arbeitsalltag einen solch aufwendigen Prozess nicht durchführen. 21. van de Bool C, Mattijssen-Verdonschot C, van Melick PP, Spruit MA, Franssen FM, Wouters EF, et al. Quality of dietary intake in relation to body composition in patients with chronic obstructive pulmonary disease eligible for pulmonary rehabilitation. Eur J Clin Nutr 2014;68(2):159-65. DOI: 10.1038/ejcn.2013.257. Ernährungsberatung ist eine der möglichen Interventionsformen in der Ernährungstherapie und wird aus leistungsrechtlicher Perspektive als Beratung gesunder Menschen bezeichnet. Bei der Ernährungstherapie handelt es sich um eine Ernährungsintervention mit therapeutischer Ausrichtung, die sich folglich richtet an Menschen mit einer Erkrankung wie Patienten mit COPD und die Ernährungsberatung</p>	<p>Empfehlungsformulierung siehe Nr. 32 Bewusste Entscheidung der Gruppe, nicht näher auf die Therapie einzugehen bzw. dazu Stellung zu nehmen, was thematisch über eine Beratung hinausgeht. Darstellung der Evidenz siehe Nr.33</p>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
			<p>beinhalten kann [3,9,22].                      22. Buchholz D, Lang C. Entstehung und Definitionen. In: VDD-Leitlinie für die Ernährungstherapie und das prozessgeleitete Handeln in der Diätetik. Band 1. Manual für den German-Nutrition Care Process (G-NCP). Ein Standardwerk für die Durchführung, Weiterentwicklung, Überprüfung und Qualitätssicherung der Diätetik in Deutschland. Hrsg: Verband der Diätassistenten – Deutscher Bundesverband e. V (VDD). Lengerich: Pabst Science Publishers, 2015. ISBN: 978-3-95853-119-2</p>	
35	<p><b>Nicht-medikamentöse Therapie</b>                      4.4 Ernährung; S. 50</p> <p>„Generell ist eine Abnahme des Körpergewichts um &gt; 10 % in den letzten 6 Monaten oder um &gt; 5% im letzten Monat als Gewichtsverlust zu werten.“</p>	<p>Laut den Kriterien der Global Leadership Initiative on Malnutrition (GLIM) 2019 ist eine ungewollte Abnahme des Körpergewichts &gt; 5 % in den letzten 6 Monaten oder &gt; 10 % in &gt; 6 Monaten als Gewichtsverlust zu werten.</p>	<p>Es sollen weltweit die gleichen Konsensus-Diagnosekriterien für Mangelernährung angewendet werden [1], die Leitlinie zur Diagnostik und Therapie von Patienten COPD 2018 [23] ist diesbezüglich veraltet. 23. Vogelmeier C, Buhl R, Burghuber O, Criege CP, Ewig S, Godnic-Cvar J, et al. [Guideline for the Diagnosis and Treatment of COPD Patients - Issued by the German Respiratory Society and the German Atemwegsliga in Cooperation with the Austrian Society of Pneumology]. Pneumologie 2018;72(4):253-308. DOI: 10.1055/s-0043-125031</p>	<p>Hintergrundtext entsprechend vorgeschlagener Textänderung anpassen.</p>
36	<p><b>Nicht-medikamentöse Therapie</b>                      4.4 Ernährung; S. 50</p> <p>„Die Definitionen für eine krankhaft bedingte Gewichtsabnahme werden in einer selektiv eingebrachten Studie [131] für Patient*innen mit COPD differenzierter dargestellt: Die hier formulierte Konsensusdefinition für Kachexie beinhaltet einen Gewichtsverlust von &gt; 5% in 12 Monaten oder einen niedrigen BMI (&lt; 20 kg/m<sup>2</sup>) zusätzlich zu drei von fünf der Kriterien verringerten Muskelkraft, Müdigkeit, Magersucht, niedrigem FFMI (fat-free-mass-index) und erhöhten Entzündungswerten.“</p>	<p>Die Definitionen für eine krankhaft bedingte Gewichtsabnahme werden in einer selektiv eingebrachten Studie [131] für Patient*innen mit COPD differenzierter dargestellt: Die hier formulierte Konsensusdefinition 2008 für Kachexie beinhaltete einen Gewichtsverlust von &gt; 5% in 12 Monaten oder einen niedrigen BMI (&lt; 20 kg/m<sup>2</sup>) zusätzlich zu drei von fünf der Kriterien verringerten Muskelkraft, Müdigkeit, Magersucht, niedrigem FFMI (fat-free-mass-index) und erhöhten Entzündungswerten.</p>	<p>Die Konsensusdefinition für Kachexie wurde 2008 formuliert [24], heutzutage sollten allererst die GLIM-Kriterien 2019 angewendet werden [1,4].                      24. Evans WJ, Morley JE, Argiles J, Bales C, Baracos V, Guttridge D, et al. Cachexia: a new definition. Clin Nutr 2008;27(6):793-9. DOI: 10.1016/j.clnu.2008.06.013. Was wird hier unter eine niedrige BMI verstanden? Deshalb Angabe übereinstimmend mit [24]. „einer 3/5“ war nicht deutlich, deshalb Korrektur in Übereinstimmung mit [24].</p>	<p>Hintergrundtext entsprechend vorgeschlagener Textänderung anpassen.</p>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
37	<p><b>Nicht-medikamentöse Therapie</b> 4.4 Ernährung; S. 50</p> <p>„Ein bereits vor Beginn der Erkrankung bzw. Diagnosestellung bestehender niedriger BMI ist keine Indikation für eine Nahrungssupplementierung.“</p>	<p>Ein bereits vor Beginn der Erkrankung bzw. Diagnosestellung bestehender niedriger BMI ist keine Indikation für eine Nahrungssupplementierung. Zur frühzeitigen Erkennung einer Mangelernährung oder eines Risikos für Mangelernährung ist bei allen COPD-Patient*innen ein regelmäßiges Screening mit einer validierten, schnell durchzuführenden Methode notwendig (<a href="https://www.dgem.de/screening">https://www.dgem.de/screening</a>). Im Krankenhaus soll das Screening standardmäßig bei Aufnahme und anschließend wöchentlich durchgeführt werden, in der Langzeitpflege soll das Screening mindestens alle 3 Monate erfolgen. In Haus- bzw. Facharztpraxen wird ein zumindest jährliches Screening empfohlen, wobei es sich anbietet Follow-Up-Untersuchungen in den Wochen 1 bis 4 nach Exazerbation und weitere Reevaluation 12-16 Wochen nach Exazerbation auch für Screening auf Mangelernährung(srisiko) zu nutzen. Bei positiver Screening soll anschließender Diagnostik (GLIM-Kriterien 2019 und ggf. zusätzlich für Sarkopenie die Kriterien der European Working Group on Sarcopenia in Older People 2019 (EWGSOP2)) stattfinden. Wenn Mangelernährung vorliegt, ist Ernährungstherapie notwendig.</p>	<p>Durch Screening mit einer validierten, einfach und schnell durchzuführenden Methode sollen Patienten mit einem Mangelernährungsrisiko oder bereits vorliegender Mangelernährung frühzeitig erkannt werden (<a href="https://www.dgem.de/screening">https://www.dgem.de/screening</a>). Im Krankenhaus soll das Screening routinemäßig bei Aufnahme und danach in wöchentlichen Intervallen erfolgen, in der Langzeitpflege mindestens alle 3 Monate. In Haus- bzw. Facharztpraxen wird insbesondere bei älteren Patienten in Abhängigkeit vom Gesundheitszustand ein zumindest jährliches Screening empfohlen.“ [3, S. 391]] Laut COPD-Leitlinie [23] finden Follow-Up-Untersuchungen in den Wochen 1 bis 4 nach Exazerbation und ggf. weitere Reevaluation 12-16 Wochen nach Exazerbation statt. Es bietet sich bei der „Evaluation der klinischen Situation“ an auch auf Mangelernährung(srisiko) zu screenen. Es sollen weltweit die gleichen Konsensus-Diagnosekriterien für Mangelernährung und Sarkopenie angewendet werden [1-4]. Mangelernährung sollte rechtzeitig festgestellt und behandelt werden [1,3 (S. 391), 5,6,9,25, DGEM-Leitlinien, weitere ESPEN-Leitlinien]. 25. Cederholm T, Barazzoni R, Austin P, Ballmer P, Biolo G, Bischoff SC, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. Clin Nutr 2017;36(1):49-64. DOI: 10.1016/j.clnu.2016.09.004.</p>	<p>Keine Änderung.</p> <p>Thema ist nicht in der Gruppe diskutiert / nicht als Versorgungsproblem wahrgenommen worden. Keine Daten für Nutzen des Screenings.</p>
38	<p><b>Nicht-medikamentöse Therapie</b> 4.4 Ernährung; S. 50</p> <p>Rationale „Die Leitliniengruppe schätzt die Evidenz so ein, dass sie prinzipiell den Vorteil von gewichtsfördernden Maßnahmen bei krankheitsbedingt untergewichtigen Menschen mit COPD belegt. Gleichwohl empfiehlt sie ausdrücklich nicht die in einigen Studien untersuchte Gabe von Steroiden oder</p>	<p>Ergänzung: hochkalorische Nahrungsergänzung und den Einsatz vieler kleiner Mahlzeiten am Tage</p>		<p>Um die evidenzbasierte Aussage der Rationale (hochkalorische Nahrungsergänzung) von der praktischen Erfahrung abzugrenzen, wird ein zusätzlicher Satz für den Hintergrundtext formuliert. Dieser kann dann lauten:</p> <p><i>Hinweis: Erfahrungsgemäß kann man den Patient*innen zur Gewichtsförderung zusätzlich auch den Einsatz mehrerer kleiner</i></p>



Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	Wachstumshormonen, sondern spricht sich für eine hochkalorische Nahrungsergänzung aus, um Gewichtszunahme zu fördern. Angesichts des deutlichen Zusammenhangs zwischen Prognose und Untergewicht sowie dem prinzipiellen Benefit der Gewichtsförderung spricht die Leitliniengruppe eine starke Empfehlung aus“			<i>Mahlzeiten am Tage sowie das Aufnehmen von fester Nahrung vor dem Trinken vorschlagen.</i>
39	<p><b>Nicht-medikamentöse Therapie</b> 4.4 Ernährung; S. 50</p> <p>Rationale „Die Leitliniengruppe geht davon aus, dass stark über- und untergewichtige Patient*innen mit COPD von einer Ernährungsberatung profitieren, um danach zu prüfen, welche Lebensstilmaßnahmen in ihrem individuellen Fall geeignet sein können.“</p>	Die Leitliniengruppe geht davon aus, dass sowohl stark über- und untergewichtige Patient*innen mit COPD, als auch normal- und leicht bis mäßig übergewichtige Patient*innen mit COPD und krankheitsbedingter (Risiko für) Mangelernährung von einer individuellen Ernährungstherapie zur Ernährungsoptimierung und Verbesserung des Ernährungszustandes profitieren, um danach zu prüfen, welche Lebensstilmaßnahmen in ihrem individuellen Fall geeignet sein können.	Laut Konsensuskriterien und Leitlinien sollen auch Patient*innen mit krankheitsbedingter (Risiko für) Mangelernährung eine Ernährungstherapie bekommen [1-3,6]. Generell: DGEM-Leitlinien: <a href="https://www.dgem.de/leitlinien">https://www.dgem.de/leitlinien</a> ESPEN-Guidelines: <a href="https://www.espen.org/guidelines-home/espen-guidelines">https://www.espen.org/guidelines-home/espen-guidelines</a> COPD geht häufig mit Begleiterkrankungen einher [8,9,23], die durch eine lebenslange Einhaltung ernährungstherapeutischer Maßnahmen günstig zu beeinflussen sind [3]. Deshalb sollten COPD-Patienten eine individuelle Ernährungstherapie [9,19,23] zur Ernährungsoptimierung [18,26] und Verbesserung des Ernährungszustandes [1,7-10,14] im multidisziplinären Rahmen nicht vorenthalten werden. Diesbezügliche gute Studien, unter anderem unter Berücksichtigung der neueren Erkenntnissen zum Qualität der Makronährstoffen [3,7,9], sind dringend erforderlich [7,8,16]. 26. McLoughlin RF, McDonald VM, Gibson PG, Scott HA, Hensley MJ, MacDonald-Wicks L, et al. The Impact of a Weight Loss Intervention on Diet Quality and Eating Behaviours in People with Obesity and COPD. <i>Nutrients</i> 2017;9(10). DOI: 10.3390/nu9101147. Siehe für Ernährungsberatung versus Ernährungstherapie unter Punkt 2.	Keine Änderung.  Siehe Nr. 34
40	<p><b>Nicht-medikamentöse Therapie</b> 4.6.3 Therapie der respiratorischen Insuffizienz Typ II; S. 54</p>	Diskussion und Ergänzung der Literatur	Die Literaturstellen [144,145] sind von 2013 und 2014, also eher alt, während es aktuelle Evidenz-Bewertungen von der ERS gibt. Ergan E et al, European Respiratory Society guidelines	Keine Änderung.  Die Gruppe hat die Daten der Cochrane Reviews geprüft und als gültig befunden. Die hier vorgeschlagene Literatur ist eine

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	„Zudem wurden in der strukturierten Recherche nach aggregierter Evidenz zwei Cochrane-Reviews identifiziert [144,145]“.		on long-term home non-invasive ventilation for management of COPD, Eur Respir J 2019; 54: 1901003, <a href="https://doi.org/10.1183/13993003.01003-2019">https://doi.org/10.1183/13993003.01003-2019</a> Diese Literaturstelle soll aufgenommen werden.	Leitlinie (nicht aus dem deutschen Kontext) und keine Evidenz. Die Begründung für die dazugehörige Empfehlung 4-18 basiert insbesondere auf einem Expert*innenkonsens inklusive Abgleich mit der S2k-Leitlinie Nichtinvasive und invasive Beatmung als Therapie der chronischen respiratorischen Insuffizienz.
74	<b>Nicht-medikamentöse Therapie</b> 4.6.3 Therapie der respiratorischen Insuffizienz Typ II; S. 54  „Zudem wurden in der strukturierten Recherche nach aggregierter Evidenz zwei Cochrane-Reviews identifiziert [144,145]“.	Diskussion und Ergänzung der Literatur	Die Literaturstellen [144,145] sind von 2013 und 2014, also eher alt, während es aktuelle Evidenz-Bewertungen von der ERS gibt. Ergan E et al, European Respiratory Society guidelines on long-term home non-invasive ventilation for management of COPD, Eur Respir J 2019; 54: 1901003, <a href="https://doi.org/10.1183/13993003.01003-2019">https://doi.org/10.1183/13993003.01003-2019</a> Diese Literaturstelle soll aufgenommen werden.	Doppelt eingegangenes Kommentar. Umgang siehe Nr. 40
41 (vorab)	<b>Medikamentöse Therapie</b> Ab S. 58	Wäre es nicht sinnvoll in diesem Abschnitt eine Excel-Tabelle mit allen Substanzen der jeweiligen Gruppe (LAMA, LABA, ICS, SAMA, SABA) aufzulisten als Hilfestellung für Nutzer der Leitlinie?? Vielleicht auch an einer anderen Stelle		Keine Änderung.  Eine fortlaufende Aktualisierung ist nicht zu gewährleisten.
42	<b>Medikamentöse Therapie</b>  Abbildung 4; S. 58 u. a. SAMA zur Symptomkontrolle bei leichter bis mittelgradiger Symptomatik	SAMA streichen	Es gibt Hinweise auf eine erhöhte Kardiotoxizität dieser Medikamentengruppe – anders als bei LAMA. Singh S, Loke Y, Furberg C. Inhaled anticholinergics and risk of major adverse cardiovascular events in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis . JAMA 2008;300:1439-50. doi: 10.1001/jama.300.12.1439	SAMA im Algorithmus belassen. Keine Änderung.  Studie wird von Experten eher als schwach eingeschätzt. Betrifft auch SABA und sollte nicht prinzipiell dazu führen, bedarfsorientiert Medikation bei leichter Symptomatik auszuschließen.
43	<b>Medikamentöse Therapie</b> 5.2.2.2 Triple-Therapie; S. 61/62  Auszug Evidenz: Ferguson et. al (KRONOS, n = 1902, Verzerrungsrisiko (RoB): 2x gering/5x	Erweiterung des Abschnitts Evidenzbeschreibung durch Text zur ETHOS Studie: Rabe et al. (Rabe et al., Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD, N Engl J Med. 2020 Jul 2;383(1):35-48. doi: 10.1056/NEJMoa1916046) untersuchten die klinische	Wichtige neue Evidenz für die COPD Therapie fehlt, Literatur im Text und: 1. Rabe et al., Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD, N Engl J Med. 2020 Jul 2;383(1):35-48. doi: 10.1056/NEJMoa1916046	Aufnahme in Hintergrundtext: <i>Nach Abschluss der Recherche zum Thema wurde ein weiterer RCT zum Thema publiziert, welcher diese Ergebnisse bestätigt [Rabe et al. 2020]</i>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	<p>unklar [168] untersuchten die Effekte der Triple-Therapie (Budesonid/Glykopyrronium/Formoterol) im Vergleich zu LAMA/LABA (Glykopyrronium/Formoterol) und LABA/ICS (Budesonid/Formoterol) bei Patient*innen mit symptomatischer COPD (n=1902). Stattgehabte Exazerbationen im vorausgegangenen Jahr waren keine Einschlussbedingung. Bei Behandlung mit der Triple-Therapie (n=640) zeigte sich eine reduzierte Exazerbationsrate von 0,46 pro Jahr im Vergleich zu LAMA/LABA (signifikant; Exazerbationsrate 0,95 /Jahr; n=627) und auch zu LABA/ICS (nicht signifikant; Exazerbationsraten 0,56/Jahr für MDI, n=316 bzw. 0,55/Jahr für DPI, n=319). In Subgruppenanalysen ergaben sich Hinweise auf einen möglichen Benefit erst ab einer Baseline-Eosinophilenzahl von 75-100 cells/mm<sup>3</sup>, wenn eine LAMA/LABA-Behandlung mit ICS eskaliert wird...</p>	<p>Wirksamkeit der Triple-Kombination Budesonid/Glykopyrronium/Formoterolfumarat in zwei verschiedenen ICS-Dosierungen (160 bzw. 320 µg) im Vergleich mit Glykopyrronium/Formoterolfumarat oder Budesonid/Formoterolfumarat an Patienten mit moderater bis sehr schwerer COPD nach prospektiver Stratifizierung von eosinophilen Granulozyten (ETHOS, n=8572). Primärer Endpunkt der Studie war die Rate moderater und schwerer Exazerbationen. Weitere Endpunkte waren COPD-Symptomatik, Lebensqualität, Gesamtmortalität sowie Sicherheitsparameter. Unter beiden Triple-Therapien zeigte sich eine statistisch signifikante Reduktion an moderaten/schweren Exazerbationen (320 µg Budesonid 1,08; 160 µg Budesonid 1,07) gegenüber LAMA/LABA (1,42; Rate ratio Dreifachtherapie 320 µg Budesonid: 0,76 (95% KI 0,69; 0,83); relative Risikoreduktion 24%; Rate ratio Dreifachtherapie 160 µg Budesonid: 0,75 (95% KI 0,69; 0,83); relative Risikoreduktion 25% Unterschied) und gegenüber ICS/LABA (1,24; Rate ratio Dreifachtherapie 320 µg Budesonid: 0,87 (95% KI 0,79; 0,95); relative Risikoreduktion 13%; Rate ratio Dreifachtherapie 160 µg Budesonid: 0,86 (95% KI 0,79; 0,95); relative Risikoreduktion 14%). Die Number-needed-to-treat zur Vermeidung einer moderaten/schweren Exazerbation war für beide ICS-Tripeldosierungen 3 gegenüber der LAMA/LABA und 7 bzw. 6 gegenüber der ICS/LABA Kombination (Rabe et al., COPD exacerbation benefits relative to pneumonia risk with budesonide/glycopyrronium/formoterol metered dose inhaler: analyses from ETHOS, European Respiratory Journal 2020 56: 5230; DOI: 10.1183/13993003.congress-2020.5230). Gegenüber ICS/LABA zeigte die 320 µg ICS-Tripeldosierung außerdem eine signifikante Reduktion der Rate an COPD-bedingten Krankenhauseinweisungen. Die Verringerung der Exazerbationsrate durch die Tripel-Therapie war generell unabhängig davon, ob die Patienten in der Vorbehandlung ICS erhalten hatten. Das Ausmaß der Exazerbationsrisikoreduzierung stieg mit höheren Eosinophilen-Spiegel. So nahm der Exazerbationsvorteil bei Patienten mit ≥150 eosinophilen Granulozyten/µl Blut unter der Dreifachkombination versus der LAMA/LABA</p>	<p>2. Rabe et al., COPD exacerbation benefits relative to pneumonia risk with budesonide/glycopyrronium/formoterol metered dose inhaler: analyses from ETHOS, European Respiratory Journal 2020 56: 5230; DOI: 10.1183/13993003.congress-2020.5230; 3. Martinez et al., Budesonide/Glycopyrrolate/Formoterol Fumarate Metered Dose Inhaler (BGF MDI) All-Cause Mortality Versus LAMA/LABA in COPD: Sensitivity Analysis of All-Cause Mortality (Secondary Endpoint) in the ETHOS Trial with Final Retrieved Vital Status Data; <a href="https://doi.org/10.1164/ajrccm-conference.2020.201.1_MeetingAbstracts.A4214">https://doi.org/10.1164/ajrccm-conference.2020.201.1_MeetingAbstracts.A4214</a>, American Journal of Respiratory and Critical Care Medicine 2020;201:A4214</p>	

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
		<p>Zweifachkombination signifikant zu. Im Studienarm der 320 µg ICS Triple-Therapie zeigte sich zudem eine signifikante Reduktion der Gesamt mortalität um 49% (nicht adjustierter p-Wert 0,0035) gegenüber dem LAMA/LABA Arm (Martinez et al., Budesonide/Glycopyrrrolate/Formoterol Fumarate Metered Dose Inhaler (BGF MDI) All-Cause Mortality Versus LAMA/LABA in COPD: Sensitivity Analysis of All-Cause Mortality (Secondary Endpoint) in the ETHOS Trial with Final Retrieved Vital Status Data; <a href="https://doi.org/10.1164/ajrccm-conference.2020.201.1_MeetingAbstracts.A4214">https://doi.org/10.1164/ajrccm-conference.2020.201.1_MeetingAbstracts.A4214</a>, American Journal of Respiratory and Critical Care Medicine 2020;201:A4214).</p>		
44	<p><b>Medikamentöse Therapie</b> 5.2.2.2 Triple-Therapie; S. 62</p> <p>Rationale Auf Basis der identifizierten Evidenz und klinischer Überlegungen sieht die Leitliniengruppe in der Triple-Therapie eine Möglichkeit der Therapie- eskalation für Patient*innen mit COPD, bei welchen – trotz Therapie mit einer LAMA/LABA- Kombination - weiterhin Exazerbationen vorrangig sind. Bei Patient*innen ohne Exazerbationen hat die Triple-Therapie dagegen keinen Stellenwert, da der Effekt auf die Symptomatik kaum untersucht wurde und nicht plausibel erscheint. Insbesondere bei einer höheren Eosinophilenzahl im Differentialblutbild sieht die Leitliniengruppe eine mögliche Indikation für die zusätzliche Gabe eines ICS (siehe den folgenden Abschnitt). Anhalts-punkte für ein eventuell erhöhtes Ansprechen auf die inhalative Steroidgabe können - neben der erhöhten Eosinophilenzahl – ein diagnostisch gesichertes</p>	<p>Ergänzung der Rationale durch</p> <p>Hinzuzufügen ist, dass Studien in den letzten Jahren eine reduzierte Mortalität mit Triple-Therapien im Vergleich zu LAMA, LABA/LAMA oder LABA/ICS gezeigt haben (Lipson et al., Am J Respir Crit Care Med. 2020 Jun 15;201(12):1508-1516. doi: 10.1164/rccm.201911-2207OC. Reduction in All-Cause Mortality with Fluticasone Furoate/Umeclidinium/Vilanterol in Patients with Chronic Obstructive Pulmonary Disease; Fabri et al., Reduction in fatal events with extrafine inhaled corticosteroid (ICS)-containing medications: results of stratified safety pooled analysis of the TRILOGY, TRINITY and TRIBUTE studies, European Respiratory Journal 2018 52: OA1659; DOI: 10.1183/13993003.congress-2018.OA1659; Rabe et al., Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD, N Engl J Med. 2020 Jul 2;383(1):35-48. doi: 10.1056/NEJMoa1916046; Global strategy for diagnosis, management, and prevention of chronic obstructive pulmonary disease 2021 Report. <a href="https://goldcopd.org/wp-content/uploads/2020/11/GOLD-REPORT-2021-v1.0-16Nov20_WMv.pdf">https://goldcopd.org/wp-content/uploads/2020/11/GOLD-REPORT-2021-v1.0-16Nov20_WMv.pdf</a>). Im Gegensatz zu früheren Studien zielen die jüngsten Studien auf Patientenpopulationen mit stärkerer Symptomatik und häufigen und/oder schweren Exazerbationen in der Vorgeschichte.</p>	<p>Wichtige neue Evidenz zur Mortalitätsreduktion bei der COPD noch nicht erwähnt, Literatur im Text und:</p> <ol style="list-style-type: none"> <li>1. Lipson et al., Am J Respir Crit Care Med. 2020 Jun 15;201(12):1508-1516. doi: 10.1164/rccm.201911-2207OC. Reduction in All-Cause Mortality with Fluticasone Furoate/Umeclidinium/Vilanterol in Patients with Chronic Obstructive Pulmonary Disease;</li> <li>2. Fabri et al., Reduction in fatal events with extrafine inhaled corticosteroid (ICS)-containing medications: results of stratified safety pooled analysis of the TRILOGY, TRINITY and TRIBUTE studies, European Respiratory Journal 2018 52: OA1659; DOI: 10.1183/13993003.congress-2018.OA1659;</li> <li>3. Rabe et al., Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD, N Engl J Med. 2020 Jul 2;383(1):35-48. doi: 10.1056/NEJMoa1916046;</li> <li>4. Global strategy for diagnosis, management, and prevention of chronic obstructive pulmonary disease 2020 Report. 2020 [cited: 2020-01-30]. <a href="https://goldcopd.org/wp-content/uploads/2019/12/GOLD-2020-FINAL-ver1.2-03Dec19_WMv.pdf">https://goldcopd.org/wp-content/uploads/2019/12/GOLD-2020-FINAL-ver1.2-03Dec19_WMv.pdf</a>).</li> </ol>	<p>Nicht berücksichtigen.</p> <p>Darstellung der Effektstärke erfolgt in NVL COPD in der Evidenzbeschreibung.</p> <p>Zitierte Literatur: - Lipton et al.: Reduction in All-Cause Mortality = Posthoc-Analyse. Dieser Endpunkt wurde vorab nicht angegeben (siehe <a href="https://clinicaltrials.gov/ct2/show/study/NCT02164513">https://clinicaltrials.gov/ct2/show/study/NCT02164513</a>); in Primäranalysen nicht betrachtet. - Fabri et al.: Kongressbeitrag - Rabe et al.: im Hintergrundtext erwähnt (siehe Nr. 43)</p>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	Asthma oder eine Atopie, erhebliche Variationen der FEV1 über einen längeren Zeitraum (mindestens 400ml), oder eine über den Tag erhebliche Variation des maximal expiratorischen Flusses (mindestens 20%) sein [12].			
45	<b>Medikamentöse Therapie</b> 5.2.2.2 Triple-Therapie; S. 62	Ergänzung Bitte aufnehmen: K.F. Rabe et al. N. Engl. J. Med.383:35-48 (2020) <a href="https://www.nejm.org/doi/10.1056/NEJMoa1916046">https://www.nejm.org/doi/10.1056/NEJMoa1916046</a>	Wichtige neue Arbeit zur Triple Therapie	Aufnahme in Hintergrundtext Nach Abschluss der Recherche zum Thema wurde ein weiterer RCT zum Thema publiziert, welcher diese Ergebnisse bestätigt [Rabe et al. 2020]  siehe Nr. 43:
75	<b>Medikamentöse Therapie</b> 5.2.2.2 Triple-Therapie; S. 62	Ergänzung Bitte aufnehmen: K.F. Rabe et al. N. Engl. J. Med.383:35-48 (2020) <a href="https://www.nejm.org/doi/10.1056/NEJMoa1916046">https://www.nejm.org/doi/10.1056/NEJMoa1916046</a>	Wichtige neue Arbeit zur Triple Therapie	Doppelt eingegangenes Kommentar. Umgang siehe Nr. 45
46	<b>Medikamentöse Therapie</b> 5.2.2.2  Vertiefende Informationen Eosinophilenzahl – Cut-Off; S. 63 „Um einen möglichen Cut-Off der Eosinophilen für oder gegen den Einsatz von ICS zu ermitteln, wurde eine zusätzliche systematische Recherche durchgeführt. Es konnten 3 RCTs identifiziert werden [172–174], die das Ansprechen auf eine Steroidgabe abhängig von der Eosinophilenzahl im Blut oder Sputum untersuchten. Die Fragestellung nach einem Cut-Off konnte mit dieser Recherche nicht eindeutig beantwortet werden, jedoch zeigten sich auch hier Hinweise für eine möglicherweise erhöhte Steroidwirkung bei höheren Eosinophilen-	Um einen möglichen Cut-Off der Eosinophilen für oder gegen den Einsatz von ICS zu ermitteln, wurde eine zusätzliche systematische Recherche durchgeführt. Es konnten 4 RCTs identifiziert werden [172–174, Rabe et al., Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD, N Engl J Med. 2020 Jul 2;383(1):35-48. doi: 10.1056/NEJMoa1916046+Supplement to: Rabe KF, Martinez FJ, Ferguson GT, et al. Triple inhaled therapy at two glucocorticoid doses in moderate-to-very-severe COPD. N Engl J Med 2020;383:35-48. DOI: 10.1056/NEJMoa1916046], die das Ansprechen auf eine Steroidgabe abhängig von der Eosinophilenzahl im Blut oder Sputum untersuchten. Die Fragestellung nach einem Cut-Off konnte mit dieser Recherche nicht eindeutig beantwortet werden, jedoch zeigten sich auch hier Hinweise für eine möglicherweise erhöhte Steroidwirkung bei höheren Eosinophilen-	Wichtige neue Evidenz zum Eosinophilenzahl – Cut-Off für ICS-Therapie-Ansprechen bei der COPD noch nicht erwähnt, Literatur im Text und: 1. Rabe et al., Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD, N Engl J Med. 2020 Jul 2;383(1):35-48. doi: 10.1056/NEJMoa1916046; 2. Supplement to: Rabe KF, Martinez FJ, Ferguson GT, et al. Triple inhaled therapy at two glucocorticoid doses in moderate-to-very-severe COPD. N Engl J Med 2020;383:35-48. DOI: 10.1056/NEJMoa1916046	Nicht annehmen (da nicht systematisch gesucht), jedoch Umgang gleich wie vorgeschlagen zur Triple Therapie.  - Im Hintergrundtext anpassen: <i>Ein nach Abschluss der systematischen Recherche selektiv eingebrachter RCT [Rabe et. al + Supplement] bestätigt diese Ergebnisse.</i>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	zahlen. Nach Einschätzung der Leitliniengruppe handelt es sich dementsprechend um fließende Übergänge. Es ergeben sich jedoch Hinweise aus den Subgruppen- und Post-hoc-Analysen, dass eine Eosinophilenzahl > 300 cells/µl im Differentialblut für ein möglicherweise besseres Ansprechen auf inhalative Steroide spricht. Steroidnaive Patient*innen mit gemessenen Eosinophilen < 100 cells/µl haben hingegen womöglich keinen zusätzlichen Nutzen von einer ICS-Gabe.“	aus der vorliegenden Evidenz, dass eine Eosinophilenzahl >150 Zellen/µl im Differentialblut für ein möglicherweise besseres Ansprechen auf inhalative Steroide spricht.		
47	<b>Medikamentöse Therapie</b> 5.3 Inhalationssysteme  Vertiefende Informationen; S. 65 Inhalationssysteme werden in Dosieraerosole, Pulverinhalatoren und elektrische Vernebler zur Feuchtinhalation unterschieden	Inhalationssysteme werden in Dosieraerosole, Pulverinhalatoren, Sprühvernebler und elektrische Vernebler zur Feuchtinhalation unterschieden	Die Klasse der Sprühvernebler ist ein etabliertes und eigenständiges Inhalationssystem mit von anderen Devices unterschiedlichen Charakteristika und Anforderungen an Patienten. Sowohl das aktuelle GOLD-Positionspapier, als auch die deutsche Atemwegsliga führen Sprühvernebler als eigene Device-Klasse (Sprühvernebler/Soft Mist Inhalatoren/Respimat). Sprühvernebler unterscheiden sich in ihrer Funktionsweise deutlich von Dosieraerosolen, Trockenpulverinhalatoren und elektrischen Verneblern und sollten als viertes Inhalationssystem eingruppiert werden. (Quellen: Wachtel et al. Respir Drug Deliv 2020;195-204; Ciciliani et al. Int J Chron Obstruct Pulmon Dis. 2017 May 26;12:1565-1577.; Fachinformation Spiolto Respimat, Stand: Dez. 2018; Fachinformation Spiriva Respimat, Stand: Okt. 2018; Fachinformation Striverdi Respimat, Stand: Okt. 2018; GOLD 2020: <a href="https://goldcopd.org/wp-content/uploads/2019/12/GOLD-2020-FINAL-ver1.2-03Dec19_WMV.pdf">https://goldcopd.org/wp-content/uploads/2019/12/GOLD-2020-FINAL-ver1.2-03Dec19_WMV.pdf</a> ; Deutsche Atemwegsliga: <a href="https://www.atemwegsliga.de/respimat.html">https://www.atemwegsliga.de/respimat.html</a> )	Anpassung im Hintergrundtext.
48	<b>Medikamentöse Therapie</b> 5.3 Inhalationssysteme  Vertiefende Informationen; S. 65	Bei der Inspiration unterscheiden sich Dosieraerosole, Sprühvernebler und elektrische Vernebler von Pulverinhalatoren:	Siehe Kommentar Nr. 1 [Nr.47]	Hintergrundtext anpassen.

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	Bei der Inspiration unterscheiden sich Dosieraerosole und Vernebler von Pulverinhalatoren:			
49	<b>Medikamentöse Therapie</b> 5.3 Inhalationssysteme  Vertiefende Informationen; S. 65 Dosieraerosole und Vernebler erfordern eine möglichst langsame Inspiration, weil eine zu hohe...	Dosieraerosole, Sprühvernebler und elektrische Vernebler erfordern eine möglichst langsame Inspiration, weil eine zu hohe...	Siehe Kommentar Nr. 1 [Nr.47]	Hintergrundtext anpassen.
50	<b>Medikamentöse Therapie</b> 5.3 Inhalationssysteme  Tabelle 15; S. 66 Vernebler: • passive Aerosolerzeugung unabhängig von der Mitarbeit des Patienten/der Patientin • Funktion auch bei geringen Atemflüssen gewährleistet • Medikamentenapplikation kann durch Aufsätze mit einer Stenoseatmung kombiniert werden	Sprühvernebler: • Passive Aerosolerzeugung durch mechanische Energie unabhängig von der Mitarbeit des Patienten/der Patientin. • Funktion auch bei geringen Atemflüssen gewährleistet Elektrische Vernebler: • passive Aerosolerzeugung durch Elektrizität unabhängig von der Mitarbeit des Patienten/der Patientin. • Funktion auch bei geringen Atemflüssen gewährleistet • Medikamentenapplikation kann durch Aufsätze mit einer Stenoseatmung kombiniert werden	Siehe Kommentar Nr. 1 [Nr.47]	Tabelle 15 wird angepasst: neue Zeile „elektrische Vernebler“ einfügt.  Die Formulierung: „passive Aerosolerzeugung durch Elektrizität“ ist redundant und wird wie folgt spezifiziert: • passive Aerosolerzeugung durch Druckluft bzw. Ultraschall.  Die Darstellung wird angepasst.
51	<b>Medikamentöse Therapie</b> 5.3 Inhalationssysteme  Hinweis; S. 66 Zur Unterstützung der Beratung und Einweisung in Inhalationssysteme wurde das Patientenblatt „Unterschiede bei Inhalier-Geräten“ (siehe Patientenblätter) entwickelt.	Ergänzung: Videos aller verfügbaren Inhalatoren kostenlos aufladbar über Deutsche Atemwegsliga	Wichtige Hilfe für Patienten, daher bereits an dieser Stelle erwähnen.	Ergänzen im Hintergrundtext: S. 66 unter "Hinweis"  <i>Zur Unterstützung der Beratung und Einweisung in Inhalationssysteme wurde das Patientenblatt „Unterschiede bei Inhalier-Geräten“ (siehe Patientenblätter) entwickelt. Zusätzlich stellt die Atemwegsliga unter <a href="http://www.atemwegsliga.de/richtig-inhalieren.html">www.atemwegsliga.de/richtig-inhalieren.html</a> verschiedene Videos über alle zur Zeit verfügbaren Inhalatoren kostenlos zur Verfügung.</i>
76	<b>Medikamentöse Therapie</b> 5.3 Inhalationssysteme	Ergänzung:	Wichtige Hilfe für Patienten, daher bereits an dieser Stelle erwähnen.	Doppelt eingegangenes Kommentar. Umgang siehe Nr. 51

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	Hinweis; S. 66 Zur Unterstützung der Beratung und Einweisung in Inhalationssysteme wurde das Patientenblatt „Unterschiede bei Inhalier-Geräten“ (siehe Patientenblätter) entwickelt.	Videos aller verfügbaren Inhalatoren kostenlos aufladbar über Deutsche Atemwegsliga		
52	<b>Medikamentöse Therapie</b> 5.3 Inhalationssysteme  Empfehlung 5-5; S. 67 Wenn für die verordneten Substanzen verfügbar, sollte für die Langzeittherapie nur ein Inhalationssystem (nur ein Typ eines Dosieraerosols oder eines Pulverinhalators) für die inhalative Medikation verordnet werden.	(nur ein Typ eines Dosieraerosols, Sprühverneblers oder eines Pulverinhalators)	Neben dem wiederverwendbaren Respimat sind auch nicht-wiederverwendbare Inhalatoren aufgrund von Re-Importen verkehrsfähig und im Handel.	Redaktionelle Änderung der Empfehlung 5-5.  Empfehlung 5-5: <i>Wenn für die verordneten Substanzen verfügbar, sollte für die Langzeittherapie nur ein Inhalationssystem (nur ein Typ eines Dosieraerosols, eines Sprühverneblers, eines elektrischen Verneblers oder eines Pulverinhalators) für die inhalative Medikation verordnet werden.</i>  Die Hintergrundtexte werden entsprechend angepasst.
53	<b>Medikamentöse Therapie</b> 5.6 Mukolytika; S. 70	Keine Evidenz zu Mukolytika. Studie H. Worth et al. Concomitant therapy with cineole (eucalyptole) reduces exacerbations in COPD. A placebo controlled double-blind trial. <i>Respir. Res.</i> 10:69(2007)	RCT mit positivem Effekt bei COPD. Kann erwähnt und diskutiert werden.	Die Fragestellung wird in der 3. Auflage der NVL bearbeitet. Es wird eine systematische Recherche zur Wirkung von Cineol (Eucalyptol) bei Patient*innen mit COPD durchgeführt.
77	<b>Medikamentöse Therapie</b> 5.6 Mukolytika; S. 70	Keine Evidenz zu Mukolytika. Studie H. Worth et al. Concomitant therapy with cineole (eucalyptole) reduces exacerbations in COPD. A placebo controlled double-blind trial. <i>Respir. Res.</i> 10:69(2007)	RCT mit positivem Effekt bei COPD. Kann erwähnt und diskutiert werden.	Doppelt eingegangenes Kommentar. Umgang siehe Nr. 53
54	<b>Medikamentöse Therapie</b> 5.9 Impfschutz bei Patient*innen mit COPD  Empfehlung 5-9; S. 71	Patient*innen mit COPD soll eine Impfung gegen Influenza angeboten werden.	Die Evidenz für einen Nutzen der Pneumokokkenimpfung bei Patient*innen mit COPD ist schlecht. Im epidemiologischen Bulletin 37/2016 schreibt die StIKo selbst auf S. 393: „Es wurden 5 kleine RCTs (ausschließlich mit PPSV23) mit überwiegend unspezifischen klinischen Endpunkten identifiziert. Die gepoolte Impfeffektivität gegen CAP	Nicht berücksichtigen. Der Suchzeitraum des identifizierten Cochrane Reviews [194] ist etwas aktueller (schließt zusätzliche 10 Monate mit ein); die Datenqualität wird hier als moderat dargestellt, die Daten sprechen für die Pneumokokkenimpfung.



Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	Patient*innen mit COPD sollen Impfungen gemäß den Empfehlungen der STIKO (aktuell Influenza und Pneumokokken) angeboten werden		jeglicher Ursache lag bei 26 % (95 % KI: -6 – 48 %), erreichte aber keine statistische Signifikanz. Der spezifischer Endpunkt Pneumokokken-Pneumonie wurde nur in einem RCT 27 untersucht. In der PPSV23-Gruppe traten unter 800 geimpften keine Fälle, in der Plazebo-Gruppe unter 798 Probanden 5 Fälle auf. Daraus resultiert eine nicht signifikante Impfeffektivität von 91 % (95 % KI: -64 – 99 %).	
55	<p><b>Medikamentöse Therapie</b></p> <p>5.9 Impfschutz bei Patient*innen mit COPD</p> <p>Empfehlung 5-9; S. 71</p> <p>Patient*innen mit COPD sollen Impfungen gemäß den Empfehlungen der STIKO (aktuell Influenza und Pneumokokken) angeboten werden</p>	Patient*innen mit COPD sollen Impfungen gemäß den Empfehlungen der STIKO (aktuell Influenza und Pneumokokken) angeboten werden. Der Pertussisimpfstatus soll überprüft und ggf. entsprechend der offiziellen Empfehlungen aufgefrischt werden.	<p>Eine Pertussisinfektion führt häufig zu Komplikationen bei Patienten mit COPD und kann eine der Ursachen für eine Exazerbation sein. COPD führt dazu, dass die Atemwege anschwellen und mit Schleim blockiert werden, was das Atmen erschweren kann. Eine Pertussisinfektion kann diese Schwellung der Atemwege und der Lunge verstärken. Die Kombination aus beidem führt oftmals zu Lungenentzündung und anderen schweren Atemwegserkrankungen. Die Pertussisimpfung ist eine der sichersten Möglichkeiten die Gesundheit von COPD Patienten zu schützen, selbst wenn Sie verschreibungspflichtige Medikamente einnehmen.</p> <p>Daher wurde die Empfehlung zur Pertussisimpfung von COPD-Patienten in die aktuelle Version der internationalen GOLD Leitlinie aufgenommen. Literatur zu diesem Thema finden Sie untenstehend.</p> <p>Global Initiative for Chronic Obstructive Lung Disease, Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease Report 2020 <a href="https://goldcopd.org/wp-content/uploads/2020/11/GOLD-REPORT-2021-v1.0-16Nov20_WMV.pdf">https://goldcopd.org/wp-content/uploads/2020/11/GOLD-REPORT-2021-v1.0-16Nov20_WMV.pdf</a> Blasi F, Bonanni P, Braido F, Gabutti G, Marchetti F, Centanni S. The unmet need for pertussis prevention in patients with chronic obstructive pulmonary disease in the Italian context. Hum Vaccin</p>	<p>Nicht berücksichtigen. Es wird kein relevantes Versorgungsproblem gesehen.</p> <p>- STIKO empfiehlt die Pertussisimpfung nicht für chronisch Kranke (wie bspw. COPD; siehe aktuelle STIKO-Empfehlungen (Epi Bull 2020;34)); aus diesem Grund nicht in Empfehlung verorten.</p>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
			<p>Immunother. 2020;16(2):340-348. doi: 10.1080/21645515.2019.1652517. Epub 2019 Sep 6. PMID: 31403385; PMCID: PMC7062424. <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7062424/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7062424/</a></p> <p>Buck PO, Meyers JL, Gordon LD, Parikh R, Kurosky SK, Davis KL. Economic burden of diagnosed pertussis among individuals with asthma or chronic obstructive pulmonary disease in the USA: an analysis of administrative claims. <i>Epidemiol Infect.</i> 2017 Jul;145(10):2109-2121. doi: 10.1017/S0950268817000887. Epub 2017 May 2. PMID: 28462763; PMCID: PMC5968309. <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5968309/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5968309/</a></p> <p>Jenkins VA, Savic M, Kandeil W. Pertussis in high-risk groups: an overview of the past quarter-century. <i>Hum Vaccin Immunother.</i> 2020 Apr 16:1-9. doi: 10.1080/21645515.2020.1738168. Epub ahead of print. PMID: 32298213. <a href="https://www.tandfonline.com/doi/pdf/10.1080/21645515.2020.1738168">https://www.tandfonline.com/doi/pdf/10.1080/21645515.2020.1738168</a></p> <p>Emmanuel Aris, Esse Ifebi Akpo, Amit Bhavsar, Lauriane Harrington, Evie Merinopoulou, Nicola Sawalhi-Leckenby, Elisa Turriani, Kinga Meszaros, Dimitra Lambrelli, Piyali Mukherjee <i>European Respiratory Journal</i> Sep 2020, 56 (suppl 64) 2468; DOI: 10.1183/13993003.congress-2020.2468 <a href="https://erj.ersjournals.com/content/56/suppl_64/2468">https://erj.ersjournals.com/content/56/suppl_64/2468</a></p> <p>Pesek R, Lockey R. Vaccination of adults with asthma and COPD. <i>Allergy.</i> 2011 Jan;66(1):25-31. doi: 10.1111/j.1398-9995.2010.02462.x. Epub 2010 Aug 17. PMID: 20716316. <a href="https://onlinelibrary.wiley.com/doi/full/10.1111/j.1398-9995.2010.02462.x">https://onlinelibrary.wiley.com/doi/full/10.1111/j.1398-9995.2010.02462.x</a></p> <p>Hashemi SH, Nadi E, Hajilooi M, Seif-Rabiei MA, Samaei A. High Seroprevalence of <i>Bordetella pertussis</i> in Patients with Chronic Obstructive Pulmonary Disease: A Case-Control Study. <i>Tanaffos.</i></p>	

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
			<p>2015;14(3):172-6. PMID: 26858762; PMCID: PMC4745185.  <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4745185/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4745185/</a>                      Mbayei SA, Faulkner A, Miner C, Edge K, Cruz V, Peña SA, Kudish K, Coleman J, Pradhan E, Thomas S, Martin S, Skoff TH. Severe Pertussis Infections in the United States, 2011-2015. Clin Infect Dis. 2019 Jul 2;69(2):218-226. doi: 10.1093/cid/ciy889. PMID: 30321305; PMCID: PMC7108152. Mbayei SA, Faulkner A, Miner C, Edge K, Cruz V, Peña SA, Kudish K, Coleman J, Pradhan E, Thomas S, Martin S, Skoff TH. Severe Pertussis Infections in the United States, 2011-2015. Clin Infect Dis. 2019 Jul 2;69(2):218-226. doi: 10.1093/cid/ciy889. PMID: 30321305; PMCID: PMC7108152.  <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7108152/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7108152/</a></p> <p>ERS- Whitebook:  <a href="https://www.erswhitebook.org/chapters/immunisation-against-respiratory-diseases/pertussis/">https://www.erswhitebook.org/chapters/immunisation-against-respiratory-diseases/pertussis/</a></p>	
56	<p><b>Medikamentöse Therapie</b></p> <p>5.9 Impfschutz bei Patient*innen mit COPD</p> <p>Empfehlung 5-9; S. 71</p> <p>Patient*innen mit COPD sollen Impfungen gemäß den Empfehlungen der STIKO (aktuell Influenza und Pneumokokken) angeboten werden</p>	<p>Patient*innen mit COPD sollen Impfungen gemäß den Empfehlungen der STIKO (aktuell Influenza und Pneumokokken) angeboten werden. Zudem wird von der STIKO eine Standardimpfung für Patient*innen ab 60 Jahren sowie eine Indikationsimpfung für COPD Patient*innen ab 50 Jahren gegen Herpes Zoster empfohlen. Neue Studiendaten aus Deutschland unterstützen, dass bei Patient*innen mit COPD und insbesondere Patient*innen unter systemischer Kortikosteroid-Therapie eine Impfung gegen Herpes Zoster in Abstimmung mit dem Arzt/Ärztin erwogen werden sollte.</p>	<p>In einer Auswertung repräsentativer nationaler Versorgungsdaten auf Basis der Versicherten der BARMER (7 Millionen Versicherte in 2018, 13 % aller GKV-Versicherten in Deutschland) konnte ein erhöhtes Risiko für eine Herpes Zoster (HZ) Inzidenz beobachtet werden. Untersucht wurden die Jahre 2008 bis 2018, berichtet werden die Ergebnisse für das aktuellste Jahr (2018). Bei einer nicht multimorbiden COPD-Kohorte wurde gegenüber einer gesunden Vergleichspopulation in der Altersgruppe ab 18 Jahren ein erhöhtes Risiko für eine HZ beobachtet (OR=1,2, 95% KI=1,10-1,30). Bei Beachtung von Multimorbidität wird für Patient*innen ab 60 Jahren mit COPD (OR=1,05, 95% KI: 1,0-1,1) ebenfalls ein erhöhtes Risiko beobachtet. Durch Gabe systemischer Kortikosteroide erhöhte sich das Risiko in derselben Altersgruppe nochmals (OR=1,21, KI:1,12-1,31). Bei jüngeren</p>	<p>Klammerausdruck weglassen. Zusätzlich wird „aktuelle“ mit in die Empfehlung aufgenommen. Diese lautet dann wie folgt:</p> <p><i>Patient*innen mit COPD sollen Impfungen gemäß den aktuellen Empfehlungen der STIKO angeboten werden.</i></p> <p>Durch das Weglassen der Klammer (Bezugnahme auf bestimmte Impfungen) werden alle von der STIKO empfohlenen Impfungen für Patient*innen mit COPD abgebildet.</p> <p>Eine Verlinkung auf das aktuelle Bulletin des RKI wird eingefügt.</p>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
			<p>COPD Patient*innen ist unter Steroidgabe das Risiko ebenfalls erhöht, etwa in der Altersgruppe von 18-49 Jahren (OR=1,09, 95% KI=0,90-1,31) sowie in der Altersgruppe von 50-59 Jahren (OR=1,02, 95% KI:0,83-1,26), allerdings nicht statistisch signifikant.</p> <p>Vergleiche:                      Batram M, Witte J, Schwarz M, Hain J, Ultsch B, Steinmann M, Amit B, Wutzler P, Criée CP, Hermann C, Wahle K, Füchtenbusch M, Greiner W. Burden of Herpes Zoster in adult patients with underlying conditions – analysis of German claims data, 2007-2018. <i>Dermatology and therapy</i> [in submission].                      Ständige Impfkommission: Empfehlungen der Ständigen Impfkommission (STIKO). <i>Epid Bull</i> 2020; 34:1-68 DOI:10.25646/7083.5].</p>	
57	<p><b>Medikamentöse Therapie</b>                      5.9 Impfschutz bei Patient*innen mit COPD; S. 72</p>	<p>Evidenzbeschreibung                      Seit 2018 empfiehlt die STIKO allgemein für alle Personen ab 60 Jahren eine Impfung gegen Herpes Zoster, sowie eine Indikations-Impfung für Personen ab 50 Jahren. Im Rahmen der Indikationsimpfempfehlung wird explizit auf COPD Patient*innen als Personen mit erhöhter gesundheitlicher Gefährdung verwiesen. Zudem wird im Zuge der Impfempfehlung eine internationale systematische Übersichtsarbeit benannt, die ein erhöhtes Herpes Zoster Risiko für COPD Patient*innen zeigt.</p> <p>Eine repräsentative, nationale Sekundärdatenanalyse hat über einen Zeitraum von 10 Jahren ebenfalls ein signifikant höheres Risiko für eine Herpes Zoster-Inzidenz bei einer nicht multimorbiden COPD-Kohorte gegenüber einer gesunden Vergleichspopulation der Altersgruppe ab 18 Jahren gezeigt (OR=1,2, 95% KI=1,10-1,30). Wird Multimorbidität berücksichtigt, zeigt sich insbesondere bei Patient*innen ab 60 Jahren ein statistisch signifikant höheres Herpes Zoster-Risiko (OR=1,05, 95% KI: 1,0-1,1). Bei Patient*innen unter systemischer Kortikosteroid-Therapie ist das</p>	<p>In Anlehnung an die bestehende Impfempfehlung der STIKO (siehe Epi.Bull.) bezieht sich die vorgeschlagene Textänderung lediglich auf die Altersgruppen 50-59 Jahre sowie die Altersgruppe ab 60 Jahren, wengleich die Analysen ebenfalls bei Patient*innen ab 18 Jahren ein erhöhtes Risiko zeigen. So wurde bei jüngeren Patient*innen von 18-49 Jahren das höchste Risiko einer Herpes Zoster Erkrankung beobachtet, allerdings auf statistisch nicht signifikantem Niveau (OR=1,09, 95% KI=0,90-1,31).</p> <p>Vergleiche:                      Ständige Impfkommission: Empfehlungen der Ständigen Impfkommission (STIKO). <i>Epid Bull</i> 2020; 34:1-68 DOI:10.25646/7083.5].                      Ständige Impfkommission (STIKO): Wissenschaftliche Begründung zur Empfehlung einer Impfung mit dem Herpes zoster-subunit-Totimpfstoff. <i>Epid Bull</i> 2018;50:541 – 567 [DOI 10.17886/EpiBull-2017-059.2].                      Batram M, Witte J, Schwarz M, Hain J, Ultsch B, Steinmann M, Amit B, Wutzler P, Criée CP, Hermann C, Wahle K, Füchtenbusch M, Greiner W.</p>	<p>Nicht berücksichtigen.</p> <ul style="list-style-type: none"> <li>- Selektiv eingebrachte Sekundärdatenanalyse noch nicht publiziert (kein peer review), daher nicht zitiert.</li> <li>- RKI EpidBull wird als Referenz angegeben → - siehe Umgang zu Nr. 56</li> </ul>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
		Zoster-Risiko nochmals erhöht (ab 60 Jahren OR=1,21, KI: 1,12-1,31 sowie von 50-59 Jahren OR=1,02, 95% KI= 0,83-1,26).	Burden of Herpes Zoster in adult patients with underlying conditions – analysis of German claims data, 2007-2018. Dermatology and therapy [in submission].	
58	<b>Medikamentöse Therapie</b> 5.9 Impfschutz bei Patient*innen mit COPD; S. 72	Vertiefende Informationen: Aus aktuellen nationalen Versorgungsdaten kann zudem gezeigt werden, dass Patient*innen mit mindestens einer Risikoeinzelkrankung wie bspw. COPD ein erhöhtes Risiko für eine Herpes-Zoster Rekurrenz aufweisen.  Dies wird auch in internationalen Arbeiten bestätigt. So zeigten eine taiwanesischen Sekundärdatenanalyse mit rund 8.500 Patient*innen (HR=3,00; 95% KI= 2,40-3,75) wie auch eine Auswertung britischer Primärversorgungsdaten mit rund 145.000 Patient*innen (OR=1,82; 95% KI: 1,58-2,1) bereits ein erhöhtes Risiko für eine Herpes Zoster Erkrankung, insbesondere bei Patient*innen unter systemischer Kortikosteroid-Therapie.	Vergleiche: Batram M, Witte J, Schwarz M, Hain J, Ultsch B, Steinmann M, Amit B, Wutzler P, Crieé CP, Hermann C, Wahle K, Füchtenbusch M, Greiner W. Burden of Herpes Zoster in adult patients with underlying conditions – analysis of German claims data, 2007-2018. Dermatology and therapy [in submission]. Forbes HJ, Bhaskaran K, Thomas SL, Smeeth L, Clayton T, Langan SM. Quantification of risk factors for herpes zoster: population based case-control study. BMJ 2014; 348: g2911 [DOI 10.1136/bmj.g2911]. Yang Y-W, Chen Y-H, Wang K-H, Wang C-Y, Lin H-W. Risk of herpes zoster among patients with chronic obstructive pulmonary disease: a population-based study. CMAJ 2011; 183(5): E275-80 [DOI 10.1503/cmaj.101137].	Nicht berücksichtigen  RKI EpidBull wird als Referenz angegeben → siehe Umgang zu Nr. 56
59	<b>Medizinische Rehabilitation</b>  Vorbemerkung; S. 73 Wichtige nicht-medikamentöse Therapiekomponenten sind Patientenschulung, medizinische Trainingstherapie, Atemphysiotherapie, Ergotherapie, Hilfsmittelberatung, psychologische Hilfen, Ernährungsberatung, Tabakentwöhnung sowie Sozial- und Berufsberatung.	Wichtige nicht-medikamentöse Therapiekomponenten sind Patientenschulung, medizinische Trainingstherapie, Atemphysiotherapie, Ergotherapie, Hilfsmittelberatung, psychologische Hilfen, Ernährungsberatung, Tabakentwöhnung sowie Sozial- und Berufsberatung.	Siehe für Ernährungsberatung versus Ernährungstherapie unter Punkt 2.  [SSc: Nr. 35]	Nicht berücksichtigen.  Gruppe hat explizit von Beratung gesprochen.
61	<b>Versorgungskoordination</b> 7.2 Ambulante Überweisungsindikatoren  Tabelle 19; S. 80	• bei klinischen Hinweisen auf therapiebedürftige schlafbezogene Atmungsstörungen (Abstimmung mit/Überweisung an schlafmedizinisch tätigen Pneumologen oder HNO-Arzt oder einen Schlafmediziner)	Zur weiteren Diagnostik bei Verdacht auf eine schlafbezogene Atmungsstörung bedarf es einer schlafmedizinischen Expertise, die nicht jeder Pneumologe und HNO-Arzt hat. Nur ein Teil der Pneumologen und HNO-Ärzte führt die hierfür notwendigen Untersuchungen (kardiorespiratorische	Keine Änderung.

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
	<ul style="list-style-type: none"> <li>• bei klinischen Hinweisen auf therapiebedürftige schlafbezogene Atmungsstörungen (Abstimmung mit/Überweisung an Pneumologie, HNO, Schlafmedizin)</li> </ul>		Polygraphie und kardiorespiratorische Polysomnographie) durch.	
62	<p><b>Versorgungskoordination</b></p> <p>7.2 Ambulante Überweisungsindikatoren</p> <p>Tabelle 19; S. 80</p>	<p><b>Neue Zeile:</b> <u>Fachgebiet:</u> Hals-Nasen-Ohrenheilkunde, <u>Konstellation:</u> rezidivierende Infekte der Nase und Nasennebenhöhlen sowie pharyngo-laryngealer Reflux als beobachtete Exacerbationstrigger und relevante Komorbiditäten. Tracheostoma und Z.n. Laryngektomie als relevante Besonderheiten.</p>	<p>In der Anamnese (Seite 15) wird auf HNO-Begleiterkrankungen abgehoben. Das lange bekannte Phänomen des „sinu-bronchialen Syndroms“, moderner „united airways“ ist eine praktisch klinische immer wieder beobachtete Tatsache, die auch in der Literatur bekannt ist. Reflux kann Hustensymptomatik verstärken und ist eine typische Komorbidität. Bei vorhandenem Tracheostoma oder Z.n. Laryngektomie ist u.a. eine HME-Versorgung wichtig. Siehe beiliegender Literatur-Review.</p>	<p>Die Tabelle 19 (7.2 Ambulante Überweisungsindikatoren) wird um das Fachgebiet Hals-Nasen-Ohrenheilkunde ergänzt. Die entsprechende Konstellation wird wie folgt abgebildet:</p> <p><u>Konstellation:</u></p> <ul style="list-style-type: none"> <li>• <i>chronische Sinusitis als beobachteter Exazerbationstrigger.</i></li> <li>• <i>Tracheostoma und Z.n. Laryngektomie als relevante Besonderheiten.</i></li> </ul> <p>Der pharyngo-laryngeale Reflux wird nicht dargestellt.</p>
63	<p><b>Versorgungskoordination</b></p> <p>7.4 Kooperation von Ärzt*innen und Apotheker*innen</p> <p>Empfehlung 7-9; S. 82</p> <p>Der Arzt oder die Ärztin soll gemeinsam mit den Patient*innen über das Inhalationssystem entscheiden. Um sicherzugehen, dass die Patientin oder der Patient das indizierte System erhält, soll bei „aut-idem“ ein Kreuz gesetzt werden.</p>	<p>„Der Arzt soll gemeinsam mit dem Patienten über das Inhalationssystem entscheiden. Falls sichergestellt werden muss, dass der Patient das gewünschte Inhalationssystem erhält, soll bei „aut-idem“ ein Kreuz gesetzt werden.“</p>	<p>Hierzu hatten wir eine intensive Diskussion (Mandatsträger/Paten). Wir sind uns einig, dass ein Wechsel des Inhalationssystems vermieden werden soll. Die aktuelle Formulierung bzgl. aut idem-Kreuz würde allerdings dazu führen, dass auch bei Erstverordnung ein aut-idem-Kreuz gesetzt werden müsste. Das erscheint uns nicht notwendig und angemessen zu sein.</p>	<p>Redaktionelle Änderung:</p> <p><i>Der Arzt oder die Ärztin soll gemeinsam mit den Patient*innen über das Inhalationssystem entscheiden. Wenn sichergestellt werden muss, dass die Patientin oder der Patient das verordnete Inhalationssystem erhält, soll bei „aut-idem“ ein Kreuz gesetzt werden.</i></p> <p>Da es wichtig ist, in diesem Zusammenhang zwischen Erst- und Folgeverordnung zu unterscheiden, wird dieser Sachverhalt nochmals deutlich im Hintergrundtext adressiert.</p> <p>Für die nächste Konsensuskonferenz der NVL COPD (3. Auflage) wird die Thematik noch einmal zur Besprechung vorgesehen.</p>

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Entscheidung der Leitliniengruppe
64	<b>Versorgungskoordination</b> 7.6 Schriftlicher Aktionsplan  Empfehlung 7-16; S. 85 Patient*innen mit COPD sollen einen schriftlichen Aktionsplan erhalten.	Wenn im Arzt-Patient eine gemeinsame therapeutische Entscheidung gefunden wurde, soll diese schriftlich fixiert werden.	Die Empfehlung generalisiert zu stark. Wenn ich allen Patient*innen in der Hausarztpraxis neben Medikations- auch noch „schriftliche Aktionspläne“ mitgeben müsste, würden wir irgendwann in Papier absaufen. Wenn – was meist der Fall ist – die Patient*innen klinisch stabil sind – oder eben nichts an ihrem Rauch- oder Ess-Verhalten ändern wollen, wofür sollten sie dann einen „Aktionsplan“ bekommen? Wenn wiederum Veränderungsbereitschaft besteht, dann ist es mit Evidenz belegt, dass eine Verschriftlichung der in der gemeinsamen Entscheidungsfindung gefundenen Absprachen hilft, das Besprochene auch umzusetzen.	Die Empfehlung wird nicht geändert.  Im Hintergrundtext wird konsequent die Formulierung „Aktionsplan“ verwendet. Es wird darauf hingewiesen, dass der Aktionsplan „einfach, klar und verständlich“ aufgebaut sein müsse.  Ein direkter Link zum Aktionsplan der Atemwegsliga ist bereits im Hintergrundtext vorhanden. Zusätzlich wird geprüft, ob in Zusammenarbeit mit der Atemwegsliga konkrete Praxishilfen hierzu erstellt werden können.
65	<b>Versorgungskoordination</b> 7.6 Schriftlicher Aktionsplan; S. 85  Rationale Ein schriftlicher Behandlungsplan beinhaltet individuelle...	Rationale Ein schriftlicher Aktionsplan beinhaltet individuelle...	Die Bezeichnung des Plans sollte in der Überschrift / Empfehlung und im Hintergrundtext gleich lauten (Behandlungsplan vs. Aktionsplan).  Es wäre hilfreich, wenn eine Vorlage für den Plan z.B. über die DMP-Dokumentation zugänglich ist bzw. generiert werden kann als fester Bestandteil der verpflichtenden Erhebungsdaten im DMP Möglicherweise analog dem COBRA Schulungsprogramm der Atemwegsliga.	Siehe weiteres Vorgehen Nr. 64.

### Anhang 11.2 Redaktionelle Kommentare

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Redaktionelle Bearbeitung
1	<b>Definition und Epidemiologie</b> S. 11 [...] Der akuten Exazerbation liegen eine entzündlich bedingte vermehrte Bronchokonstriktion und/oder Schleimproduktion mit Überblähung zugrunde. [...]	Akut streichen	Exazerbation ist als Akutereignis definiert.	Vorgeschlagene Textänderung wurde übernommen.
66	<b>Definition und Epidemiologie</b> S. 11	Akut streichen	Exazerbation ist als Akutereignis definiert.	Doppelt eingegangenes Kommentar. Umgang siehe Nr. 1

Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Redaktionelle Bearbeitung
	[...] Der akuten Exazerbation liegen eine entzündlich bedingte vermehrte Broncho- konstriktion und/oder Schleimproduktion mit Überblähung zugrunde. [...]			
3	<b>Diagnostik und Monitoring</b> Abbildung 1; S. 14 [...]Post BD: post Bronchodilatator, FEV1/FVC: Einsekundenkapazität/forcierte Vitalkapazität (Tiffeneau-Index), LLN: Lower Limit of Normal, GLI: Global Lung Initiative, GKP: Ganzkörperplethysmografie, DLCO: Diffusionskapazität für Kohlenstoffmonoxid, TLC: totale Lungenkapazität	Kohlenmonoxid	Gebräuchliche Bezeichnung in der Literatur und im Sprachgebrauch	Vorgeschlagene Textänderung wurde über- nommen.
67	<b>Diagnostik und Monitoring</b> Abbildung 1; S. 14 [...]Post BD: post Bronchodilatator, FEV1/FVC: Einsekundenkapazität/forcierte Vitalkapazität (Tiffeneau-Index), LLN: Lower Limit of Normal, GLI: Global Lung Initiative, GKP: Ganzkörperplethysmografie, DLCO: Diffusionskapazität für Kohlenstoffmonoxid, TLC: totale Lungenkapazität	Kohlenmonoxid	Gebräuchliche Bezeichnung in der Literatur und im Sprachgebrauch	Doppelt eingegangenes Kommentar. Umgang siehe Nr. 3
19	<b>Tabakentwöhnung</b> Empfehlung 3-6: (S. 34) Die patientengerechte Erklärung individuel- ler Gesundheitsparameter in Bezug auf das Rauchen wie z. B. das Besprechen von Lungenfunktionsparametern und CO kann einen positiven Einfluss auf den Erfolg der Tabakentwöhnung haben.	CO- Messungen	Verständlichkeit	Vorgeschlagene Textänderung wurde über- nommen.  Die Empfehlung lautet somit: <i>Die patientengerechte Erklärung individuel- ler Gesundheitsparameter in Bezug auf das Rauchen wie z. B. das Besprechen von Lungenfunktionsparametern und CO-Mes- sungen kann einen positiven Einfluss auf den Erfolg der Tabakentwöhnung haben.</i>
68	<b>Tabakentwöhnung</b> Empfehlung 3-6: (S. 34)	CO- Messungen	Verständlichkeit	Doppelt eingegangenes Kommentar. Umgang siehe Nr.19



Nr.	NVL	Vorgeschlagene Textänderung	Begründung (mit Literaturangaben)	Redaktionelle Bearbeitung
	Die patientengerechte Erklärung individueller Gesundheitsparameter in Bezug auf das Rauchen wie z. B. das Besprechen von Lungenfunktionsparametern und CO kann einen positiven Einfluss auf den Erfolg der Tabakentwöhnung haben.			
23	<b>Tabakentwöhnung</b> 3.3 E-Zigaretten; S. 35 [...] Mögliche kardiovaskuläre Effekte der E-Zigarette wurden von Skotsimara et. al angedeutet [...]	[...] Mögliche kardiovaskuläre Effekte der E-Zigarette wurden von Skotsimara et. al beschrieben. [...]	Auch an anderer Stelle der LL wurde bei vergleichbarer Qualität der Evidenz nicht „angedeutet“ genutzt.	Vorgeschlagene Textänderung wurde übernommen.
60	<b>Medizinische Rehabilitation</b> 6.1.1 Rehabilitationssport; S. 75  Nach den Empfehlungen der Deutschen Atemwegsliga und der Arbeitsgemeinschaft Lungensport in Deutschland zum Sport und körperlichen Training bei Patient*innen mit obstruktiven Atemwegserkrankungen ist vor der Teilnahme an Sport- oder Trainingsprogrammen eine ärztliche Untersuchung erforderlich [202].	Austausch der Literaturstelle 202	Neue Sportempfehlung ersetzt die alte (2020)  H. Worth et al. Ambulanter Lungensport und körperliches Training bei Patienten mit Atemwegs- und Lungenkrankheiten. Empfehlungen der Arbeitsgemeinschaft Lungensport und der Deutschen Atemwegsliga. Pneumologie(2020)	Literatur geprüft und aktualisiert. Inhalte stützen die Formulierung weiterhin.
78	<b>Medizinische Rehabilitation</b> 6.1.1 Rehabilitationssport; S. 75  Nach den Empfehlungen der Deutschen Atemwegsliga und der Arbeitsgemeinschaft Lungensport in Deutschland zum Sport und körperlichen Training bei Patient*innen mit obstruktiven Atemwegserkrankungen ist vor der Teilnahme an Sport- oder Trainingsprogrammen eine ärztliche Untersuchung erforderlich [202].	Austausch der Literaturstelle 202	Neue Sportempfehlung ersetzt die alte (2020)  H. Worth et al. Ambulanter Lungensport und körperliches Training bei Patienten mit Atemwegs- und Lungenkrankheiten. Empfehlungen der Arbeitsgemeinschaft Lungensport und der Deutschen Atemwegsliga. Pneumologie(2020)	Doppelt eingegangenes Kommentar. Umgang siehe Nr. 60

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