NATIONALE VERSORGUNGS LEITLINIEN

Nationale VersorgungsLeitlinie

COPD

Recherchedokumentation + Evidenztabellen
Kapitel 8:Exazerbationen
Kapitel 9: Operative und interventionelle Verfahren

Ergänzung zur 2. Auflage
AWMF-Register-Nr. nvl-003

Träger:

Bundesärztekammer

Kassenärztliche Bundesvereinigung

Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften

BUNDESÄRZTEKAMMER KBV AWMF

Inhaltsverzeichnis

1 Evidenzbasis

Evidenzbasis Kapitel 8 Exazerbationen und Kapitel 9 Operative und interventionelle Verfahren

Die hier veröffentlichten Recherchestrategien und Evidenztabellen beziehen sich auf die aktuelle Bearbeitung der Kapitel Exazerbationen sowie Operative und interventionelle Verfahren. Diese beiden Kapitel wurden nach Bekanntgabe der Auflösung des ÄZQ zum 31.12.2024 als Ergänzung zur 2. Auflage der NVL COPD [1] veröffentlicht. Die Recherchestrategien und Evidenztabellen für die in der 2. Auflage der NVL COPD (2021) bereits veröffentlichten Kapitel sind im zugehörigen Leitlinienreport zur 2. Auflage [2] dargestellt.

Für die gesamte NVL erfolgte eine themenübergreifende Recherche nach systematischen Übersichtsarbeiten und Metaanalysen,die durch das IQWiG (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen), die Cochrane Collaboration, das National Institute for Health and Care Excellence (NICE), und durch die Agency for Healthcare Research and Quality (AHRQ) erstellt wurden. Die für die Kapitel Exazerbationen sowie Operative und interventionelle Verfahren relevanten Treffer werden in diesem Dokument dargestellt. Zusätzlich wurden Beschlüsse des Gemeinsamen Bundesausschusses (G-BA) herangezogen. Weitere systematische Recherchen erfolgten

- zur D-Dimer-Testung bei Patient*innen mit Exazerbation der COPD zur differentialdiagnostischen Erkennung einer Lungenembolie (diagnostische Genauigkeit);
- zum Einsatz von CRP, Sputum oder Procalcitonin in der Therapiesteuerung einer antibiotischen Behandlung;
- zur Wirksamkeit und Sicherheit von Opioiden in der Akutversorgung;
- zur präinterventionellen Rehabilitation vor einem operativen oder interventionellen Eingriff;
- zur gezielten Lungendenervation.

Grundlage der Diskussionen für die Kapitel Exazerbationen sowie Operative und interventionelle Verfahren bildeten die Ergebnisse der hier dargestellten systematischen Recherchen, die identifizierte Evidenz und die zugehörigen Diskussionen der 2. Auflage der NVL COPD, themenverwandte bzw. weiterführende AWMF-Leitlinien, die klinische Erfahrung der Leitliniengruppe, sowie gute klinische Praxis.

2 Recherchedokumentation

2.1 Themenübergreifende strukturierte Recherche nach systematischen Übersichtsarbeiten

2.1.1 PICO-Fragestellung

Population Patient*innen mit COPD

Intervention keine Einschränkungen

Comparison keine Einschränkungen

Outcome Priorisierte Endpunkte der Leitliniengruppe:

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

Studientyp systematische Übersichtsarbeiten/Metaanalysen, HTA

Recherchequellen

Als Quellen für die themenübergreifende systematische Recherche nach hochwertigen systematischen Übersichtsarbeiten wurden folgende Institutionen aufgrund ihrer evidenzbasierten Vorgehensweise, ihrer hohen Berichtsqualität, ihrer wissenschaftlichen Unabhängigkeit, eines weitergehenden Einblicks in Studiendossiers sowie ggf. ihres Bezugs zum deutschen bzw. europäischen Versorgungskontext ausgewählt:

- Cochrane
- AHRQ (Agency for Healthcare Research and Quality)
- NICE (National Institute for Health and Care Excellence)
- IQWiG (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen)
- Zusätzlich wurden die Seiten des G-BA (Gemeinsamer Bundesausschuss, https://www.g-ba.de/) herangezogen.

Ein- und Ausschlusskriterien

Einschluss	**E**	Einschluss: Fragestellung passend, Studientyp passend
	Ep	noch nicht veröffentlicht (Protokoll, Berichtsplan o. Ä. vorhanden)
	Ez	zurückgestellt für iteratives Vorgehen (z.B. Detailfragestellung)
Ausschluss	Aa	thematisch nicht passend: andere Erkrankung/ Fragestellung/Thema
	Ap	Studientyp nicht passend
	Aq	Methodische Qualität
	Ad	Doppelpublikation / bereits in 2. Auflage inkludiert
	As	Sprache nicht deutsch oder englisch
	Ap	Publikationstyp (z.B. Protokoll, thematisch nicht passend)
	Aw	zurückgezogen
	Av	Systematische Übersichtsarbeit mit gleicher Fragestellung und aktuellerem Suchzeitraum vorhanden

2.1.2 Recherchestrategien

Die Recherchestrategien (z. B. Datenbanksuche, Schlagwortsuche, einfaches Screening) richteten sich nach den Möglichkeiten der jeweiligen Recherchequelle.

2.1.2.1 Cochrane Library (06. März 2024)

Die im Januar 2019 durchgeführte allgemeine Recherche zum Thema COPD in der Cochrane Library wurde für die geplante Wiederaufnahme der Arbeiten zur Version 3 der NVL COPD wiederholt; eine Einschränkung des Suchzeitraumes ab 01/2019 wurde angewendet.

Nr.	Suchfrage	Anzahl
#6	**#1 or #2 or #3 or #4 in Cochrane Protocols; Publication date from 01/01/2019**	**11**
#5	**#1 or #2 or #3 or #4 in Cochrane Reviews; Publication date from 01/01/2019**	**32**
#4	((obstruct*) near/3 (pulmonary or lung* or airway* or airflow* or bronch* or respirat*)):ti (Word variations have been searched)	9001
#3	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	8300
#2	(COAD):ti,ab,kw	100
#1	(COPD):ti,ab,kw	19488

Update 2024: Für das Kapitel 8 Exazerbationen wurden n = 1 und für das Kapitel 9 Operative und interventionelle Verfahren n = 0 Reviews eingeschlossen.

Recherche 01/2019 (inklusive Recherche 09/2017; siehe auch Leitlinienreport zur 2. Auflage): Für das Kapitel 8 Exazerbationen wurden n = 7 und für das Kapitel 9 Operative und interventionelle Verfahren n = 2 Reviews eingeschlossen.

2.1.2.2 IQWiG (28.05.2024)

Kategorie	
Filter	Projekte und Ergebnisse (Resort/Bereich: alle; Anwendungsgebiet: alle; Status: alle; Jahr: 2019 – 2024)
Suchzeitraum	Ab Januar 2019
Suchbegriff: COPD	
Treffer	2019 A18-79: Fluticasonfuroat/Umeclidinium/Vilanterol (COPD) - Nutzenbewertung gemäß § 35a SGB V (Bearbeitung abgeschlossen; 02.05.2019) https://www.iqwig.de/projekte/a18-79.html A19-27: Fluticasonfuroat/Umeclidinium/Vilanterol (COPD) - Addendum zum Auftrag A18-79 (Bearbeitung abgeschlossen; 02.05.2019) https://www.iqwig.de/projekte/a19-27.html 2020 V19-01: Leitliniensynopse für das DMP COPD (Bearbeitung abgeschlossen; 06.05.2020) 2021 **N20-02: High-Flow-Therapie zur Selbstanwendung bei fortgeschrittener COPD oder chronischer respiratorischer Insuffizienz Typ** 1 (Bearbeitung abgeschlossen; 13.07.2021) https://www.iqwig.de/projekte/n20-02.html 2022 Keine Treffer 2023 Keine Treffer 2024 Keine Treffer
Eingeschlossene Treffer	3
Suchbegriff: Lungenvolumenreduktion	2019 – 2024 Keine Treffer
Eingeschlossene Treffer	0
Suchbegriff: Emphysem	2019 – 2024 Keine Treffer
Eingeschlossene Treffer	0
Suchbegriff: Exazerbation	2019 – 2024 Keine Treffer
Eingeschlossene Treffer	0

Relevante Treffer für Kapitel 8 oder 9: n = 1

Einschluss nach Volltextscreening: n = 0

- N20-02: High-Flow-Therapie zur Selbstanwendung bei fortgeschrittener COPD oder chronischer respiratorischer Insuffizienz Typ 1 (Bearbeitung abgeschlossen; 13.07.2021) https://www.iqwig.de/projekte/n20-02.html
  - ➔ Az (Noch keine weiterführenden Resultate: “Für den Abschlussbericht waren jedoch keine Daten verfügbar, die für eine Nutzenbewertung ausreichend gewesen wären. Da die HFT die gesetzlichen Anforderungen für ein Potenzial erfüllt, formuliert das IQWiG Eckpunkte für zwei Erprobungsstudien: für COPD mit respiratorischer Insuffizienz Typ I und für Typ I”)

2.1.2.3 G-BA (29.05.2024)

	Suchfrage
Suchzeitraum	Keine Einschränkung
Suchbegriff:	Lungenvolumenreduktion
Filter	Bewertungsverfahren
Treffer	7
Eingeschlossene Treffer	Chirurgische Lungenvolumenreduktion beim schweren Lungenemphysem Letzter Beschluss: 15.02.2018 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/65/) Bronchoskopische Lungenvolumenreduktion mittels Einlage von Spiralen (Coils) beim schweren Lungenemphysem mit einem pulmonalen Residualvolumen von mindestens 225 % vom Soll Letzter Beschluss: 20.12.2018 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/209/) Bronchoskopische Lungenvolumenreduktion mittels Einlage von Ventilen beim schweren Lungenemphysem Letzter Beschluss: 20.12.2018 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/208/) Bronchoskopische Lungenvolumenreduktion beim Lungenemphysem mittels Applikation von Polymerschaum Letzter Beschluss: 20.02.2020 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/312/) Bronchoskopische Lungenvolumenreduktion beim schweren Lungenemphysem mittels Thermoablation Letzter Beschluss: 17.09.2020 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/223/) Bronchoskopische Lungenvolumenreduktion mittels Thermoablation beim schweren Lungenemphysem Letzter Beschluss: 15.10.2020 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/222/) Bronchoskopische Lungenvolumenreduktion mittels Einlage von Spiralen (Coils) beim schweren Lungenemphysem mit einem pulmonalen Residualvolumen von unter 225 % vom Soll Letzter Beschluss: 11.01.2024 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/212/)
Suchbegriff:	Emphysem
Filter	Nutzenbewertungsverfahren; ab Januar 2019
Treffer	33

Eingeschlossene Treffer	Nutzenbewertung zum Wirkstoff Fluticasonfuroat/Umeclidinium/Vilanterol (neues Anwendungsgebiet COPD, keine ausreichende Kontrolle mit LAMA und LABA) Beginn des Verfahrens: 15.11.2018; Beschlussfassung: 02.05.2019; Datum letzte Aktualisierung: 09.03.2020 (https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/413/) Nutzenbewertung zum Wirkstoff Fluticasonfuroat/Umeclidinium/Vilanterol (COPD) Beginn des Verfahrens: 01.03.2018; Beschlussfassung: 16.08.2018; Datum letzte Aktualisierung: 19.02.2020 (https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/352/)
Suchbegriff:	COPD
Filter	Bewertungsverfahren; ab Januar 2019
Treffer	2
Eingeschlossene Treffer	**High-Flow-Therapie bei chronisch obstruktiver Lungenerkrankung (COPD) und chronisch respiratorischer Insuffizienz Typ 1** Letzter Beschluss: 17.02.2022 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/259/) **High-Flow-Therapie bei chronisch obstruktiver Lungenerkrankung (COPD) und chronisch respiratorischer Insuffizienz Typ 2** Letzter Beschluss: 17.02.2022 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/260/)
Filter	Nutzenbewertungsverfahren
Treffer	264
Eingeschlossene Treffer	Nutzenbewertung zum Wirkstoff Umeclidinium (COPD); Beginn des Verfahrens: 01.02.2016; Beschlussfassung: 21.07.2016 Datum letzte Aktualisierung: 04.02.2020 https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/214/ Nutzenbewertung zum Wirkstoff Olodaterol (COPD); Beginn des Verfahrens: 15.05.2014, Beschlussfassung: 17.07.2014; Datum letzte Aktualisierung: 04.02.2020 (https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/114/) Nutzenbewertung zum Wirkstoff Tiotropium/Olodaterol (COPD) Beginn des Verfahrens: 15.08.2015; Beschlussfassung: 04.02.2016; Datum letzte Aktualisierung: 04.02.2020 (https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/183/) Nutzenbewertung zum Wirkstoff Aclidiniumbromid/Formoterol (COPD) Beginn des Verfahrens: 01.02.2015; Beschlussfassung: 16.07.2015; Datum letzte Aktualisierung: 04.02.2020 (https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/156/) Nutzenbewertung zum Wirkstoff Umeclidinium/Vilanterol (COPD) Beginn des Verfahrens: 15.07.2014; Beschlussfassung: 08.01.2015 Datum letzte Aktualisierung: 04.02.2020 (https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/124/) Nutzenbewertung zum Wirkstoff Indacaterol/Glycopyrronium (COPD)

	Beginn des Verfahrens: 15.11.2013; Beschlussfassung: 08.05.2014; Datum letzte Aktualisierung: 03.02.2020 (https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/86/) Nutzenbewertung zum Wirkstoff Fluticasonfuroat/Umeclidinium/Vilanterol (COPD) Beginn des Verfahrens: 01.03.2018; Beschlussfassung: 16.08.2018; Datum letzte Aktualisierung: 19.02.2020 (https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/352/) Nutzenbewertung zum Wirkstoff Aclidiniumbromid (Erneute Nutzenbewertung § 14: COPD) Beginn des Verfahrens: 15.10.2015; Beschlussfassung: 07.04.2016; Datum letzte Aktualisierung: 04.02.2020 (https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/198/) Nutzenbewertung zum Wirkstoff Fluticasonfuroat/Vilanterol-Trifenatat (Asthma bronchiale, COPD) Beginn des Verfahrens: 01.01.2014; Datum letzte Aktualisierung: 03.02.2020 (https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/97/) Nutzenbewertung zum Wirkstoff Fluticasonfuroat/Umeclidinium/Vilanterol (neues Anwendungsgebiet COPD, keine ausreichende Kontrolle mit LAMA und LABA) Beginn des Verfahrens: 15.11.2018; Beschlussfassung: 02.05.2019; Datum letzte Aktualisierung: 09.03.2020 (https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/413/) → Ad

Nach Ende des Suchzeitraumes für die themenübergreifende systematische Recherche wurde ein aktueller Beschluss zum Bewertungsverfahren Bronchoskopische Lungenvolumenreduktion mittels Einlage von Spiralen (Coils) beim schweren Lungenemphysem mit einem pulmonalen Residualvolumen von unter 225 % vom Soll veröffentlicht (Beschlussdatum: 17.10.2024; noch nicht in Kraft getreten; https://www.g-ba.de/bewertungsverfahren/methodenbewertung/212/).

Relevante Treffer für **Kapitel 8 und 9:** n = 9

Einschluss nach Volltextscreening: n = 7

- Chirurgische Lungenvolumenreduktion beim schweren Lungenemphysem
- Letzter Beschluss: 15.02.2018 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/65/)
- Bronchoskopische Lungenvolumenreduktion mittels Einlage von Spiralen (Coils) beim schweren Lungenemphysem mit einem pulmonalen Residualvolumen von mindestens 225 % vom Soll
- Letzter Beschluss: 20.12.2018 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/209/)
- Bronchoskopische Lungenvolumenreduktion mittels Einlage von Ventilen beim schweren Lungenemphysem
- Letzter Beschluss: 20.12.2018 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/208/)
- Bronchoskopische Lungenvolumenreduktion beim Lungenemphysem mittels Applikation von Polymerschaum
- Letzter Beschluss: 20.02.2020 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/312/)
- Bronchoskopische Lungenvolumenreduktion beim schweren Lungenemphysem mittels Thermoablation
- Letzter Beschluss: 17.09.2020 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/223/)
- Bronchoskopische Lungenvolumenreduktion mittels Thermoablation beim schweren Lungenemphysem
- Letzter Beschluss: 15.10.2020 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/222/)
- Bronchoskopische Lungenvolumenreduktion mittels Einlage von Spiralen (Coils) beim schweren Lungenemphysem mit einem pulmonalen Residualvolumen von unter 225 % vom Soll
- Letzter Beschluss: 13.06.2024 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/212/)

Ausschluss nach Volltextscreening: n = 2

- High-Flow-Therapie bei chronisch obstruktiver Lungenerkrankung (COPD) und chronisch respiratorischer Insuffizienz Typ 1
- Letzter Beschluss: 17.02.2022 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/259/)
  - ➔ Az (Noch keine weiterführenden Resultate: “Ermittlung von an der Erprobung beteiligten Medizinprodukteherstellern und Unternehmen”)
- High-Flow-Therapie bei chronisch obstruktiver Lungenerkrankung (COPD) und chronisch respiratorischer Insuffizienz Typ 2
- Letzter Beschluss: 17.02.2022 (https://www.g-ba.de/bewertungsverfahren/methodenbewertung/260/)
  - ➔ Az (Noch keine weiterführenden Resultate: “Ermittlung von an der Erprobung beteiligten Medizinprodukteherstellern und Unternehmen”)

Die anderen identifizierten Treffer sind für das Kapitel Medikamentöse Therapie relevant; dieses wurde aktuell nicht bearbeitet.

2.1.2.4 NICE (28.05.2024)

	Suchfrage
Suchbegriffe	**COPD**
Suchzeitraum	Ab Januar 2019
Filter	guidance (clinical guidelines, diagnostic guidance, NICE guidelines, Public health guidelines, Technology appraisal guidance, interventional procedure guidance, medical technology guidance, social care guideline, Antimicrobial prescribing guidelines, Health technology evaluations, Highly specialised technologies guidance) published
Treffer	19
Eingeschlossene Treffer	5 - **Endobronchial nerve ablation** for chronic obstructive pulmonary disease Interventional procedures guidance [IPG714]; Published: 15 December 2021 (https://www.nice.org.uk/guidance/ipg714) - myCOPD for managing chronic obstructive pulmonary disease Medical technologies guidance [MTG68]; Published: 31 March 2022 (https://www.nice.org.uk/guidance/mtg68) - Digital technologies to deliver pulmonary rehabilitation programmes for adults with COPD: early value assessment Health technology evaluation HTE18; Published: 30 April 2024 (https://www.nice.org.uk/guidance/hte18) - Chronic obstructive pulmonary disease in over 16s: diagnosis and management NICE guideline [NG115]; Published: 05 December 2018; Last updated: 26 July 2019 (https://www.nice.org.uk/guidance/ng115) - **Bronchoscopic thermal vapour** ablation for upper-lobe emphysema Interventional procedures guidance [IPG652]; Published: 12 June 2019 (https://www.nice.org.uk/guidance/ipg652)
Suchbegriffe	**Lung volume reduction**
Suchzeitraum	Ab Januar 2019
Filter	interventional procedure guidance, published
Treffer	6

Eingeschlossene Treffer	2 - **Bronchoscopic thermal vapour** ablation for upper-lobe emphysema Interventional procedures guidance [IPG652]; Published: 12 June 2019 (https://www.nice.org.uk/guidance/ipg652) - Extracorporeal carbon dioxide removal for acute respiratory failure Interventional procedures guidance [IPG776]; Published: 15 November 2023 (https://www.nice.org.uk/guidance/ipg776)

Relevante Treffer für Kapitel 8 und 9: **n = 2**

Einschluss nach Volltextscreening: n = 0

- Endobronchial nerve ablation for chronic obstructive pulmonary disease; Interventional procedures guidance [IPG714]; Published: 15 December 2021 (https://www.nice.org.uk/guidance/ipg714):

  Inkludierte Studien geprüft; keine neue Evidenz zur durchgeführten systematischen Recherche zum Thema Lungendenervation von 09/2021, daher nicht herangezogen → Ad
- Bronchoscopic thermal vapour ablation for upper-lobe emphysema; Interventional procedures guidance [IPG652]; Published: 12 June 2019 (https://www.nice.org.uk/guidance/ipg652):

  Dampfablation zum Zeitpunkt der Erstellung des Kapitels nicht im dt. Versorgungskontext zugelassen/zur Verfügung; siehe auch G-BA-Beschlüse zur Thermoablation beim schweren Lungenemphysem → Aa

2.1.2.5 AHRQ (29.05.2024)

Kategorien	Suchbegriffe/ Filter (Ab Januar 2019)	Treffer	Eingeschlossene Treffer
Technology Assessment Program (completed)	Sichtung der Ergebnisliste ohne Eingabe von Suchbegriffen	8	1
Evidence-based Practice Center Reports	COPD	2	1
	„chronic obstructive“	17	2
	„lung volume reduction“	12 (Ad: n=3)	1

Anzahl der Treffer nach Titel-Screening: 5

- Noninvasive Positive Pressure Ventilation in the Home (https://www.cms.gov/medicare-coverage-database/view/technology-assessments.aspx?TAId=108&bc=AAAIAAAAAAAA&
- **Pharmacologic and Nonpharmacologic Therapies in Adult Patients With Exacerbation of COPD**; Date: October 2019; Report Type: Comparative Effectiveness Reviews; Affiliation: Mayo Clinic; Report Status: Final; (https://effectivehealthcare.ahrq.gov/products/copd/research?_gl=1*hwb1gj*_ga*MjYzNjk3MjU2LjE3MTU1OTU2MTM.*_ga_1NPT56LE7J*MTcxNjk4Mjg0MC4yLjEuMTcxNjk4MzM4My4wLjAuMA..) → E (für nicht-medikamentöse Terapie)
- Screening for Chronic Obstructive Pulmonary Disease: A Targeted Evidence Update for the U.S. Preventive Services Task Force; Date: May 2022; Report Type: U.S. Preventive Services Task Force Evidence Syntheses; Affiliation: Kaiser Permanente Research Affiliates; Report Status: Final (https://www.uspreventiveservicestaskforce.org/uspstf/document/final-evidence-review/chronic-obstructive-pulmonary-disease-screening)
- Integrating Palliative Care in Ambulatory Care of Noncancer Serious Chronic Illness: A Systematic Review; Date: February 2021; Report Type: Comparative Effectiveness Reviews; Affiliation: Johns Hopkins University; Report Status: Final (https://effectivehealthcare.ahrq.gov/products/palliative-care-integration/research?_gl=1*11h4fa6*_ga*MjYzNjk3MjU2LjE3MTU1OTU2MTM.*_ga_1NPT56LE7J*MTcxNjk4Mjg0MC4yLjEuMTcxNjk4MzcwOC4wLjAuMA..)
- Screening for Lung Cancer With Low-Dose Computed Tomography: An Evidence Review for the U.S. Preventive Services Task Force; Date: March 2021; Report Type: U.S. Preventive Services Task Force Evidence Syntheses; Affiliation: RTI International—University of North Carolina at Chapel Hill; Report Status: Final (https://www.uspreventiveservicestaskforce.org/uspstf/document/final-evidence-review/lung-cancer-screening)

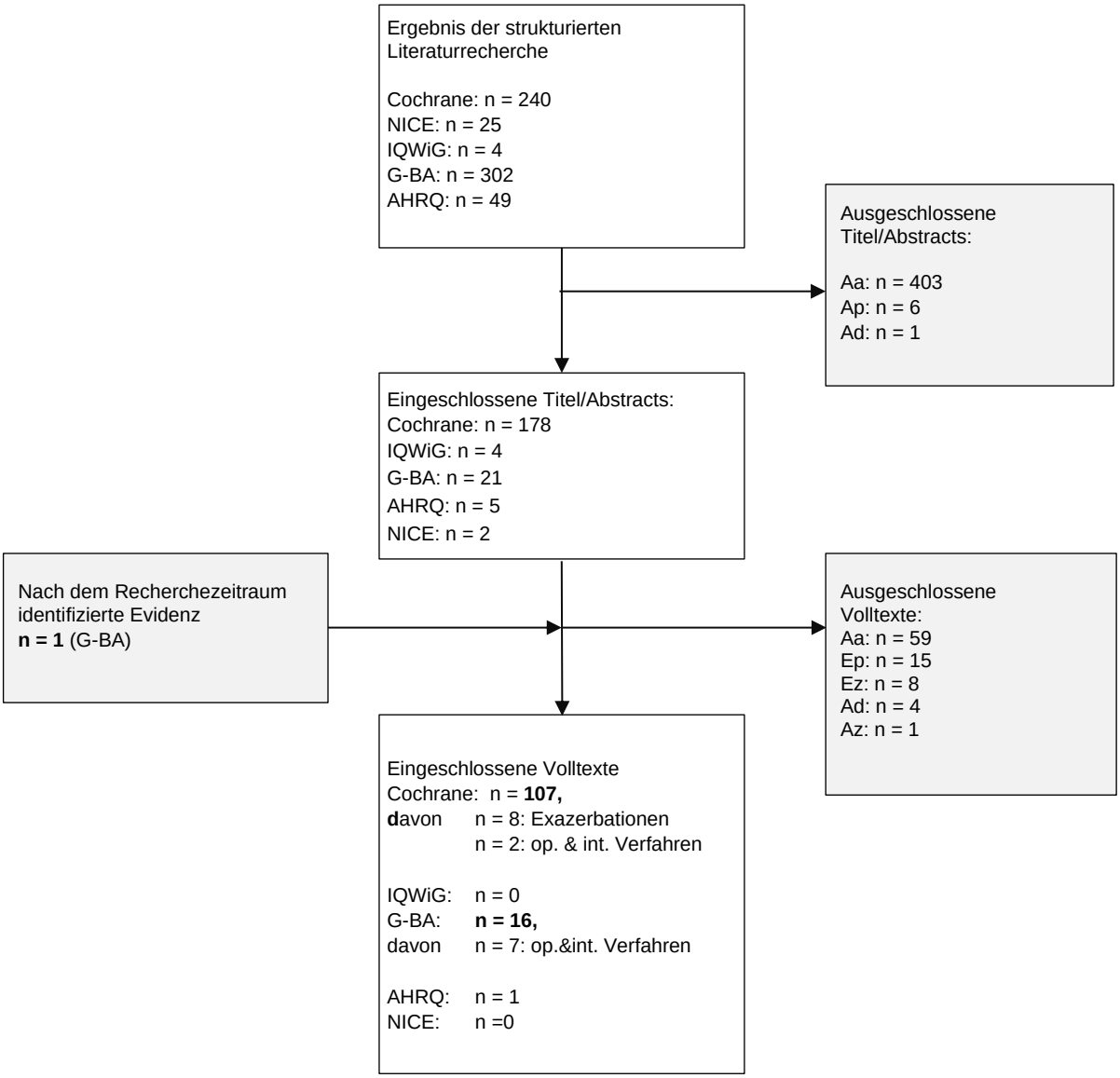
Relevante Treffer: n = 1

Einschluss nach Volltextscreening: n = 1

2.1.3 Übersicht der eingeschlossenen Treffer für Kapitel 8 und 9

	IQWiG	G-BA	NICE	Cochrane	AHRQ
E	0	7	0	13	1

2.1.4 Flowchart



2.2 Atemphysiotherapie (u.a. Selbsthilfetechniken)

Um zu klären, ob die Atemphysiotherapie bereits während der Exazerbation oder erst nach einigen Tagen eingesetzt werden kann, wurden die Daten aus der bereits durchgeführten systematischen Recherche für das Unterkapitel Atemphysiotherapie (2. Auflage) geprüft (siehe Leitlinienreport zur 2. Auflage [2]).

2.2.1 PICO-Fragestellung

Population Patient*innen mit COPD; evtl. mit Exazerbation

Intervention Atemtechniken (längerfristige und Notfalltechniken)

Comparison Jegliche

Outcome Priorisierte Endpunkte der Leitliniengruppe:

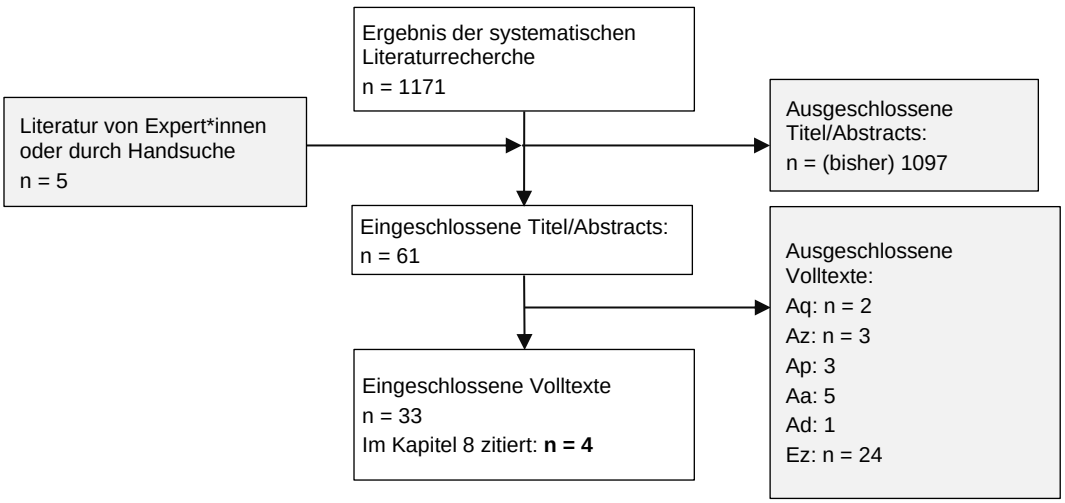
- krankheitsspezifische Mortalität
- Morbidität
  - Symptomatik: Atemnot, Husten und Auswurf
  - Mobilität/Funktionalität (Körperliche Belastbarkeit, Fähigkeit Treppen zu steigen, Exercise Tolerance)
  - soziale Teilhabe
  - Exazerbationen
  - Reduktion des zukünftigen Krankheitsrisikos: COPD-bedingte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

Studientyp Systematische Übersichtsarbeiten, RCTs

2.2.2 Recherchestrategien

Siehe Leitlinienreport zur 2. Auflage [2].

2.2.3 Flowchart



2.3 D-Dimer-Testung

2.3.1 PICO-Fragestellung

Population Patient*innen mit COPD und Exazerbation

Intervention D-Dimer-Test

Comparison

Outcome Diagnostische Genauigkeit; Erkennung Lungenembolie (DD)

Studientyp aggregierte Evidenz, ggf. RCT und andere Primärstudien

2.3.2 Recherchestrategien

Patient*innen mit Verdacht auf Exazerbation; stationäre Aufnahme ins Krankenhaus; D-Dimer-Testung zur Differentialdiagnostik (Lungenembolie).

Medline via Pubmed (www.pubmed.gov) (09. September 2021)

Nr.	Suchfrage	Anzahl
#19	**Search: #14 NOT (#17 OR #18)**	**65**
#18	**Search: (#14 AND #16) NOT #17**	**1**
#17	**Search: #14 AND #15**	**4**
#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]	1,404,060
#15	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 study[pt] OR validation study[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])	537,245
#14	Search: #7 AND #10 AND #13	70
#13	Search: #11 OR #12	13,671
#12	Search: "fibrin fragment D" [Supplementary Concept]	6,124
#11	Search: D-Dimer [tiab]	12,606
#10	Search: #8 OR #9	61,622
#9	Search: Pulmonary [tiab] AND (embolism* [tiab] OR thromboembolism* [tiab])	46,530
#8	Search: "Pulmonary Embolism" [Mesh]	40,824
#7	Search: #1 OR #2 OR #3 OR #4 OR #5 OR #6	118,484
#6	Search: "Air trapping" [tiab]	1,429
#5	Search: COAD [tiab]	613
#4	Search: COPD [tiab]	51,404
#3	Search: Emphysem* [tiab]	29,091

#2	Search: „Pulmonary Disease, Chronic Obstructive" [Mesh]	60,225
#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])))	68,167

Anzahl der Treffer: 4 Aggregierte Evidenz; 1 RCTs, 65 Sonstige

Datenbanken der Cochrane Library (09. September 2021)

Nr.	Suchfrage	Anzahl
#13	**(#7 and #10 and #11) NOT (conference abstract):pt in Trials**	**7**
#12	**(#7 and #10 and #11) NOT (conference abstract):pt in Cochrane Reviews, Cochrane Protocols**	**0**
#11	(D-Dimer):ti,ab,kw (Word variations have been searched)	2464
#10	#8 or #9	4442
#9	((Pulmonary and (embolism* or thromboembolism*))):ti,ab,kw (Word variations have been searched)	4442
#8	MeSH descriptor: [Pulmonary Embolism] explode all trees	1069
#7	#1 or #2 or #3 or #4 or #5 or #6	24136
#6	("air trapping" or airtrapping):ti,ab,kw (Word variations have been searched)	158
#5	((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*)):ti,ab,kw (Word variations have been searched)	17958
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1590
#3	(COAD):ti,ab,kw	85
#2	(COPD):ti,ab,kw	17200
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	6043

Cochrane Reviews • Review • Protocol	 0 0
Trials	7

Epistemonikos (09. September 2021)

Nr.	Suchanfrage	Anzahl
#1	(title:((title:(((chronic* [tiab]) AND ((obstruct* [tiab]) AND (pulmonary[tiab] OR lung* [tiab] OR airway* [tiab] OR airflow* [tiab] OR bronchi* [tiab] OR respirat* [tiab])))) OR abstract:(((chronic* [tiab]) AND ((obstruct* [tiab]) AND (pulmonary[tiab] OR lung* [tiab] OR airway* [tiab] OR airflow* [tiab] OR bronchi* [tiab] OR respirat* [tiab])))) OR (title:(Emphysem*) OR abstract:(Emphysem*)) OR (title:(COPD) OR abstract:(COPD)) OR (title:(COAD) OR abstract:(COAD)) OR (title:("Air trapping") OR abstract:("Air trapping"))) OR abstract:((title:(((chronic* [tiab]) AND ((obstruct* [tiab]) AND (pulmonary[tiab] OR lung* [tiab] OR airway* [tiab] OR airflow* [tiab] OR bronchi* [tiab] OR respirat* [tiab])))) OR abstract:(((chronic* [tiab]) AND ((obstruct* [tiab]) AND (pulmonary[tiab] OR lung* [tiab] OR airway* [tiab] OR airflow* [tiab] OR bronchi* [tiab] OR respirat* [tiab])))) OR (title:(Emphysem*) OR abstract:(Emphysem*)) OR (title:(COPD) OR abstract:(COPD)) OR (title:(COAD) OR abstract:(COAD)) OR (title:("Air trapping") OR abstract:("Air trapping")))) AND (title:((Pulmonary AND (embolism* OR thromboembolism*))) OR abstract:((Pulmonary AND (embolism* OR thromboembolism*)))) AND (title:(D-Dimer) OR abstract:(D-Dimer))	12

Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Epistemonikos	Summe
Aggregierte Evidenz	65	0		65
RCTs	1	7		8
Sonstige Primär	4		12	16
GESAMT				**89**

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

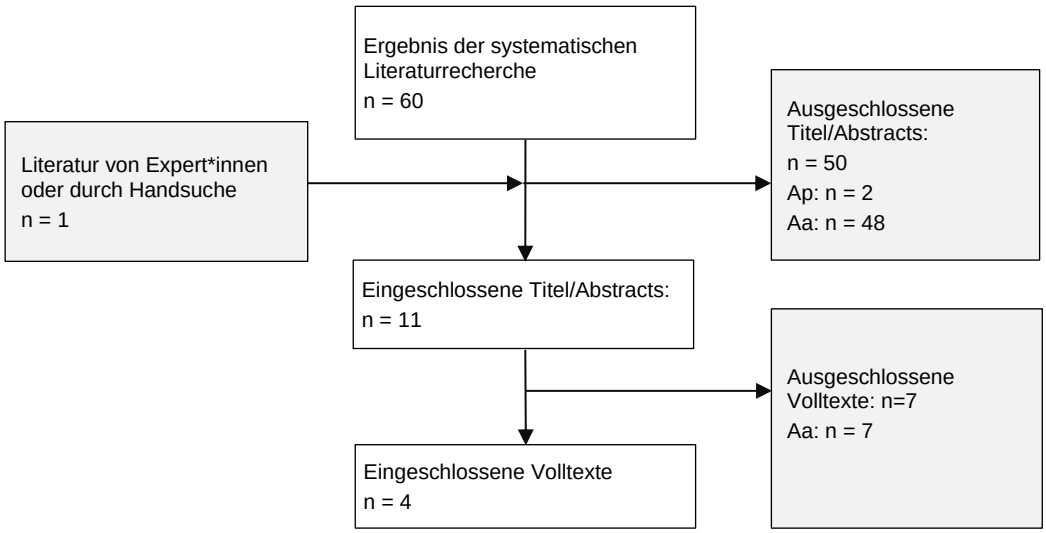
A1 (Dubletten): 13

A2 (nicht englisch/deutsch): 16

Eingeschlossene Treffer insgesamt nach Ausschlüssen: 60

Nach dem Recherchezeitraum wurde von der Leitliniengruppe selektiv eine weitere Studie eingebracht.

2.3.3 Flowchart



2.4 CRP, Sputum oder Procalcitonin

2.4.1 PICO-Fragestellung

Population Patient*innen mit COPD

Intervention CRP oder Sputumpurulenz oder PCT

Comparison

Outcome Cut-Offs für Therapieinitialisierung oder –anpassung; insbesondere für Antibiotika

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

2.4.2 Recherchestrategien

Vorüberlegung

Da die erste systematische Recherche zum Thema bereits 08/2018 durchgeführt wurde, wurde für die Bearbeitung der Fragestellung eine Update-Recherche durchgeführt. Hierbei wurde sukzessiv vorgegangen: zunächst wurde nach systematischen Übersichtsarbeiten zum Thema gesucht; falls diese Recherche keine Treffer erbrachte, wurde auf Ebene der Primärstudien weiter recherchiert. Der SIGN-Filter für Kohortenstudien und der McMaster Filter für diagnostische Studien wurde für diese Recherche adaptiert.

Medline via Pubmed (www.pubmed.gov) (11. November 2020)

Nr.	Suchfrage	Anzahl
#22	**Search: (#12 AND #21) NOT (#17 OR #18) Sort by: Most Recent**	**2**
#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] OR randomised [tiab] Sort by: Most Recent	1,374,313
#20	**Search: (#12 AND #16) NOT (#17 OR #18 OR #19) Sort by: Most Recent**	**47**
#19	**Search: (#12 AND #15) NOT (#17 OR #18) Sort by: Most Recent**	**244**
#18	**Search: (#12 AND #14) NOT #17 Sort by: Most Recent**	**70**
#17	**Search: #12 AND #13 Sort by: Most Recent**	**42**
#16	Search: (sensitiv*[Title/Abstract] OR "sensitivity and specificity"[MeSH] OR (predictive[Title/Abstract] AND value*[Title/Abstract]) OR "predictive value of tests"[MeSH] OR accuracy*[Title/Abstract]) Sort by: Most Recent	2,119,109
#15	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])) Sort by: Most Recent	3,340,653
#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] Sort by: Most Recent	1,335,449
#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 study[pt] OR validation study[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]	483,041

	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]) Sort by: Most Recent	
#12	Search: #7 AND #10 Filters: from 2018/8/17 - 3000/12/12 Sort by: Most Recent	685
#11	Search: #7 AND #10 Sort by: Most Recent	4,969
#10	Search: #8 OR #9 Sort by: Most Recent	140,389
#9	Search: "sputum"[MeSH Terms] OR "sputum"[tiab] Sort by: Most Recent	39,292
#8	Search: CRP[tiab] OR "c-reactive protein"[tiab] OR "C-Reactive Protein"[Mesh] OR PCT[tiab] OR procalcitonin[tiab] OR pro-calcitonin[tiab] Sort by: Most Recent	101,808
#7	Search: #1 OR #2 OR #3 OR #4 OR #5 OR #6 Sort by: Most Recent	112,251
#6	Search: "Air trapping" [tiab] OR airtrapping[tiab] Sort by: Most Recent	1,370
#5	Search: COAD[tiab] Sort by: Most Recent	478
#4	Search: COPD[tiab] Sort by: Most Recent	47,850
#3	Search: Emphysem*[tiab] Sort by: Most Recent	28,100
#2	Search: "Pulmonary Disease, Chronic Obstructive"[Mesh] Sort by: Most Recent	56,641
#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]) Sort by: Most Recent	63,958

Anzahl der Treffer: 42 Aggregierte Evidenz; 70 RCTs, 244 Beobachtungsstudien, 47 Diagnostische Studien

Datenbanken der Cochrane Library (11. November 2020)

Nr.	Suchfrage	Anzahl
#17	**(#7 and #15) NOT (conference abstract):pt in Trials with Publication Year from 2018 to present**	**207**
#16	**(#7 and #15) NOT (conference abstract):pt in Cochrane Reviews, Cochrane Protocols with publication date from Aug 2018 to present**	**7**
#15	#10 or #13 or #14	31364
#14	(PCT or procalcitonin or pro-calcitonin):ti,ab,kw (Word variations have been searched)	1550
#13	#11 or #12	5983
#12	(Sputum*):ti,ab,kw (Word variations have been searched)	5983
#11	MeSH descriptor: [Sputum] explode all trees	1269
#10	#8 or #9	24663
#9	MeSH descriptor: [C-Reactive Protein] explode all trees	4610
#8	(CRP or "c-reactive protein"):ti,ab,kw	24663
#7	#1 or #2 or #3 or #4 or #5 or #6	22775
#6	("air trapping" or airtrapping):ti,ab,kw (Word variations have been searched)	151
#5	((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*)):ti,ab,kw (Word variations have been searched)	16742
#4	(Emphysem*):ti,ab,kw	1512
#3	(COAD):ti,ab,kw	81
#2	(COPD):ti,ab,kw	16209
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	5738

Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
Aggregierte Evidenz	42	7	49
RCTs	70	207	277
Beobachtungsstudien	244		244
Diagnostische Studien	47		47
GESAMT:			**617**

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 63

A2 (nicht englisch/deutsch): 36

A3 (Conference Abstracts): 1

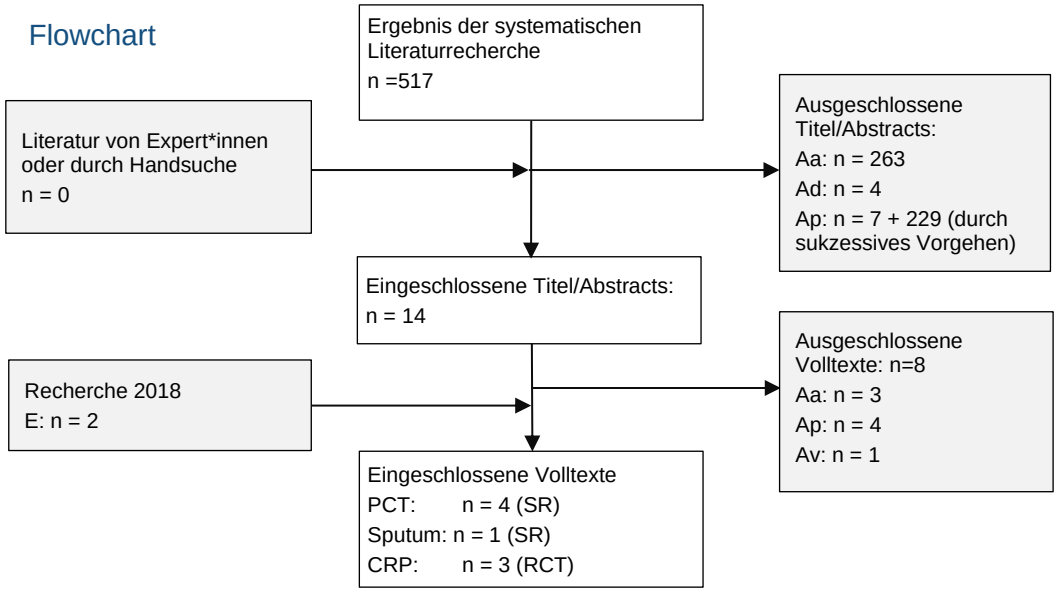
Eingeschlossene Treffer insgesamt nach Ausschlüssen: 517

Zusammenfassung

Recherche 2018: In einem iterativem Recherchevorgang wurde für n = 43 aggregierte Evidenzen ein Title/Abstract-Screening und darauf folgend für n = 13 ein Volltext-Screening durchgeführt. Für die Suche nach einem geeigneten Cut-Off für die Therapieinitialisierung oder –anpassung mittels Sputumpurulenz oder CRP-Werten, konnte je eine Evidenz identifiziert werden. Diese wurden jedoch zurückgestellt (Ez), da diese keine Anhaltspunkte bzw. Aussagen über Therapiesteuerung oder zur Diagnostik bereithalten. Es wurden n = 2 systematische Übersichtsarbeiten zu Procalcitonin identifiiziert.

Recherche 2021: Es wurden n = 2 systematische Übersichtsarbeiten zu Procalcitonin und n = 1 systematische Übersichtsarbeit zum Thema Sputum identifiziert. Zum Thema CRP wurde zusätzlich auf Primärstudienebene gescreent: hier konnten 3 RCTs zum Thema gefunden werden.

2.4.3 Flowchart



2.5 Opioide

2.5.1 PICO-Fragestellung

Population Patient*innen mit COPD

Intervention Opiate und Opioide: Anwendung in

- einer akuten Situation (Exazerbation) und/oder
- als Dauertherapie (insbesondere Morphin, Hydromorphon, Fentanyl- und Buprenorphinpflaster, Oxycodon)

Comparison keine Einschränkung

Outcome Priorisierte Endpunkte der Leitliniengruppe:

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

Studientyp Systematische Übersichtsarbeiten; ggf. RCTs und andere Primärstudien (wenn keine adäquate aggregierte Evidenz zu identifizieren ist.)

2.5.2 Recherchestrategien

Vorüberlegung

Sukzessives Vorgehen: Zunächst wurde nach systematischen Übersichtsarbeiten gesucht, falls hier keine entsprechenden Publikationen identifiziert werden konnten, wurde auf Ebene von RCTs und/oder anderen Arten von Primärstudien weiter recherchiert.

Medline via Pubmed (www.pubmed.gov) (08.01.2021)

Nr.	Suchfrage	Anzahl
#21	**Search: #15 NOT (#18 OR #19) Sort by: Publication Date**	**472**
#19	**Search: (#15 AND #17) NOT #18 Sort by: Publication Date**	**100**
#18	**Search: #15 AND #16 Sort by: Publication Date**	**35**
#17	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] Sort by: Publication Date	1,347,819
#16	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 study[pt] OR validation study[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]	492,448

	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]) Sort by: Publication Date	
#15	Search: #7 AND #14 Sort by: Publication Date	607
#14	Search: #8 OR #9 OR #10 OR #11 OR #12 OR #13 Sort by: Publication Date	224,591
#13	Search: Morphine[tiab] OR Hydromorphone[tiab] OR Fentanyl[tiab] OR Buprenorphine[tiab] OR Oxycodone[tiab] Sort by: Publication Date	76,733
#12	Search: opioid*[tiab] OR opiate*[tiab] Sort by: Publication Date	113,283
#11	Search: "Opioid Peptides"[Mesh] Sort by: Publication Date	31,420
#10	Search: "Analgesics, Opioid" [Pharmacological Action] Sort by: Publication Date	119,567
#9	Search: "Analgesics, Opioid"[Mesh] Sort by: Publication Date	46,191
#8	Search: "Opiate Alkaloids"[Mesh] Sort by: Publication Date	87,088
#7	Search: #1 OR #2 OR #3 OR #4 OR #5 OR #6 Sort by: Publication Date	113,416
#6	Search: "Air trapping" [tiab] OR airtrapping[tiab] Sort by: Publication Date	1,381
#5	Search: COAD[tiab] Sort by: Publication Date	502
#4	Search: COPD[tiab] Sort by: Publication Date	48,535
#3	Search: Emphysem*[tiab] Sort by: Publication Date	28,284
#2	Search: "Pulmonary Disease, Chronic Obstructive"[Mesh] Sort by: Publication Date	57,102
#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]))) Sort by: Publication Date	64,744

Anzahl der Treffer: 35 Aggregierte Evidenz; 100 RCTs, 472 Sonstige

Datenbanken der Cochrane Library (08.01.2021)

Nr.	Suchfrage	Anzahl
#15	**(#7 and #13) not "conference abstract":pt in Trials**	**234**
#14	**(#7 and #13) in Cochrane Reviews, Cochrane Protocols**	**2**
#13	#8 or #9 or #10 or #11 or #12	47091
#12	(Morphine or Hydromorphone or Fentanyl or Buprenorphine or Oxycodone):ti,ab,kw (Word variations have been searched)	30715
#11	(opioid* or opiate*):ti,ab,kw (Word variations have been searched)	26603
#10	MeSH descriptor: [Opioid Peptides] explode all trees	646
#9	MeSH descriptor: [Analgesics, Opioid] explode all trees	7605
#8	MeSH descriptor: [Opiate Alkaloids] explode all trees	10914
#7	#1 or #2 or #3 or #4 or #5 or #6	23168
#6	("air trapping" or airtrapping):ti,ab,kw (Word variations have been searched)	154
#5	(((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*):ti,ab,kw (Word variations have been searched)	17086
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1530
#3	(COAD):ti,ab,kw	81

#2	(COPD):ti,ab,kw	16488
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	5786

Epistemonikos (11.01.2021)

Nr.	Suchanfrage	Anzahl
#1	(title:((chronic* AND ((obstruct*) AND (pulmonary OR lung* OR airway* OR airflow* OR bronchi* OR respirat*)))) OR abstract:((chronic* AND ((obstruct*) AND (pulmonary OR lung* OR airway* OR airflow* OR bronchi* OR respirat*))))) OR (title:(Emphysem OR COPD OR COAD OR (air trapping) OR airtrapping) OR abstract:(Emphysem OR COPD OR COAD OR (air trapping) OR airtrapping)) AND (title:(opioid* OR opiate* OR Morphine OR Hydromorphone OR Fentanyl OR Buprenorphine OR Oxycodone) OR abstract:(opioid* OR opiate* OR Morphine OR Hydromorphone OR Fentanyl OR Buprenorphine OR Oxycodone)) Filter: systematic reviews	8

Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Epistemonikos	Summe
Aggregierte Evidenz	35	2	8	45
RCTs	100	234		334
Sonstige Primär	472			472
Gesamt				**851**

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 97

A2 (nicht englisch/deutsch): 1

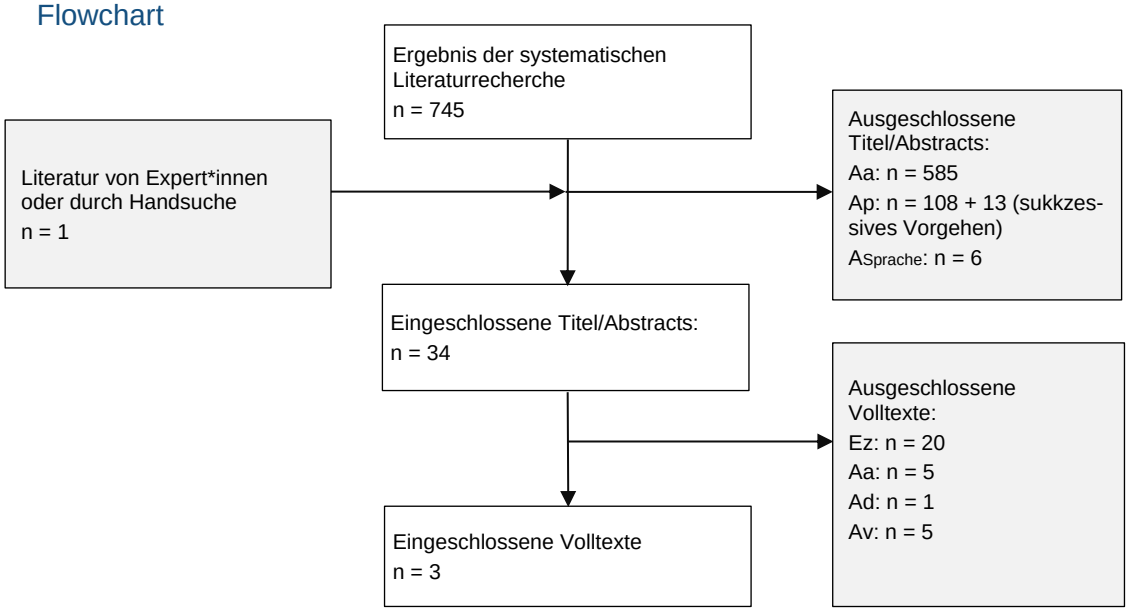
A3 (Conference Abstracts): 8

Eingeschlossene Treffer insgesamt nach Ausschlüssen: 745

Zusammenfassung

Für die Dauertherapie mit Opiaten und Opioiden konnten 2 aktuellere Metaanalysen identifiziert werden; für die Frage nach dem Einsatz von Opiaten und Opioiden in der Akutsituation (Exazerbation) wurde die Recherche auf Ebene der Primärstudien weitergeführt; die hier identifizierte Studie beantwortet jedoch nicht die Fragestellung, könnte aber möglicherweise zur Diskussion von Sicherheitsaspekten zur Gabe von Opioiden in einem akuten Setting herangezogen werden.

2.5.3 Flowchart



2.6 Prärehabilitation

2.6.1 PICO-Fragestellung

Population	Pat. mit COPD
Intervention	präinterventionelle Rehabilitationsmaßnahmen
Comparison	keine präinterventionelle Rehabilitation
Outcome	operatives Outcome, funktionale Kriterien präoperativ
Studientyp	aggregierte Evidenz, RCT, ggf. andere Primärstudien

2.6.2 Recherchestrategien

Medline via Pubmed (www.pubmed.gov) (18. Mai 2022)

Nr.	Suchfrage	Anzahl
#32	**Search: #27 NOT (#30 OR #31)**	**761**
#31	**Search: (#27 AND #29) NOT #30**	**171**
#30	**Search: #27 AND #28**	**58**
#29	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]	1,459,400
#28	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 study[pt] OR validation study[pt]	583,389

	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])	
#27	Search: #7 AND #22 AND #26	990
#26	Search: #23 OR #24 OR #25	519,943
#25	Search: Rehab*[tiab] OR exercis*[tiab]	519,376
#24	Search: Prerehab*[tiab] OR pre-rehab*[tiab] OR prehab* [tiab]	1,338
#23	Search: "Preoperative Exercise"[Mesh]	253
#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	1,728,521
#21	Search: Lung[tiab] AND (translantation*[tiab] OR graft*[tiab])	7,902
#20	Search: „lung denervation" [tiab] OR TLD [tiab]	2,553
#19	Search: (endoscopic*[tiab] OR bronchoscopic*[tiab]) AND reduction*[tiab]	6,370
#18	Search: valve*[tiab] OR coil*[tiab] OR AeriSeal[tiab] OR (lung*[tiab] AND sealant[tiab]) OR "Biologic Lung Volume Reduction"[tiab] OR (bronchoscopic*[tiab] AND ablation[tiab]) OR BLVR[tiab]	228,988
#17	Search: airway*[tiab] AND (bypass*[tiab] OR stent*[tiab])	3,281
#16	Search: pneumoplasty[tiab] OR pneumonectomy[tiab]	11,062
#15	Search: LVRS[tiab] OR LVR[tiab]	1,134
#14	Search: "lung volume reduct*"[tiab] OR "lung reduct*"[tiab] OR "volume reduct*"[tiab]	8,382
#13	Search: Surgery[tiab]	1,386,669
#12	Search: "Thoracic Surgery"[Mesh]	13,359
#11	Search: "Pulmonary Surgical Procedures"[Mesh]	77,422
#10	Search: "Pneumonectomy"[Mesh]	28,258
#9	Search: "Stents"[Mesh]	86,251
#8	Search: "Thoracic Surgery, Video-Assisted"[Mesh]	8,162
#7	Search: #1 OR #2 OR #3 OR #4 OR #5 OR #6	123,387
#6	Search: "Air trapping" [tiab]	1,484
#5	Search: COAD [tiab]	786
#4	Search: COPD [tiab]	54,221

#3	Search: Emphysem* [tiab]	29,812
#2	Search: „Pulmonary Disease, Chronic Obstructive" [Mesh]	63,348
#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])))	71,522

Datenbanken der Cochrane Library (19.05.2022)

Nr.	Suchfrage	Anzahl
#29	**(#7 AND #23 AND #27) NOT (conference abstract):pt in Trials**	**315**
#28	**#7 AND #23 AND #27 in Cochrane Reviews, Cochrane Protocols**	**5**
#27	#24 or #25 or #26	154767
#26	((Rehab* or exercis*)):ti,ab,kw (Word variations have been searched)	154685
#25	((Prerehab* or pre-rehab* or prehab*)):ti,ab,kw (Word variations have been searched)	511
#24	MeSH descriptor: [Preoperative Exercise] explode all trees	38
#23	#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	249286
#22	((Lung and (translantation* or graft*))):ti,ab,kw (Word variations have been searched)	1486
#21	((“lung denervation“ or TLD)):ti,ab,kw (Word variations have been searched)	67
#20	(BLVR):ti,ab,kw	15
#19	((((endoscopic* or bronchoscopic*) and reduction*))):ti,ab,kw (Word variations have been searched)	2207
#18	(((valve* or coil* or AeriSeal or (lung* and sealant) or "Biologic Lung Volume Reduction" or (bronchoscopic* and ablation)))):ti,ab,kw (Word variations have been searched)	11743
#17	(((airway* and (bypass* or stent*)))):ti,ab,kw (Word variations have been searched)	421
#16	(((“reduction Pneumoplasty“ or pneumonectomy))):ti,ab,kw (Word variations have been searched)	858
#15	(((LVRS or LVR))):ti,ab,kw	180
#14	(((“lung volume reduction“ or “lung reduction“ or “volume reduction“))):ti,ab,kw (Word variations have been searched)	1193
#13	("Surgery*"):ti,ab,kw (Word variations have been searched)	236707
#12	MeSH descriptor: [Thoracic Surgery] explode all trees	176
#11	MeSH descriptor: [Pulmonary Surgical Procedures] explode all trees	1595
#10	MeSH descriptor: [Pneumonectomy] explode all trees	595
#9	MeSH descriptor: [Stents] explode all trees	4521
#8	MeSH descriptor: [Thoracic Surgery, Video-Assisted] explode all trees	300
#7	#1 or #2 or #3 or #4 or #5 or #6 (Word variations have been searched)	24794
#6	((("air trapping" or airtrapping))):ti,ab,kw	145
#5	(((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*))):ti,ab,kw (Word variations have been searched)	18526
#4	(Emphysem*):ti,ab,kw	1626
#3	(COAD):ti,ab,kw	89
#2	(COPD):ti,ab,kw	17603

#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	6283

Epistemonikos (www.epistemonikos.org) (19.Mai 2022)

Nr.	Suchfrage	Anzahl
#1	(title:(((chronic* AND (obstruct* AND (pulmonary OR lung* OR airway* OR airflow* OR bronchi* OR respirat*))) OR Emphysem OR COPD OR COAD OR "air trapping" OR airtrapping) AND (Prerehab* OR pre-rehab* OR prehab* OR ((perioperati* OR preoperativ*) AND (rehab* OR exercis*)))) OR abstract:(((chronic* AND (obstruct* AND (pulmonary OR lung* OR airway* OR airflow* OR bronchi* OR respirat*))) OR Emphysem OR COPD OR COAD OR "air trapping" OR airtrapping) AND (Prerehab* OR pre-rehab* OR prehab* OR ((perioperati* OR preoperativ*) AND (rehab* OR exercis*))))) Publication type: systematic Review	2

Übersicht der eingeschlossenen Treffer

	Medline	Cochrane	Epistemonikos	Summe
Aggregierte Evidenz	58	5	2	65
RCTs	171	315		486
Sonstige Primär	761			761
GESAMT				**1312**

Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 123

A2 (nicht englisch/deutsch): 120

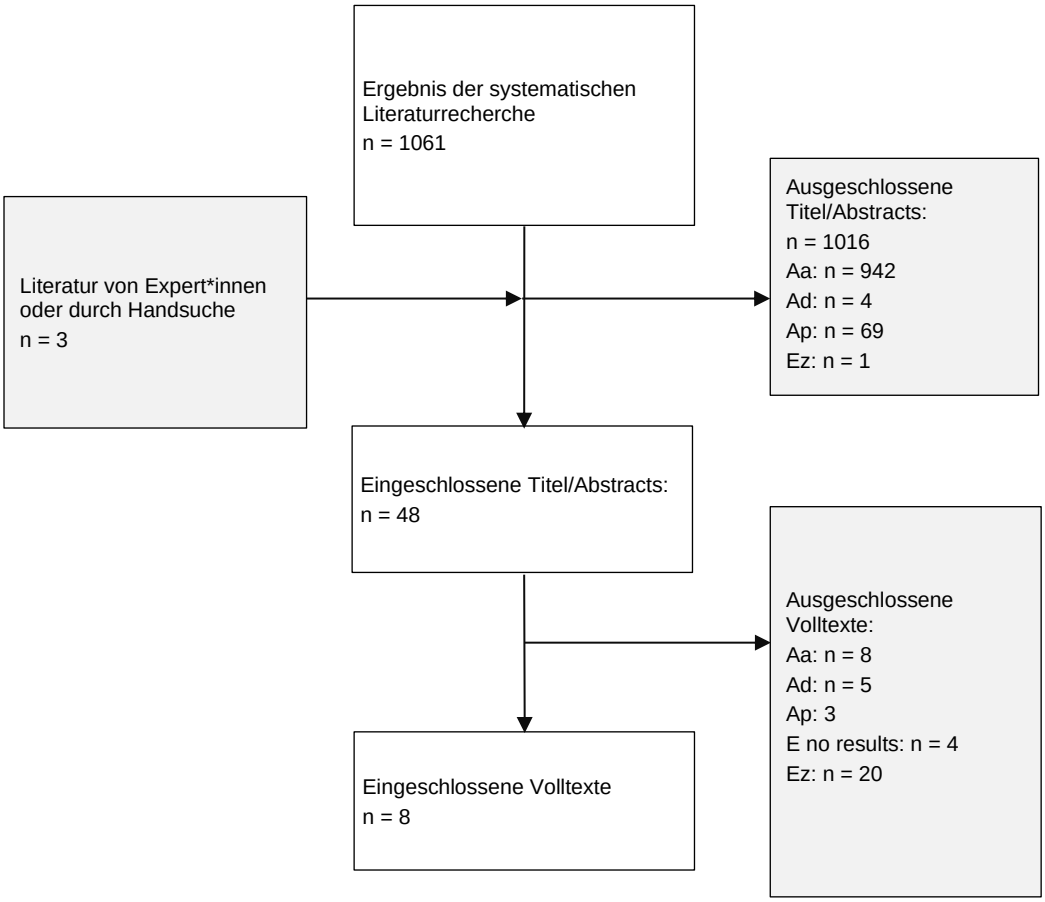
A3 (Conference Abstracts): 8

Eingeschlossene Treffer insgesamt nach Ausschlüssen: 1061

Zusammenfassung

Ein großer Anteil aller identifizierten Studien betrachtet Patient*innen mit COPD und einer Lungenkrebserkrankung; der chirurgische Eingriff bezieht sich ebenso auf diese Population.

2.6.3 Flowchart



2.7 Gezielte Lungendenervierung

2.7.1 PICO-Fragestellung

Population Patient*innen mit COPD

Intervention Gezielte Lungendenervierung (TLD: Targeted Lung Denervation)

Comparison

Outcome Priorisierte Endpunkte der Leitliniengruppe:

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

Studientyp Primärstudien (RCT, ggf. andere Primärstudien für Sicherheitsaspekte)

2.7.2 Recherchestrategien

Zusammenfassung

In einem ersten Schritt erfolgte eine strukturierte Suche nach Übersichtsarbeiten bei ausgewählten Institutionen. Auf Grund ihrer evidenzbasierten Vorgehensweise, ihrer hohen Berichtsqualität, ihrer wissenschaftlichen Unabhängigkeit, eines weitergehenden Einblicks in Studiendossiers und ihres Bezugs zum deutschen bzw. europäischen Versorgungskontext: IQWiG; NICE; Cochrane Collaboration; AHRQ. Auf Grundlage der dabei identifizierten Evidenz wurde in einem 2. Schritt eine zusätzliche systematische Update-Recherche durchgeführt. Suchzeitraum: ab 2018 (Veröffentlichung des Addendum zum Thema vom IQWiG (IQWiG-Berichte – Nr. 622/ H18-02).

Es konnten keine neuen RCTs anderer Studiengruppen zum Thema gezielte Lungendenervierung identifiziert werden. Follow up-Publikationen der AIRFLOW-1 und AIRFLOW-2 Studie werden hier aufgeführt.

Medline via Pubmed (www.pubmed.gov) (14.09.2021)

Nr.	Suchfrage	Anzahl
#13	**Search: #10 NOT #12**	**14**
#12	**Search: #10 AND #11**	**6**
#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]	1,405,039
#10	Search: #7 AND #8 Filters: from 2018/1/1 - 3000/12/12	20
#9	Search: #7 AND #8	35
#8	Search: „lung denervation" [tiab] OR TLD [tiab]	2,486
#7	Search: #1 OR #2 OR #3 OR #4 OR #5 OR #6	118,560
#6	Search: "Air trapping" [tiab]	1,431
#5	Search: COAD [tiab]	615
#4	Search: COPD [tiab]	51,448
#3	Search: Emphysem* [tiab]	29,106
#2	Search: „Pulmonary Disease, Chronic Obstructive" [Mesh]	60,279
#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])))	68,223

Anzahl der Treffer: 6 RCTs, 14 Sonstige

Datenbanken der Cochrane Library (14.09.2021)

Nr.	Suchfrage	Anzahl
#9	**#7 AND #8 NOT (conference abstract):pt in Trials - Year first published: from 2018**	**9**
#8	(("lung denervation" or TLD)):ti,ab,kw (Word variations have been searched)	66
#7	#1 or #2 or #3 or #4 or #5 or #6	24136
#6	(("air trapping" or airtrapping)):ti,ab,kw (Word variations have been searched)	158
#5	((((pulmonary or lung* or airway* or airflow* or bronchi* or respirat*) and obstruct*) and chronic*)):ti,ab,kw (Word variations have been searched)	17958
#4	(Emphysem*):ti,ab,kw (Word variations have been searched)	1590
#3	(COAD):ti,ab,kw	85
#2	(COPD):ti,ab,kw	17200
#1	MeSH descriptor: [Pulmonary Disease, Chronic Obstructive] explode all trees	6043

Übersicht der eingeschlossenen Treffer

	Medline	Cochrane Datenbanken	Summe
RCTs	6	9	15
Sonstige Primär	14		14
GESAMT			**29**

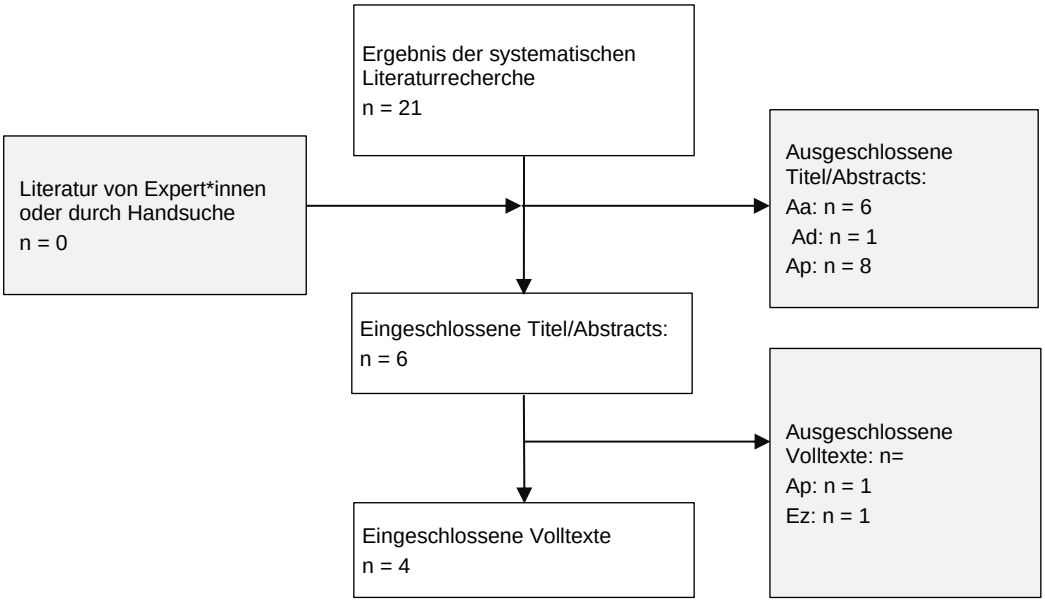
Anzahl der ausgeschlossenen Publikationen nach Ausschlussgrund:

A1 (Dubletten): 7

A2 (nicht englisch/deutsch): 1

Eingeschlossene Treffer insgesamt nach Ausschlüssen: 21

2.7.3 Flowchart



2.8 Häufigkeit von Exazerbationen

Gezielte Recherche zur Häufigkeit von Exazerbationen speziell in Deutschland. Hierzu wurden Daten aus COSYCONET und DACCORD herangezogen. Zusätzlich wurden auch Veröffentlichungen von u.a. RKI, NaKo und DMP zum Thema geprüft. Suche nach Schlüsselwörtern: COPD; Exazerbation.

- **Zi/Versorgungsatlas**: https://www.versorgungsatlas.de/. Letzte Recherche: 20.06.2024.

  5 Treffer; 1 Einschluss: https://www.versorgungsatlas.de/fileadmin/ziva_docs/99/VA_19-06_Bericht-COPD_2019-08-20_V2_1.pdf
- **NaKo:** https://nako.de/. Letzte Recherche: 20.06.2024.

  Keine Publikationen zur Fragestellung.
- **RKI:** https://www.rki.de/DE/Content/Gesundheitsmonitoring/Themen/Chronische_Erkrankungen/lungenerkrankungen/lungenerkrankungen_node.html. Letzte Recherche: 20.06.2024.

  Keine Publikationen zur Fragestellung .
- **DMP:** https://www.kbv.de/html/8456.php. Letzte Prüfung: 16.09.2024: Update vom 11.7.2024 publiziert

  1 Treffer: https://www.kbv.de/media/sp/DMP_COPD_Ergebnisse_QS.pdf
- **COSYCONET:** http://www.asconet.net/html/cosyconet. Letzte Recherche: 20.06.2024.

  http://www.asconet.net/html/cosyconet/publik/manus --> 42 Publikationen gescreent; 2 Volltexte, 1 Einschluss
  - Kahnert K, Alter P, Welte T, Huber RM, Behr J, Biertz F, Watz H, Bals R, Vogelmeier CF, Jörres RA. Uric acid, lung function, physical capacity and exacerbation frequency in patients with COPD: a multi-dimensional approach. Respir Res. 2018 Jun 4;19(1):110. doi: 10.1186/s12931-018-0815-y. 20. → Aa
  - Karch A, Vogelmeier C, Welte T, Bals R, Kauczor HU, Biederer J, Heinrich J, Schulz H, Glaser S, Hol-le R, et al. The German COPD cohort COSYCONET: aims, methods and descriptive analysis of the study population at baseline: Table 2→ E

  Update 20.06.2024: http://www.asconet.net/html/cosyconet-2: Zugang zum Portal nur mit Passwort und Benutzername möglich
- **DACCORD**
  - The ‘real-life’ COPD patient in Germany: The DACCORD study Ref ID 29219
  - A year in the life of German patients with COPD: the DACCORD observational study
  - A two-year evaluation of the ‘real life’ impact of COPD on patients in Germany: The DAC-CORD observational study

  Letzte Prüfung: 21.06.2024: keine neuen Publikationen identifiziert.

2.9 Recherche im AWMF-Leitlinienregister

Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)

Gezielte Recherche nach themenverwandten AWMF-Leitlinien: Leitliniensuche unter https://register.awmf.org/de/start bei Anmeldung der NVL und intermittierend während der Bearbeitung der einzelnen Themenbereiche.

- Zeitpunkt der letzten Suche: 21.06.2024
- Suchbegriff: COPD
- Status: alle
- Dokumententyp: alle
- Entwicklungsstufe: alle
- Gesellschaft: alle
- Organisation: alle
- Sortieren nach: Relevanz

Eingeschlossene Leitlinien: n = 10

3 Evidenztabellen Exazerbationen

3.1 Cochrane Reviews

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit der Evidenz	Kommentar
Kopsaftis Z. Oxygen therapy in the pre-hospital setting for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2020; 1(1):CD005534. dx.doi.org/10.1002/14651858.CD005534.pub3. https://www.ncbi.nlm.nih.gov/pubmed/31934729.	**Fragestellung:** 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). **Suchzeitraum:** 09/ 2019 **Population:** people with acute exacerbations of COPD (AECOPD) **Intervention:** titrated oxygen therapy **Vergleich:** high-flow oxygen therapy **eingeschlossene Studien**: 1 RCT, n=214 participants	• **Baseline-Charakteristika:** mean age 68 years • **mortality (respiratory- related and allcause)** - 21/1000 vs. 94/1000; RR 0,22 (95% KI 0,05; 0,97); 1 RCT, n=214; **GRADE: low** - number needed to treat for an additional beneficial outcome (NNTB): 14 (95% KI 12; 355) with titrated oxygen therapy • **Arterial blood gas (pH);** - MD **0.06 pH** (-0.04 to 0.16), 1 RCT, n=214; **GRADE: low** - high-flow oxygen therapy: mean arterial blood gas (pH) was 7.29 • **Ventilation of any type** - 6/1000 vs. 143/1000; RR 0.67 (95% KI 0,29; 1,55); 1 RCT, n=189, **GRADE: low** • **Length of hospital stay**; - MD -**0.88 days** (-2.25 to 0.49), 1 RCT, n=214; **GRADE: low** - high-flow oxygen therapy: mean length of hospital stay was 6.3 days >> 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 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 elect of oxygen therapies in the pre-hospital setting for people with AECOPD.	AMSTAR-2: Qualität des Reviews: - high AMSTAR-Score kritische Kriterien: - 5/5 3 Items nicht gewertet, da keine Metaanalyse durchgeführt wurde Evidenzqualität siehe endpunktspezifische GRADE- Bewertung des Reviews	
Osadnik CR. Non-invasive ventilation for the management of acute hypercapnic respiratory failure due to exacerbation of chronic obstructive pulmonary	**Fragestellung:** To compare the efficacy of NIV applied in conjunction with usual care versus usual care involving no mechanical ventilation alone in adults with AHRF due to AECOPD. AHRF: acute hypercapnic respiratory failure **Suchzeitraum:** 01/2017 **Population:** adults with AHRF due to AECOPD **Einschlusskriterien:** acute hospital setting	**Non-invasive ventilation versus usual medical care** - Mortality: 99/1000 vs. 183/1000; RR 0.54 (0.38 to 0.76), I^2 = 0%, 12 RCTs, n = 854, **GRADE: moderate** - Need for endotracheal intubation: 123/1000 vs. 341/1000; RR 0.36 (0.28 to 0.46), I^2 = 0%, 17 RCTs, n = 1105, **GRADE: moderate** - Length of hospital stay (days): MD -3.39 (- 5.93 to -0.85), I^2 = 84%, 10 RCTs, n = 888; **GRADE: moderate**	AMSTAR-2: Qualität des Reviews: - low AMSTAR-Score kritische Kriterien: 6/7 PY=1 N=0	

disease. Cochrane Database of Systematic Reviews 2017;(7).	**Interventionen:** usual care plus NIV (BiPAP) **Vergleich:** usual care alone **eingeschlossene Studien:** 17 RCT (n = 1264) **Definition AHRF:** mean admission pH < 7.35 and mean partial pressure of carbon dioxide (PaCO2) > 45 mmHg (6 kPa)		Evidenzqualität siehe endpunktspezifische GRADE- Bewertung des Reviews	
Brown CD. Inhaled short-acting beta2-agonists versus ipratropium for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2001;(1).	**Fragestellung:** 1. To assess the efficacy of short-acting beta-2 agonists against placebo ; 2. Compare the efficacy of short-acting beta-2 agonists and ipratropium. **Suchzeitraum:** 02/2002 **Population**: patients with acute exacerbations of COPD **Interventionen:** short-acting beta-2 agonists **Vergleich**: placebo or ipratropium **eingeschlossene Studien:** 3 Studies (n = 103)	**Baseline-Charakteristika:** - beta2-agonists used were: fenoterol and metaproterenol Symptom or dyspnoea scores were not reported and there were no data on length of hospital stay. Adverse drug reactions were reported by a minority of subjects in all 3 studies. Backman 1985 had one person in each group describe an unexplained “strange feeling” after using ipratropium bromide or fenoterol. Dry mouth and tremor were the most commonly reported reactions by Karpel 1990 and Rebuck 1987. One subject in each group experienced dry mouth in the study conducted by Karpel 1990; Rebuck 1987 reports 4 patients in the beta-2 agonist group, and 1 in the ipratropium bromide group for the same reaction. Tremor occurred in similar numbers with 2 in each of the groups of Karpel 1990 and 3 each for those reported by Rebuck 1987. **RoB der eingeschlossenen Studien (**GRADE nicht durchgeführt) - Backmann 1985: Allocation concealment: unclear; double-blind - Karpel 1990: Allocation concealment: low, double-blind - Rebuck 1987: Allocation concealment: low, double-blind	Qualität des Reviews: - critically low AMSTAR II-Score kritische Kriterien: 4/7 PY=2 N=1	keine von der LL-Gruppe priorisierten Endpunkte betrachtet (hier Parameter wie: FEV1, PEFR, pO2, pCO2)
McCrory DC. Anticholinergic bronchodilators versus beta2-sympathomimetic agents for acute exacerbations of chronic obstructive pulmonary disease.	**Fragestellung:** To assess the effect of anti-cholinergic agents on lung function and dyspnea in patients with acute exacerbations of COPD, compared with placebo or short-acting beta-2 agonists. **Suchzeitraum:** na (Date of most recent amendment 18.11.2004) **Population:** patients with acute exacerbations **Interventionen:** inhaled ipratropium bromide or	**Baseline-Charakteristika:** - 4 studies permitted a direct comparison of ipratropium to an inhaled beta2-agonist - 5 studies compared a combination of ipratropium and a short-acting beta2-agonist to use of a beta2-agonist alone Adverse drug reactions were reported by only a minority of the included studies (n = 4). The reaction described dry mouth and tremor (Karpel 1990, Rebuck 1987), and a 'strange feeling' after drug administration (Backman 1985). O'Driscoll 1989 and Karpel 1990 speci cally looked at hemodynamic changes and found no differences between the treatment groups.	AMSTAR-2 Qualität des Reviews: - critically low AMSTAR II-Score kritische Kriterien: 3/7 PY=2 N=2	keine von der LL-Gruppe priorisierten Endpunkte betrachtet (hier Parameter: FEV1, PEFR, paO2, paCO2)

Cochrane Database of Systematic Reviews 2003;(1).	oxitropium bromide **Vergleich:** placebo or short-acting beta-2 agonists **eingeschlossene Studien:** 8 studies	**Authors' conclusions:** There was no evidence that the degree of bronchodilation achieved with ipratropium bromide was greater than that using a shortacting beta2-agonist. The combination of a beta2-agonist and ipratropium did not appear to increase the effect on FEV1 more than either used alone. **RoB der eingeschlossenen Studien** (GRADE nicht durchgeführt) Lloberes 1988: Allocation concealment D, single-blinded Moayyedi 1995: Allocation concealment B, single-blinded Patrick 1990: Allocation concealment B, double-blind O'Driscoll 1989: Allocation concealment C, double-blind Rebuck 1987: Allocation concealment A, not blinded at Shretha 199: Allocation concealment A, double-blind Backman 1985: Allocation concealment B, double-blind Karpel 1990: Allocation concealment A, double-blind		
van-Geffen WH. Bronchodilators delivered by nebuliser versus pMDI with spacer or DPI for exacerbations of COPD. Cochrane Database of Systematic Reviews 2016;(8).	• **Fragestellung:** To compare the effects of nebulisers versus pressurised metered dose inhalers (pMDI) plus spacer or dry powder inhalers (DPI) in bronchodilator therapy for exacerbations of COPD. • Metaanalyse, RCTs of both parallel and crossover designs included • **Suchzeitraum:** 07/2016 • **Population:** Patienten mit COPD (Exazerbation) • **Einschlusskriterien:** participants with an exacerbation of COPD receiving treatment at home, in the clinic or in hospital • **Ausschlusskriterien:** - RCTs involving mechanically ventilated patients	• primärer Endpunkt: serious adverse events - similar frequencies of serious adverse events: OR 1.00 (0.18 to 5.53) (2 studies, 70 participants; **GRADE: Low**) • sekundärer Endpunkt: adverse events - non-significant odds ratio of 1.65 (95% CI 0.42 to 6.48) in favour of the pMDI plus spacer group. (n=3 studies; n= 110 participants; **GRADE: Low**)	Qualität des Reviews: -moderate Evidenzqualität siehe endpunktspezifische GRADE- Bewertung des Reviews	keine durch die Leitliniengruppe priorisierten Endpunkte betrachtet
Walters-Julia AE. Systemic corticosteroids for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2014;(9).	**Fragestellung:** To assess the effects of corticosteroids administered orally or parenterally for treatment of acute exacerbations of COPD, and to compare the efficacy of parenteral versus oral administration. **Suchzeitraum:** 05/2014 **Population:** people with AECOPD **Interventionen:** - corticosteroids (orally or parenterally) vs. appropriate placebo	**Systemic corticosteroid compared with placebo** - Treatment failure: 154/1000 vs. 276/1000, OR 0.48 (0.35 to 0.67), I^2 = 32%, 9 studies, n = 917 ; **GRADE: high** - Relapse: 174/1000 vs. 215/1000; OR 0.77 (0.51 to 1.17), I^2 = n.a., 5 studies; n = 596, **GRADE: moderate** - Decreased breathlessness - early effect: SMD 0.35 (95% CI 0.05 to 0.64); I^2 = 31%; 3 studies, n = 178, **GRADE: moderate** - Adverse drug effect (Follow-up: 2-26 weeks): 481/1000 vs. 285/1000, OR 2.33 (1.59 to 3.43), I^2 = 24%, 8 studies, n = 736, **GRADE: high** - Hyperglycaemia: 282/1000 vs. 124/1000; OR 2.79 (1.86 to 4.19); I^2 = 24%, 6 studies, n = 804, **GRADE: high**	AMSTAR-2: Qualität des Reviews: - moderate AMSTAR II-Score kritische Kriterien: 7/7 Evidenzqualität siehe endpunktspezifische GRADE- Bewertung des Reviews	

	or - oral corticosteroids with parenteral corticosteroids **eingeschlossene Studien:** 16 studies (n = 1787) **Primary outcomes** 1. Treatment failure: defined as necessity to intensify pharmacological treatment, hospital admission during outpatient treatment or return to emergency department during outpatient treatment. 2. Relapse: defined as treatment or hospital admission for a COPD exacerbation after completion of study treatment. 3. Mortality.	**Intravenous corticosteroid compared with oral corticosteroid** - Treatment failure: 115/1000 vs. 162/1000, OR 0.67 (0.34 to 1.3), I² = 0%, 3 studies, n = 298, **GRADE: moderate** - Relapse: 149/1000 vs. 155/1000, OR 0.95 (0.5 to 1.8),I² = 0%, 3 studies, n = 298, **GRADE: moderate** - breathlessness (VAS): MD 0.62 (-0.55, 1.78), I² = 0%, 2 studies, n = 75, **GRADE: low** - Mortality after discharge (1-3 months): 37/1000 vs. 27/1000, OR 1.4 (0.44 to 4.51), I² = 17%, 3 studies, n = 298, **GRADE: moderate** - Adverse drug effect - hyperglycaemia: 550/1000 vs. 200/1000, OR 4.89 (1.2 to 19.94), 1 study, n = 40, **GRADE: moderate**		
Walters-Julia AE. Different durations of corticosteroid therapy for exacerbations of chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2018;(3).	Fragestellung: To compare the efficacy of short-duration (seven or fewer days) and conventional longer-duration (longer than seven days) systemic corticosteroid treatment of adults with acute exacerbations of COPD. Suchzeitraum: 03/2017 Population: Adults with AECOPD Ausschlusskriterien: Studies with participants requiring assisted ventilation Interventionen: short durations of systemic corticosteroid (≤ 7 days) Vergleich: longer durations of systemic corticosteroid (> 7 days) Settings: hospital-initiated treatment eingeschlossene Studien für Metaanalyse: 5 studies (n= 519) Primary outcomes 1. Treatment failure (e.g. the need for additional treatment, hospital admission/re-admission for index episode, return to emergency department, unscheduled physician visit for the index episode). 2. Relapse after treatment (e.g. treatment for	**Baseline-Charakteristika:** - Mean ages: 65 to 73 years, proportion of male: 58% to 84% - COPD was classified as severe or very severe **SCS treatment for 7 or fewer days compared with SCS treatment for longer than 7 days for** - Treatment failure: 61/1000 vs. 83/1000, OR 0.72 (0.36 to 1.46), I² = 0%, 4 studies, n = 457, **GRADE: moderate** - Relapse: 304/1000 vs. 295/1000; OR 1.04 (0.7 to 1.56), I² = 0%, 4 studies, n = 478, **GRADE: moderate** - Adverse drug effect hyperglycaemia: 439/1000 vs. 442/1000, OR 0.99 (0.64 to 1.53), I² = 0%, 2 studies, n = 345, **GRADE: moderate** - Adverse drug effects: 75/1000 vs. 84/1000, OR 0.88 (0.46 to 1.7), I² = 0%, 5 studies, n = 503, **GRADE: low** - Mortality: 71/1000 vs. 77/1000, OR 0.91 (0.4 to 2.06), I² = n.a., 2 studies, n = 336, **GRADE: moderate** - Length of hospitalisation: MD -0.61 days (95% CI -1.51 to 0.28); I² = 0%, 3 studies, n = 421, **GRADE: moderate** - Health- related quality of life (QOL): MD 0.06 (-0.6 to 0.28), 1 study, n = 271, **GRADE: moderate**	AMSTAR-2: Qualität des Reviews: -moderate AMSTAR-Score kritische Kriterien: 7/7 Evidenzqualität siehe endpunktspezifische GRADE- Bewertung des Reviews	Die hier eingeschlossenen Primärstudien wurden hinsichtlich der Effektivität einzelner Dosierungen von Corticosteroiden bei Exazerbationen ausgewertet.

	new acute exacerbation, re-admission or hospitalisation for COPD). 3. Adverse drug effects.			
Vollenweider DJ. Antibiotics for exacerbations of chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2018;(10).	**Fragestellung:** To assess effects of antibiotics on treatment failure as observed between seven days and one month after treatment initiation (primary outcome) for management of acute COPD exacerbations, as well as their effects on other patient-important outcomes (mortality, adverse events, length of hospital stay, time to next exacerbation). **Suchzeitraum:** 09/2018 **Population:** people with acute COPD exacerbations **Einschlusskriterien:** providing follow-up of at least seven days **Interventionen:** antibiotic therapy **Vergleich:** placebo **eingeschlossene Studien:** 19 trials (n = 2663 participants); 11 with outpatients, seven with inpatients, and one with ICU patients **Primary outcomes** - Treatment failure as observed between seven days and one month after treatment initiation (no resolution or deterioration of symptoms after trial medication of any duration, or death, when explicitly stated, due to exacerbation or additional course of antibiotics or another medication)	**Outpatients: antibiotics compared to placebo** - Treatment failure within 4 weeks - current drugs only: 212/1000 vs. 295/1000, RR 0.72 (0.56 to 0.94), I² = 31%, 7 RCTs, n = 1194, **GRADE: low** **(**Antibiotics: amoxicillinclavulanic acid, trimethoprim-sulphamethoxazole, oxytetracycline, amoxicillin- cotrimoxazole, doxycycline, ciprofloxacin, or amoxicillin) - All-cause mortality: 66/1000 vs. 53/1000, OR 1.27 (0.49 to 3.30), 1 RCT, n = 301, **GRADE: low** (Antibiotics: doxycycline) **Inpatients: antibiotics compared to placebo** - Treatment failure within 4 weeks - current drugs only - **inpatient:** 204/1000 vs. 314/1000, RR 0.65 (0.38 to 1.12), I² = 50%, 4 RCTs, n = 576, **GRADE: moderate** (Antibiotics: amoxicillinclavulanic acid, trimethoprim/ sulphamethoxazole, doxycycline, tetracycline hydrochloride, chloramphenicol, penicillin, streptomycin, piperacillin-sulbactam, ceftazidime, or levofloxacin) - Treatment failure within 4 weeks - drugs not currently used - **ICU:** 107/1000 vs. 565/1000; RR 0.19 (0.08 to 0.45), 1 RCT, n = 93, **GRADE: moderate** (Antibiotics: ofloxacin) - Duration of hospital stay (days) - **inpatients**: MD 0.09 (-0.79 to 0.96), I² = 0%, 3 RCTs, n = 300, **GRADE: high** (Antibiotics: piperacillin-sulbactam, ceftazidime, levofloxacin, amoxicillinclavulanic acid, trimethoprim/ sulphamethoxazole, or cefaclor) - Duration of hospital stay (days) - **ICU patients**: MD -9.60 (-12.84 to -6.36); 1 RCT, n = 94, **GRADE: moderate** (Antibiotics: ofloxacin) - All-cause mortality - **inpatients:** 41/1000 vs. 31/1000, OR 2.48 (0.94 to 6.55), I² = 0%, 2 RCTs, n = 214; **GRADE: moderate** (Antibiotics: tetracycline hydrochloride, chloramphenicol, penicillin, streptomycin, chloramphenicol, doxycycline, piperacillin-sulbactam, ceftazidime, or levofloxacin) - All-cause mortality - **ICU patients**: 45/1000 vs. 217/1000, OR 0.21 (0.06 to 0.72), 1 RCT, n = 93, **GRADE: moderate** (Antibiotics: ofloxacin) **Antibiotics compared to placebo overall** - Adverse events - diarrhoea: 52/1000 vs. 31/1000, OR 1.68 (0.92 to 3.07), I² = 0%, 5 RCTs, n = 1099, **GRADE: moderate** (Antibiotics: amoxicillinclavulanic acid, amoxicillin, ofloxacin, piperacillin-sulbactam, ceftazidime, or levofloxacin-doxycycline)	AMSTAR-2: Qualität des Reviews: - low AMSTAR-Score kritische Kriterien: 6/7 PY=1 Evidenzqualität siehe endpunktspezifische GRADE- Bewertung des Re-views	

		- Adverse events - overall: 151/1000 vs. 129/1000, OR 1.20 (0.89 to 1.63), I^2 = 7%, 6 RCTs, n = 1544, **GRADE: moderate** (Antibiotics: amoxicillinclavulanic acid, doxycycline, amoxicillin, or ofloxacin)		
Osadnik CR. Airway clearance techniques for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2012;(3). https://pubmed.ncbi.nlm.nih.gov/22419331/	**Fragestellung:** To assess the safety and efficacy of ACTs for individuals with AECOPD and stable COPD **Body of Evidence:** n=28 eingeschlossene RCTs und randomised cross-over trials (n= 907 eingeschlossene Patient*innen); n= 12 für Metaanalyse **Suchzeitraum:** inception to 10/ 2011 (PEDro 10/2009) **Population:** individuals with AECOPD and stable COPD **Interventionen:** - 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). **Control:** intervention, sham intervention or coughing alone **Primäre Endpunkte:** - beneficial effects on exacerbations, hospitalisation and HRQoL **Sekundäre Endpunkte:** - evectiveness: airway clearance techniques - airway clearance techniques are safe for individuals with AECOPD and stable COPD. **Definitonen**: classified the effects of ACTs as 'immediate' (less than 24 hours), 'short-term' (24 hours to eight weeks) or 'long-term' (greater than eight weeks)	**>> Ergebnisse für Patient*innen mit Exazerbation:** Airway clearance techniques (ACT) use was associated with small but significant short-term reductions in: • the need for increased ventilatory assistance (OR 0.21, 95% CI 0.05 to 0.85; 26/1000 vs. 112/1000; 4 studies; n = 171; I^2 = 0%; **GRADE: low**), • the duration of ventilatory assistance (mean difference (MD) -2.05 days, 95% CI -2.60 to -1.51; mean duration for control groups seven days; 2 studies; n = 54; I^2 = 0%; **GRADE low:** • **hospital length of stay** (MD -0.75 days, 95% CI -1.38 to -0.11; mean duration for control groups nine days; 1 study on 35 people; **GRADE: low**). • Data from a limited number of studies revealed no significant long-term benefits of ACTs on **the number of exacerbations or hospitalisations**, nor any short-term beneficial effect on **HRQoL** (via SGRQ) total score (MD -2.30, 95% CI -11.80 to 7.20; 1 study; n = 59; **GRADE: na)** **Sensitivitätsanalyse:** • Removal of studies with inadequate or unclear allocation concealment […] resulted in a loss of significance for the duration of ventilatory assistance and sputum weight (acute COPD). • Removal of studies with inadequate assessor blinding resulted in the loss of all data for quantitative analysis except participant withdrawal […] • In AECOPD, removal of studies with incomplete data or no evidence of ITT analysis did not affect the significance of findings for the need for increased ventilatory assistance or hospital LOS, however no data were available for quantitative analysis for any other outcome >> Ergebnisse für Patient*innen mit stabiler COPD: exacerbations and hospitalisations - 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). - 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). HRQoL 1 study (n=15 participants) investigated the effect of a PEP-based ACT on	AMSTAR II: 14/16 AMSTAR-Score kritische Kriterien: 7/7 Aussagesicherheit der Evidenz: siehe endpunktspezifische Bewertung des Reviews	Ref 118 in 2.Aufl. NVL COPD; zusätzlich Ergebnisse für Patient*innen mit AECOPD dargestellt

		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) Symptoms - 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) mortality (all-cause) No data were available for analysis. Safety - 5 Studies clearly reported no negative effects from ACTs - 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) - 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.		
Ni H. Magnesium sulfate for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2022; 5(5):CD013506. dx.doi.org/10.1002/14651858.CD013506.pub2. https://www.ncbi.nlm.nih.gov/pubmed/35616126.	**Fragestellung**: To assess the effects of magnesium sulfate for acute exacerbations of chronic obstructive pulmonary disease in adults. **Suchzeitraum:** 08/2021 **Population:** adults with COPD exacerbations **Intervention:** magnesium sulfate (i.v. or nebulised) **Control:** placebo or ipratropium bromide (1 study) **Body of Evidence:** 11 RCTs (10 double-blind and 1 single-blind) with a total 762 participants	**Intravenous magnesium sulfate versus placebo** hospital admission - Fewer people may require hospital admission with magnesium infusion compared to placebo - OR 0.45 (95% CI 0.23; 0.88); number needed to treat for an additional beneficial outcome (NNTB) = 7; 3 studies, n =170 ; **low-certainty evidenc**e). requirement for non-invasive ventilation - Intravenous magnesium may result in little to no difference in the requirement for non-invasive ventilation OR 0.74 (95% CI 0.31; 1.75); **very low-certainty evidence**). - There were no reported cases of endotracheal intubation (2 studies, 107 participants) or serious adverse events (1 study, 77 participants) in either group. length of hospital stay Magnesium infusion may reduce the length of hospital stay by a mean difference (MD) of 2.7 days (95% CI 4.73 days to 0.66 days; 2 studies, 54 participants; **low-certainty evidence**) and improve dyspnoea score by a standardised mean difference of -1.40 (95% CI -1.83 to -0.96; 2 studies, 101 participants; **low-certainty evidence**). lung function or oxygen saturation We were uncertain about the effect of magnesium infusion on improving lung function or oxygen saturation. AEs	AMSTAR 2: Qualität des Reviews: - high AMSTAR-Score kritische Kriterien: - 7/7 Evidenzqualität siehe endpunktspezifische GRADE- Bewertung des Reviews	Nicht zitiert: zu speziell für NVL

		For all adverse events, the Peto OR was 0.14 (95% CI 0.02 to 1.00; 102 participants); however, the event rate was too low to reach a robust conclusion. **Nebulised magnesium sulfate versus placebo** hospital admission Magnesium inhalation may have little to no impact on hospital admission - OR 0.77, 95% CI 0.21 to 2.82; **very low-certainty evidence**) need for ventilatory support (NIV or mechanical ventilation) Magnesium inhalation may have little to no impact on need for ventilatory support - OR 0.33, 95% CI 0.01 to 8.20; **very low-certainty evidence**). ICU admissions It may result in fewer ICU admissions compared to placebo - OR 0.39 (95% CI 0.15; 1.00); **very lowcertainty evidence**) dyspnoea It may result in fewer improvement in dyspnoea - MD -14.37, 95% CI -26.00 to -2.74; 1 study, 20 participants; **very low-certainty evidence**). SAEs There were no serious adverse events reported in either group. There was one reported death in the placebo arm in one trial, but the number of participants was too small for a conclusion. There was limited evidence about the effect of magnesium inhalation on length of hospital stay, lung function outcomes or oxygen saturation. Included studies did not report adverse events. **Magnesium sulfate vs. ipratropium bromide** - n=1 study with 124 participants assessed nebulised magnesium sulfate plus intravenous magnesium infusion vs. nebulised ipratropium plus intravenous normal saline. - little to no difference between these groups in terms of hospital admission (OR 1.62, 95% CI 0.78 to 3.37), endotracheal intubation (OR 1.69, 95% CI 0.61 to 4.71) and length of hospital stay (MD 1.10 days, 95% CI -0.22 to 2.42), **all with very low-certainty evidence.** There were no data available for non-invasive ventilation, ICU admission and serious adverse events. Adverse events were not reported		
Greenstone M. Doxapram for ventilatory failure due to exacerbations of chronic	**Fragestellung:** The objective of this review was to assess the effects of doxapram on gas exchange and clinical outcomes in people with ventilatory failure due to acute exacerbations of chronic obstructive pulmonary disease.	**Baseline-Charakteristika:** Comparisons - 1 study (Moser 1973): doxapram vs. placebo. - 2 studies (Angus 1996;Newman 2001): doxapram vs. NIPPV - 1 study (Edwards 1967): doxapram vs. four other respiratory stimulants: etamivan, amiphenazole, prethcamide and nikethamide.	y-n-y-y-y-y-y-y-n-n-n Qualität des Reviews: - low	Nicht zitiert, da Behandung mit Doxapram nicht mehr relevant

obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2002;(3).	**Suchzeitraum:** 10/ 2003 **Population:** people with ventilatory failure due to AECOPD **Interventionen:** doxapram **Vergleich:** other treatments or placebo **eingeschlossene Studien:** 4 trials (n = 176)	**Effektivität:** Doxapram vs. placebo, Outcome: Intubation/ventilation - 15/40 vs. 12/38; Peto OR 1.29 [95%CI 0.51, 3.27], 1 study, n = 78 (Moser 1973) Doxapram vs. NIPPV, Outcome: Mortality at 24 hours - 3/8 vs. 0/9; Peto OR 11.34 [95% CI 1.00, 128.02], 1 study, n = 17 (Angus 1996) **RoB der eingeschlossenen Studien** (GRADE nicht durchgeführt) - Angus 1996: not blinded; allocation concealment: unclear - Edwards 1967: double-blinded; allocation concealment: unclear - Moser 1973: double-blinded; allocation concealment: unclear - Newman 2001: unblinded parallel group study; allocation concealment: unclear	AMSTAR II-Score kritische Kriterien: 3/5 PY=2	- relativ alter Review; Vergleiche anwendbar? (Bsp. Studie Edwards 1967: Doxapram vs. nikethamide) - teilweise sehr geringe Studiengrößen (Bsp. Angus 1996: n = 17) - Mortalität als einziger von der Leitliniengruppe priorisierter Endpunkt in diesem Review
Jeppesen E. Hospital at home for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2012;(5).	• **Fragestellung:** To evaluate the efficacy of hospital at home compared to hospital inpatient care in acute exacerbations of COPD. • **Suchzeitraum:** October 2010 • **Population:** patients presented to the emergency department with an exacerbation of COPD • **Einschlusskriterien:** 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) • **Interventionen**: hospital at home - under the care of a specialist respiratory nurse (under guidance of the hospital medical team) - provided with the treatment as deemed appropriate at the time of initial assessment on presentation to the emergency department - would have regular scheduled visits by the nurse as well as additional visits as requested by the patient or deemed appropriate by the nurse	**Readmission to hospital (inpatient)** - significant reduction in readmission rates for hospital at home compared with hospital inpatient care of acute exacerbations of COPD - RR 0.76; 95% CI from 0.59 to 0.99; P=0.04; n=8 studies; 870 participants; **GRADE: moderate** **Mortality** - trend towards lower mortality in the hospital at home group, but the pooled effect estimate did not reach statistical significance - RR 0.65, 95% CI 0.40 to 1.04, P = 0.07; n=7 studies; 845 participants; **GRADE: moderate** **Patient satisfaction** (follow-up: 0 to 2 weeks after discharge) - RR 1.06 (95% CI 0.96 to 1.17); n=2 studies; 158 participants; **GRADE: low** **Carer satisfaction** (follow-up: 2 weeks after discharge) - RR 0.97 (95% CI 0.79 to 1.19); n=1 study; 34 participants; **GRADE: very low** • 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. **Authors' conclusions** Selected patients presenting to hospital emergency departments with acute exacerbations of COPD can be safely and successfully treated at home with	Qualität des Reviews: AMSTAR Score: 8/11 y-n-y-y-y-y-y-y-y-n-n Evidenzqualität siehe endpunktspezifische GRADE- Bewertung des Reviews	Nicht zitiert, da nicht anwendbar auf deutschen Versorgungskontext

	or the medical team - should be visited by the respiratory nurse until discharged from care • **Vergleich:** hospital inpatient care (treated as usual) • **eingeschlossene Studien:** 8 RCTs (870 participants)	support from respiratory nurses.[...]		
Barr RG. Methylxanthines for exacerbations of chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2003;(2).	**Fragestellung:** To determine the benefit of methylxanthines compared to placebo for COPD exacerbations. **Suchzeitraum:** 03/2005 **Population:** patients with AECOPD Ein- und Ausschlusskriterien **Interventionen:** methylxanthines (oral or intravenous) + standard of care **Vergleich:** placebo plus standard care **eingeschlossene Studien:** 4 RCTs (n = 169)	Data on clinical outcomes were sparse. Trends toward improvements in hospitalisation and length-of stay were offset by a trend toward more relapses at one week. Changes in symptom scores were not significant. Methylxanthines caused more nausea and vomiting than placebo (OR: 4.6; 95% CI: 1.7 to 12.6) and trended toward more frequent tremor, palpitations, and arrhythmias. **RoB der eingeschlossenen Studien** (GRADE nicht durchgeführt) - Dolcetti 1988: Allocation concealment: B, Double-blinded - Ram 2000: Allocation concealment: B, Double-blinded - Rice 1987: Allocation concealment: B, Double-blinded, with the exception of one investigator who adjusted theophylline and placebo infusion rates. - Seiden eld 1984: Allocation concealment: B, Double-blinded	AMSTAR-2: y-n-y-y-y-y-y-n-y-y-n Qualität des Reviews: - critically low AMSTAR II-Score kritische Kriterien: 4/7 PY=2 N=1	Nicht zitiert, Therapieoption nicht mehr relevant

3.1.1 Walters 2018 – Detailbetrachtung Primärstudien

Der bereits eingeschlossene und diskutierte Cochrane Review von Walters et.al 2018 (Different durations of corticosteroid therapy for exacerbations of chronic obstructive pulmonary disease) wurde hinsichtlich der Effektivität einzelner Dosierungen von Corticosteroiden bei Exazerbationen geprüft: Effektivität einzelner eingeschlossener Studien wurden extrahiert.

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
Chen 2005	**Studiendesign:** parallel group; n=87 **Interventionen:** - SCS ≤ 7 days: prednisolone 30 mg/d 7 days + placebo 7 days - SCS > 7 days: prednisolone 30 mg/d 10 days + 15 mg/d 5 days **Delivery:** oral **Dauer der Studie:** 14 days **Setting:** inpatients in China, unknown number of centres	**SCS treatment for 7 or fewer days compared with SCS treatment for longer than 7 days for** **- Treatment failure: OR** 0.56 (95%CI 0.12; 2.49); n=87 **- Relapse: OR** 1.33 (95%CI 0.28; 6.34); n=87 **- Length of hospitalisation: MD** 0.10 (95%CI -1.50; 1.70); n=87	**Selection bias** Random sequence generation: **low risk** Allocation concealment: **low risk** **Performance bias + Detection bias** Blinding: **low risk** **Attrition bias** Incomplete outcome data: **low risk** **Reporting bias** Selective reporting: **unclear risk**	
Leuppi 2013	**Studiendesign:** parallel; n=314 **Interventionen:** - SCS≤ 7 days: 5 days: day 1: IV methylprednisolone 40 mg/d, days 2 - 5: oral prednisolone 40 mg/d, days 6 - 14: placebo - SCS > 7 days: 14 days: day 1: IV methylprednisolone 40 mg/d, days 2 - 14: oral 40 mg/d **Setting:** Switzerland, recruited in 5 teaching hospitals **Dauer der Studie:** 14 days **Follow up:** 180 days	**SCS treatment for 7 or fewer days compared with SCS treatment for longer than 7 days for** **- Treatment failure: OR** 0.67 (95%CI 0.28; 1.61); n=311 **- Relapse: OR** 0.96 (95%CI 0.61; 1.53); n=311 - Time to re-exacerbation: HR 0.95 (95%CI 0.66; 1.37); n=311 **- Adverse drug effect hyperglycaemia: OR** 0.99 (95%CI 0.63; 1.54); n=311 **- Mortality: OR** 0.91 (95%CI 0.40; 2.06); n=311 **- Length of hospitalisation: MD** -1.00 (95%CI -2.16; 0.16); n=311	**Selection bias** Random sequence generation: **low risk** Allocation concealment: **low risk** **Performance bias + Detection bias** Blinding: **low risk** **Attrition bias** Incomplete outcome data: **low risk** **Reporting bias** Selective reporting: **low risk**	

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
Sayiner 2001	**Studiendesign:** parallel, n=36 **Interventionen:** - SCS ≤ 7: methylprednisolone, 0.5 mg/kg IV 6-hourly for 3 days, followed by normal saline solution as placebo treatment IV twice daily for the following 3 days and once daily for the final 4 days - SCS > 7: methylprednisolone, 0.5 mg/kg IV 6-hourly for the first 3 days, followed by 0. 5 mg/kg 12-hourly for 3 days and 0.5 mg/kg once daily for 4 more days (total 10 days) **Setting:** Izmir, Turkey. 1 tertiary centre **Dauer der Studie:** 6 month	**SCS treatment for 7 or fewer days compared with SCS treatment for longer than 7 days for** **- Treatment failure: OR** 3.18 (95%CI 0.12; 83.76); n=34 **- Relapse:** 1.31 (95%CI 0.31; 5.53); n=34 **- Adverse drug effect hyperglycaemia: OR** 1.00 (95%CI 0.12; 8.06); n=34	**Selection bias** Random sequence generation: **low risk** Allocation concealment: **low risk** **Performance bias + Detection bias** Blinding: **low risk** **Attrition bias** Incomplete outcome data: **low risk** **Reporting bias** Selective reporting: **low risk**	i.v. Gabe beachten
Sirichana 2008	**Studiendesign:** parallel; n=48 **Interventionen:** - SCS ≤ 7: 5-day group received prednisolone 30 mg/d for 5 days - SCS > 7: 10-day group was administered 30 mg/d prednisolone for 10 days **Setting:** Thailand, single tertiary-care centre **Dauer der Studie:** 30 days	**SCS treatment for 7 or fewer days compared with SCS treatment for longer than 7 days for** **- Relapse: OR** 1.40 (95%CI 0.37; 5.29); n=46	**Selection bias** Random sequence generation: **unclear risk** Allocation concealment: **low risk** **Performance bias + Detection bias** Blinding: **high risk** **Attrition bias** Incomplete outcome data: **high risk** **Reporting bias** Selective reporting: **unclear risk**	Schwache methodische Qualität
Wood-Baker 1997	**Studiendesign:** parallel 3-group design, n=38 **Intervention:** - SCS ≤ 7: prednisolone 2.5 mg/kg orally daily for 3 days followed by 11 days placebo - SCS > 7: prednisolone 0.6 mg/kg orally daily for 7 days followed by prednisolone 0.3 mg/kg orally daily for 7 days **Setting:** hospitalised patients, 2 centres in Australia/ New Zealand	**SCS treatment for 7 or fewer days compared with SCS treatment for longer than 7 days for** **- Treatment failure: OR** 1.09 (95%CI 0.06; 19.63); n=25 **- Length of hospitalisation: MD** 0.54 (95%CI -3.40; 2.32; n=23	**Selection bias** Random sequence generation: **low risk** Allocation concealment: **unclear risk** **Performance bias + Detection bias** Blinding: **low risk** **Attrition bias**	

Zitat	Studiencharakteristika	Studienergebnisse	Methodische Qualität	Kommentar
	Dauer der Studie: 14 days		Incomplete outcome data: **low risk** **Reporting bias** Selective reporting: **low risk**	

Drei andere Studien wurden aufgrund schwacher methodischer Qualität nicht in die Metaanalyse des Cochrane Reviews einbezogen; daher auch in dieser Zusammenfassung Aq (Ausschluss aufgrund schwacher methodischer Qualität).

3.2 Atemphysiotherapie und körperliches Training

3.2.1 Primärstudien (systematische Recherche; 2.Auflage)

Zitat	Studiencharakteristika	Ergebnisse	Methodische Qualität
Cross JL. Evaluation of the effec-tive-ness of man-ual chest physi-other-apy tech-niques on quality of life at six months post exacer-bati-on of COPD (MATREX): A randomi-sed control-led equiva-lence trial. BMC Pulm Med 2012; 12:33. https://www.ncbi.nlm.nih.gov/pub-med/22748085.	• **Ziel:** Manual chest physiotherapy: assessed its effectiveness on disease-specific quality of life. • **Studiendesign: r**andomised controlled equivalence trial • **Population:** patients hospitalised with AECOPD; n=526 • **Intervention:** Manual chest physiotherapy(MCP) + advice on airway clearance • **Vergleich:** advice on chest clearance alone >active cycle of breathing techniques (ACBT) was used in both arms • **Follow-up:** 6 months • Studienzeitraum: November 21, 2005, and April 30, 2008 • UK; multicentre • Messmethoden: SGRQ	• Baseline-Patientencharakteristika: hinsichtlich Alter, Geschlecht; Rauchstatus; SGRQ Baseline weitestgehend ausgeglichen - All patients were included in the analyses, of which 372 (71%) provided evaluable data for the primary outcome. - effect size of 0.3 standard deviations in SGRQ score was specified as the threshold for superiority - ITT analyses indicated no significant difference at 6 months post randomisation in -- total SGRQ score [adjusted effect size (no MCP - MCP) 0.03 (95% confidence interval, CI -0.14 to 0.19)], -- SGRQ symptom score [adjusted effect size 0.04 (95% CI -0.15 to 0.23)], -- SGRQ activity score [adjusted effect size -0.02 (95% CI -0.20 to 0.16)] or -- SGRQ impact score [adjusted effect size 0.02 (95% CI -0.15 to 0.18)]. • authors conclusion: 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.	**Selection bias** Randomisierung: **gering** Allocation concealment: **gering** **Performance bias** Verblindung von Teilnehmern und Personal: **hoch** **Detection bias** Verblindung der Ergebnisevaluation: **unklar** **Attrition bias** Verlust von Studienteilnehmern/ fehlende Daten: **gering** ITT-Analyse: durchgeführt **Reporting bias** selektive Ergebnisdarstellung: **unklar** **Andere Biasursachen** Baseline imbalance: **gering** Interessenkonflikte/ Sponsoring: angegeben

Zitat	Studiencharakteristika	Ergebnisse	Methodische Qualität
Basri R. Short-term effects of chest physi-otherapy in acute exa-cerbation of chronic obstructive pulmonary disease. Journal of medical sciences (peshawar) 2017; 25(3):323–7. www.jmedsci.com/index.php/Jmedsci/article/view/31.	• **Ziel:** To find out the short-term effects of chest physiotherapy in acute exacerbation of COPD • **Studiendesign:** double blinded RCT • **Population:** patients with AECOPD; n=60 • **Intervention:** 2 weeks - active chest physiotherapy techniques along with medical treatment > included Breathing control exercise; Thoracic expansion exercises (incl. pursed lips), Forced expiration technique) • **Vergleich:** - only medical treatment • Pakistan • **Messmethoden:** - visual analogue scale (VAS) for breathlessness - Peak Expiratory Flow Rates (PEFR) - Oxygen saturation level (SaO2)	• Baseline-Patientencharakteristika: leichte Differenzen bezüglich Alter und Exazerbations-Historie - Mean age: group A 53±3.7 / group B Mean 55±3.8 **Experimental group:** - VAS for breathlessness: MD 4.78±1.12 with P=0.03 - PEFR: MD -5.35±5.35 with P=0.02 - SaO2: MD -3.64±3.20 with P=0.01 with 95% CI. **Control group:** - VAS: MD 0.40±0.63 with P=0.03 - PEFR: MD 2.00±25.89 with P=0.76 - SaO2: MD -3.7±3.10 with P=0.00 using 95% CI. 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<0.05). Experimental group showed more improvement on - Peak Expiratory Flow Rates (PEFR) (P<0.05), - SaO2 (P>0.05) - VAS for breathlessness (P<0.05). **Conclusion:** Active chest physiotherapy technique along with medical treatment is more effective in acute exacerbation of COPD than medical treatment alone	**Selection bias** Randomisierung: **gering** Allocation concealment: **gering** **Performance bias** Verblindung von Teilnehmern und Personal: **gering** **Detection bias** Verblindung der Ergebnisevaluation: **gering** **Attrition bias** Verlust von Studienteilnehmern/ fehlende Daten: **unklar** ITT-Analyse: nicht durchgeführt **Reporting bias** selektive Ergebnisdarstellung: **unklar** **Andere Biasursachen** Baseline imbalance: **unklar** Interessenkonflikte/ Sponsoring: angegeben (keine)
Goktalay T. Does high-frequency chest wall oscillation therapy ha-ve any im-pact on the infective exacerbations of chronic obstructive pulmonary disease? A randomized controlled single-blind study. Clin Rehabil 2013;	• **Ziel:** To investigate the impact of high-frequency chest wall oscillation in chronic obstructive pulmonary disease patients with infective exacerbation. • **Studiendesign**: randomized controlled single-blind study • **Population:** Stage III-IV COPD patients hospitalized with acute infective exacerbation; n=50 patients randomised • **Intervention:** group 2: usual exacerbation protocol + received additional high-frequency chest wall oscillation therapy (20 minutes three times a day for 5 days) • **Vergleich:** group 1: usual exacerbation protocol >> All patients have been treated with bronchodilators, antibiotics, if necessary oxygen and patient education, as part of acute chronic obstructive pulmonary disease exacerbation protocol. • **Follow-up:** five-days	• **Baseline-Patientencharakteristika:** bezüglich Alter, Gewicht; BODE Index baseline, 6MWD weitestgehend ausgeglichen - Mean (SD) age of the 50 participants (one (2%) female and 49 (98%) male) was 65.06 years (7.39) (range 45–80). - 50 (100%) patients (25 in Group I and 25 in Group II) were followed up for five days. - Application of high-frequency chest wall oscillation therapy resulted in no significant advantage in all outcomes (p > 0.05). - Mean (SD) baseline **BODE index v**alue in Group I was 7.72 (1.76), in Group II (Intervention) was 7.72(1.89) (p = 0.55). - On the fifth-day assessment, mean (SD) **BODE index** value in Group I (usual protocol) was 7.24 (1.83), in group II was 6.44 (2.46) (p = 0.18). • "authors conclusion ": The application of high-frequency chest wall oscillation therapy offers no additional advantages on infective exacerbations in chronic obstructive pulmonary disease.	**Selection bias** Randomisierung: **unklar** Allocation concealment: **gering** **Performance bias** Verblindung von Teilnehmern und Personal: **unklar** **Detection bias** Verblindung der Ergebnisevaluation: **unklar** **Attrition bias** Verlust von Studienteilnehmern/ fehlende Daten: **unklar** ITT-Analyse: nicht durchgeführt **Reporting bias** selektive Ergebnisdarstellung: **unklar**

Zitat	Studiencharakteristika	Ergebnisse	Methodische Qualität
27(8):710–8. https://www.ncbi.nlm.nih.gov/pubmed/23503735.	• Studienzeitraum: April 2009 to July 2011 • Türkei • BODE; SGRQ		**Andere Biasursachen** Baseline imbalance: **gering** Interessenkonflikte/ Sponsoring: angegeben
Reychler G. Intrapulmonary Percussive Ventilation as an Airway Clearance Technique in Subjects With Chronic Obstructive Airway Diseases. Respir Care 2018; 63(5):620–31. https://www.ncbi.nlm.nih.gov/pubmed/29692351.	• **Fragestellung:** to summarize the physiological and clinical effects related to the use of IPV as an airway clearance technique in chronic obstructive airway diseases • **Suchzeitraum:** to May 2017 • **Population:** Subjects > 5 y old with obstructive disease (cystic fibrosis, asthma, **COPD**, bronchiectasis), stable or exacerbated • **Interventionen:** Use of intrapulmonary percussive ventilation as airway clearance technique • **Vergleich:** No airway clearance technique used, placebo or other airway clearance techniques • **eingeschlossene Studien**: n=12 studies; n= 278 participants - für COPD: n=6 studies (RCTs, controlled, observational); n=178 participants	• systematischer Review ohne Meta-Analyse • Baseline-Charakteristika COPD-Studien: - 3 studies were performed in ICUs during an exacerbation, - 2 studies were performed in stable out-patients. **Cardiorespiratory Parameters, Lung Function, and Lung Mechanics in COPD** - 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) [...] - After 1 d of treatment in stable subjects, 1 study showed an improvement in inspiratory and expiratory muscle strength. **Length of Hospital Stay and Other Clinical Outcomes in COPD** - 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. - In 1 study, a decrease in the need for mechanical ventilation was observed. **Adverse Effects and Drop-Outs in COPD.** In subjects with COPD, - 2 studies revealed complications or discomfort. - Even though some subjects were intubated after inclusion in 1 study, it was not related to IPV. - In another study, 2 subjects did not tolerate settings with a higher frequency of percussions (1.220 cm H2O-350 c/min and 1.840 cm H2O-350 c/min). The main findings showed that IPV improves gas exchange during exacerbation and could reduce the hospital length of stay for patients with COPD. >> CONCLUSIONS: The systematic use of IPV as an airway clearance technique in chronic obstructive airway diseases is not supported by suffi-	AMSTAR-2 Qualität des Reviews: - critically low AMSTAR-Score gesamt: 7/13 PY=1 N=5 AMSTAR-Score kritische Kriterien: 2/75 PY=1 N=2 Only one of the included studies had a sample size > 50 subjects.

Zitat	Studiencharakteristika	Ergebnisse	Methodische Qualität
		ciently 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.	

3.2.2 AHRQ (themenübergreifende Recherche 2024)

Zitat	Studiencharakteristika	Studienergebnisse	Aussagesicherheit	Kommentar
Dobler, Claudia C. et al.: Pharmacologic and Nonpharmacologic Therapies in Adult Patients With Exacerbation of COPD: A Systematic Review. Agency for Healthcare Research and Quality (US). Rockville (MD) (AHRQ Comparative Effectiveness Reviews, 21). https://pubmed.ncbi.nlm.nih.gov/31657888/.	**AHRQ** **Key Question 2 (KQ2).** In adult patients with exacerbation of COPD, what are the benefits and harms of emerging and other pharmacologic and nonpharmacologic therapies compared with placebo or standard care? **Suchzeitraum:** 02/2019 **Population:** Adults aged 18 years and above with an acute exacerbation of COPD **Interventionen:** • Early pulmonary rehabilitation/exercise • Chest physiotherapy • Nutritional support • Whole body vibration • Neuromuscular electrical stimulation • Combinations of the above **Vergleiche:** Placebo or standard care **SOE=** Overall Strength of Evidence	**Chest physiotherapy** is commonly prescribed in patients hospitalized for ECOPD; however,the evidence-base for chest physiotherapy, as shown in our review, is weak. There was no evidence of improved final health outcomes, other than reduced hospital admission, from relatively small, low quality trials in our review. **Chest Physiotherapy (Breathing Technique) vs. Management Without Chest Physiotherapy** • hospital admission: Chest physiotherapy using a specific breathing technique significantly reduced hospital admission at the longest followup compared with management without chest physiotherapy (low SOE): Rate Ratio: 0.91; 95% CI: 0.83 to 0.99, I^2=79.5%; 2 RCTs with 581 patients; Low SOE supporting reduction (High ROB, and inconsistency) There were no statistically significantly differences between the intervention and management without chest physiotherapy group for other outcomes, including: • mortality at end of followup: OR: 0.97; 95% CI: 0.06 to 16.20, I^2= N/A; 1 RCT with 59 patients; SOE: Insufficient evidence (High ROB and severe imprecision) • mortality at the longest followup: OR: 0.90; 95% CI: 0.54 to 1.49, I^2= N/A; 1 RCT1 with 522 patients; Low SOE supporting no difference (Intermediate ROB and imprecision) • dyspnea based on a questionnaire (MRC): WMD: 0.40; 95% CI: -0.24 to 1.04, I^2= N/A; 1 RCT110 with 59 patients; SOE: Insufficient evidence (High ROB and severe imprecision) • dyspnea based on a numeric scale (VAS, Borg): SMD: -0.42; 95%CI: -0.89 to 0.05, I^2=98.92%; 2 RCT with 119 patients; SOE: Insufficient evidence (High ROB, inconsistency and severe imprecision) • QoL(SGRQ): SMD: -0.02; 95%CI: -0.18 to 0.14, I^2=0.00%; 2 RCTs with 581 patients; SOE: Insufficient evidence (High ROB and severe imprecision) **Chest Physiotherapy using Vibration, Percussion, or Massage vs. management without chest physiotherapy** There was no difference between the intervention and management without chest physiotherapy group for all evaluated outcomes including:	Methodische Qualität: AMSTAR II: high Aussagesicherheit: Siehe Review-spezifische Bewertung	did not include studies conducted in an intensive care unit (ICU), chronic ventilator unit, or respiratory care unit,

		• dyspnea at the end of the intervention(MRC, MMRC): SMD: 0.15; 95% CI: -0.29 to 0.60, I^2= 0.00%; 2 RCTs with 80 patients; SOE: Insufficient evidence (High ROB and severe imprecision) • dyspnea at the longest followup (MMRC): WMD: -0.24; 95% CI: -0.73 to 0.25, I^2= N/A; 1 RCT103 with 50 patients; SOE: Insufficient evidence (High ROB and severe imprecision) • 6-minute walking distance at the end of the intervention: WMD: 56.20; 95% CI: -8.18 to 120.58, I^2= N/A; 1 RCT with 30 patients; SOE nicht angegeben (additional outcome) No patient withdrew during the study **Chest Physiotherapy using Positive Expiratory Pressure vs. management without positive expiratory pressure** There was no difference between the intervention and management without positive expiratory pressure group for all evaluated outcomes including: • mortality at the end of the intervention: OR: 1.00; 95% CI: 0.06 to 16.48, I^2= N/A; 1 RCT with 92 patients; Low SOE supporting no difference (Severe imprecision) • mortality at the longest followup: OR: 1.58; 95% CI: 0.41 to 6.00, I^2= N/A; 1 RCT with 92 patients; Low SOE supporting no difference (Severe imprecision) • dyspnea (MMRC) at the end of the intervention: WMD: 0.40; 95% CI: - 0.16 to 0.96, I^2= N/A; 1 RCT with 92 patients; Low SOE supporting no difference (Severe imprecision) • dyspnea (MMRC) at the longest followup: WMD: 0.50; 95% CI: -0.06 to 1.06, I^2= N/A; 1 RCT with 92 patients; Low SOE supporting no difference (Severe imprecision) • 6-minute walking distance at the end of the intervention: WMD: -26.00; 95% CI: -89.61 to 37.62, I^2= N/A; 1 RCT with 92 patients; SOE nicht angegeben (additional outcome) • quality (SGRQ) of life at the longest followup: WMD: -1.50; 95% CI: -5.99 to 8.99, I^2= N/A; 1 RCT with 92 patients; SOE nicht angegeben (additional outcome) • No statistically significant difference on withdrawals, withdrawals due to AEs, and total number of AEs was found (Appendix Table H.9.). • Serious AEs (serious clinical deterioration) were reported in 9 patients in the chest physiotherapy compared with 6 patients in the management without positive expiratory pressure group **Exercise Using Resistance Training Versus Management Without Resistance Training** Exercise using resistance training was associated with statistically significantly • better dyspnea (modified Borg): WMD: -2.11; 95% CI: -3.50 to -0.72, I^2= N/A; 1 RCT with 60 patients; Low SOE supporting improvement (Intermediate ROB and imprecision) • better QoL (EQ-5D VAS): WMD: 18.70; 95% CI: 5.06 to 32.34,I^2= N/A; 1 RCT with 60 patients; Low SOE supporting improvement (Intermediate ROB and imprecision) • higher 6-minute walking distance: WMD: 74.42; 95% CI: 46.85 to 101.99, I^2=95.42%; 2 RCTs with 86 patients; SOE nicht angegeben (additional outcome)		

at the end of the intervention, compared with management without resistance training.

There was no difference between the intervention and management without resistance training group for all other evaluated outcomes including:

- mortality at the longest followup: OR: 0.22; 95% CI: 0.01 to 4.81, I^2= N/A; 1 RCT with 46 patients; SOE: Insufficient evidence (Intermediate ROB and severe imprecision)
- hospital admissions at the longest followup: OR: 1.23; 95% CI: 0.35 to 4.31, I^2= N/A; 1 RCT with 40 patients; SOE: Insufficient evidence (High ROB and severe imprecision)

No statistically significant difference was found on number of withdrawals

Exercise Using Aerobic Training Versus Management Without Aerobic Training

Aerobic exercise was associated with significantly improved

- dyspnea (Questionnaire: Transitional Dyspnea Index): WMD: 7.20; 95% CI: 4.53 to 9.87, I^2= N/A; 1 RCT with 46 patients; Low SOE supporting better outcome (High ROB and imprecision)
- quality of life at the end of intervention (CRQ): WMD: 38.00; 95% CI: 24.51 to 51.49, I^2= N/A; 1 RCT with 46 patients; Low SOE supporting better outcome (High ROB and imprecision)
- worse dyspnea at the longest followup: (Questionnaire: MRC): WMD: 1.20; 95% CI: 0.33 to 2.07, I^2= N/A; 1 RCT with 29 patients; Low SOE supporting worse outcome (Intermediate ROB and imprecision)
- statistically significant improvement in 6 minute walking distance: WMD: 28.71; 95% CI: 10.91 to 46.50, I^2= 98.4%; 2 RCTs with 75 patients; SOE nicht angegeben (additional outcome)
- number of steps walked per day: WMD: 663.03; 95% CI: 496.34 to 829.72, I2= N/A; 1 RCT with 58 patients; SOE nicht angegeben (additional outcome)
- endurance based on a 30-second sit-to-stand test: WMD: 4.63; 95% CI: 2.54 to 6.72, I^2= N/A; 1 RCT with 58 patients; SOE nicht angegeben (additional outcome)

compared with management without aerobic exercise.

There was no difference between the intervention and control group for

- mortality: OR: 1.00; 95% CI: 0.06 to 17.02, I^2= N/A; 1 RCT with 46 patients; SOE: Insufficient evidence (High ROB and severe imprecision)
- hospital admissions: Rate Ratio: 0.96; 95% CI: 0.39 to 2.37, I^2= N/A; 1 RCT with 29 patients; SOE: Insufficient evidence (Intermediate ROB and severe imprecision)
- repeat exacerbations: OR: 0.74; 95% CI: 0.22 to 2.49, I^2= 0.0%; 2 RCTs with 75 patients; SOE: Insufficient evidence (High ROB and severe imprecision)

Exercise Using Combined Aerobic + Resistance Training Versus Management Without Exercise Training

Low-intensity and moderate-to-high intensity aerobic and resistance training was not associated with a statistical difference in FEV1 percent predicted, 3-minute walking distance

		test, and upper limb muscle strength at the end of the intervention compared with management without exercise training. There was no statistical difference in total number of AEs **Chest Physiotherapy + Exercise Combined Versus Management Without Exercise Training** One study evaluated the effectiveness of chest physiotherapy and exercise (breathing technique and range of motion exercises) combined compared with management without exercise training in patients with moderate to severe ECOPD. The chest physiotherapy and exercise combination group was found to have statistically significantly more improvements in quality of life at the end of the intervention. No other statistically significant difference was found. • Dyspnea (Numeric Scale: Modified Borg Scale): WMD: 1.15; 95% CI: -0.61 to 2.91, I^2= N/A; 1 RCT with 60 patients; SOE: Insufficient evidence (Intermediate ROB and severe imprecision) • QoL (EQ-5D): WMD: 14.89; 95% CI: 5.30 to 24.50, I^2= N/A; 1 RCT with 60 patients: Low SOE supporting improvement (Intermediate ROB and imprecision)		

3.3 D-Dimere

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit der Evidenz	Kommentar
Gunen H. Venous thromboemboli and exacerbations of COPD. Eur Respir J 2010; 35(6):1243–8. https://www.ncbi.nlm.nih.gov/pubmed/19926740.	**Fragestellung:** to determine the prevalence of and risk factors for venous thromboembolism (VTE) in exacerbations of chronic obstructive pulmonary disease (COPD) **Studiendesign:** u.a. auch diagnostische Genauigkeitsstudie; prospektiv; konsekutiver Einschluss **Population:** COPD patients hospitalised with an exacerbation **Diagnostik:** - clinical evaluations (including the calculations for PE risk stratification: classified using the Wells and Geneva criteria) - BGA; detailed biochemical and haematological parameters, including D-dimer levels - Conventional chest radiographs and spirometric measurements - dynamic computed tomography (CT) scanning (CT	**Baseline:** - mean age 67.1±10.1 yrs; n=27 (20.6%), female ; n=34 (26%) nonsmokers. - n=138 were included; **n=131** patients completed the study. (Exclusion: n =7 due to technical problems with their angiographic and ultrasonographic scans and contrast allergy) - Deep vein thrombosis (VTE): n=14/131 (10.6%; 95% CI 5.3–15.9%) - Pulmonary embolism (PE): n=18/131 (13.7%; 95% CI7.8–19.6%) - The prevalence of VTE was three times higher in patients with an exacerbation of unknown origin than in patients with an exacerbation of known origin (p=0.016). -Of patients with VTE, 20 (95%) had high D-dimer levels. - The negative predictive value of D-dimer testing was 0.98. **Diagnostische Genauigkeit**	Beurteilung mit QUADAS II Domain 1: patient Selection ●consecutive or random: yes (consecutive) ●case-control-design: no ●avoiding inapproprate exclusions: yes **Could the selection of patients have introduced bias? Low** Domain 2: Index Test(s) ●interpretation of index test blinded: unclear ●threshold pre-specified: yes **Could the conduct or interpretation of the index test have introduced bias? unclear** Domain 3: Reference Standard ●reference standard likely to correctly classify the target condition: yes ●interpretation of reference test blinded: unclear	

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit der Evidenz	Kommentar
	angiography) - ECG recordings and echocardiographic examination Studienzeitraum: n.a. Malatya, Turkey D-dimer levels of <0.5 µg/ml were considered to be within the normal range	- D-Dimer = Index; CT = Referenztest The mean D-dimer level was significantly higher in the VTE group (5.2±4.5 versus 1.2±1.8 mg/mL-1; p<0.001). Except for one patient, D-dimer levels were elevated (>0.5 µg/mL-1) in all patients with VTE. At cut-off level 0.5 µg/mL: sensitivity: 0.95 specificity: 0.37 PPV: 0.22 NPV: 0.98 >> Analysis of D-dimer levels for better sensitivity, specificity, PPV and NPV did not demonstrate any better D-dimer cut-off levels. According to the **Wells criteria**, none (0/71) of the patients with low-risk determination, 20.7% (11/53) of the patients with moderate-risk determination and all (7/7) of the patients with high-risk determination were found to have PE	**Could the reference standard, its conduct, or its interpretation have introduced bias? unclear** Domain 4: Flow and Timing: ●appropriate interval between index test(s) and reference standard?: unclear (<24h) ●Did all patients receive a reference standard?: yes ●Did patients receive the same reference standard?: yes ●Were all patients included in the analysis?: yes **Could the patient flow have introduced bias?: low** ●possible concerns regarding applicability: low Evidenzqualität: Qualität der Evidenz: niedrig (diagnostische Genauigkeit) Ausgangsniveau: niedrig 1)Verzerrungsrisiko: moderat 2) Präzision: unklar 3) Direktheit/Übertragbarkeit: gut 4) Konsistenz: n.a.	
Akpinar EE. Should the cut-off value of D-dimer be elevated to exclude pulmonary embolism in acute exacerbation of COPD? J Thorac Dis 2013; 5(4):430–4. https://www.ncbi.nlm.nih.gov/	**Fragestellung:** evaluate the D-dimer levels in patients with AECOPD with and without pulmonary embolism (PE) and to attempt to define a new cut-off value for D-dimer to exclude the diagnosis of PE in patients with COPD exacerbation. **Studiendesign:** cross-sectional study, consecutive inclusion; u.a. auch diagnostische Genauigkeit **Population:** patients with COPD exacerbation **Diagnostik:** - D-dimer levels - computed tomography angiography (CTA) and Doppler ultrasonography (US) of the lower extremities	**Baseline** - mean participant age: 73.3±8.5 years (108 (73%) males) - patient distribution according to the GOLD stages 1: 0%, 2: 43.92%, 3: 25.68%, 4: 30.4% - n=53/148 patients (36%) who did not have PE had higher than normal (>0.5 pg/mL) D-dimer levels. - D-dimer levels of the COPD patients with PE were significantly higher than those of the patients without PE (2.38±2.80 vs. 1.06±1.51 pg/mL) (P<0.001). - cut-off value for D-dimer in diagnosing PE in the COPD patients was 0.95 pg/mL. The area under the receiver operating characteristic (ROC) curve was 0.752±0.040 (95% CI: 0.672-0.831) (P<0.001).	Beurteilung mit QUADAS II **Domain 1: patient Selection** ●consecutive or random: yes ●case-control-design: no ●avoiding inapproprate exclusions: yes **Could the selection of patients have introduced bias? low** **Domain 2: Index Test(s)** ●interpretation of index test blinded: unclear ●threshold pre-specified: yes (normal= <0.5 pg/mL) **Could the conduct or interpretation of the index test have introduced bias? unclear** Domain 3: Reference Standard	

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit der Evidenz	Kommentar
pubmed/23991298.	**Ausschlusskriterien:** - hematological diseases, coagulation disorders, hepatic or renal diseases, under oral antiplatelet or oral anti-coagulant therapy, known malignancies or collagen vascular diseases at admission, undergone surgery or transfusion in the previous 3 months **Studienzeitraum:** 06/2012 - 01/2013 Ankara, Turkey usual: normal D-dimer levels of <0.5 pg/mL	**Authors conclusion:** This study showed that the D-dimer concentrations of COPD patients who are in the exacerbation period may be higher than normal, even without PE. The cut-off level for D-dimer was 0.95 pg/mL (sensitivity 70%, spesificity 71%) for the exclusion of PE in the patients with COPD exacerbation. The D-dimer cut-off value that is used to exclude PE in patients with acute exacerbation of COPD should be reevaluated to prevent the excessive use of further diagnostic procedures	●reference standard likely to correctly classify the target condition: yes ●interpretation of reference test blinded: unclear **Could the reference standard, its conduct, or its interpretation have introduced bias? unclear** **Domain 4: Flow and Timing:** ●appropriate interval between index test(s) and reference standard?:yes (<4h) ●Did all patients receive a reference standard?: yes ●Did patients receive the same reference standard?: yes ●Were all patients included in the analysis?: yes **Could the patient flow have introduced bias?: low** ●possible concerns regarding applicability: low Evidenzqualität: Qualität der Evidenz: niedrig (diagnostische Genauigkeit) Ausgangsniveau: niedrig 1)Verzerrungsrisiko: moderat 2) Präzision: unklar 3) Direktheit/Übertragbarkeit: gut 4) Konsistenz: n.a.	
Sadeghi S. Diagnostic Value of D-dimer in Detecting Pulmonary Embolism in Patients with Acute COPD Exacerbation. Tanaffos 2020; 19(4):371–9. https://www.ncbi.nlm.nih.gov/	**Fragestellung:** diagnostic value of D-dimer for diagnosis of pulmonary embolism during acute exacerbation in patients with COPD was investigated. **Studiendesign:** cross-sectional Diagnostic accuracy **Population:** patients with acute COPD exacerbations (n=112) **Diagnostik:** -Wells criteria and D-dimer serum levels - CT angiography (CTA) and ultrasonography	**Baseline:** - mean age 69.57 ± 6.35 years and 91 patients (81.3%) were males. The appropriate cut-off for D-dimer and the Wells score for diagnosis of PTE in COPD patients were >990 µg/L and 3, respectively **Diagnostics performance of D-dimer and wells score** Wells score: Cut-off point >3 Sensitivity: 69.12% Specifity: 75.27%	Beurteilung mit QUADAS II Domain 1: patient Selection ●consecutive or random: unclear ●case-control-design: no ●avoiding inapproprate exclusions: unclear (Patients with no venous thrombosis evidenced by CTA and the diagnosis of thrombosis using Doppler Vein ultrasound were excluded from the study) **Could the selection of patients have introduced bias? unclear** Domain 2: Index Test(s)	

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit der Evidenz	Kommentar
pubmed/33959175.	**Ausschlusskriterien:** hematologic disorders, such as hemostatic dysfunction, renal and gastrointestinal diseases, malignancies, collagen vascular disease, autoimmune disease, drug history of anticoagulants or glucocorticoids use, and also patients with a specific cause of acute COPD exacerbation (lobar pneumonia, etc.) Studienzeitraum: n.a. Iran	Positive Predictive value: 36.1% Negative Predictive value: 92.1% <u>D-dimer: Cut-off point >990 µg/l</u> Sensitivity: 68.42% Specifity: 61.18% Positive Predictive value: 28.3% Negative Predictive value: 89.7% <u>Wells score and D-dimer: Cut-off point >3 and >990 µg/l</u> Sensitivity: 47.37% Specifity: 88.17% Positive Predictive value: 5.0% Negative Predictive value: 89.1%	●interpretation of index test blinded: unclear ●threshold pre-specified: yes **Could the conduct or interpretation of the index test have introduced bias? unclear** Domain 3: Reference Standard ●reference standard likely to correctly classify the target condition: yes ●interpretation of reference test blinded: unclear **Could the reference standard, its conduct, or its interpretation have introduced bias? unclear** Domain 4: Flow and Timing: ●appropriate interval between index test(s) and reference standard?: unclear (in first 48 h) ●Did all patients receive a reference standard?: yes ●Did patients receive the same reference standard?: yes ●Were all patients included in the analysis?: yes **Could the patient flow have introduced bias?: low** ●possible concerns regarding applicability: low <u>Evidenzqualität:</u> Qualität der Evidenz: niedrig (diagnostische Genauigkeit) Ausgangsniveau: niedrig 1)Verzerrungsrisiko: moderat 2) Präzision: unklar 3) Direktheit/Übertragbarkeit: gut 4) Konsistenz: n.a.	
Jiménez D. Effect of a Pulmonary Embolism Diagnostic Strategy on Clinical Outcomes in	Significance of Pulmonary Embolism in COPD Exacerbations **(SLICE)** trial **Fragestellung:** To compare usual care plus an active strategy for diagnosing PE with usual care alone in patients hospitalized for COPD exacerbation.	**Baseline-Patientencharakteristika:** - mean (SD) age 70.4 (9.9) years, n=195 (26%) women - All patients in the control group and all patients in the intervention group without PE during the initial diagnostic period received at least 1 prophylactic dose of low-molecular-weight heparin. - Hinsichtlich Alter, Geschlecht, Rauchstatus, stattgehabte	<u>RoB</u> Selection bias Randomisierung (Generierung): low Allocation concealment (verdeckte Zuteilung): low	

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit der Evidenz	Kommentar
Patients Hospitalized for COPD Exacerbati-on. JAMA 2021 https://pubmed.ncbi.nlm.nih.gov/34609451/	**Studiendesign:** RCT; multicenter, open-label **Population:** patients hospitalized for COPD exacerbation **Intervention:** Usual care plus an active strategy for diagnosing PE (D-dimer testing and, if positive, computed tomography pulmonary angiogram); n=370 (ITT) **Kontrolle**: usual care (n=367; ITT) **primärer Kompositendpunkt:** nonfatal symptomatic venous thromboembolism (VTE), readmission for COPD, or death within 90 days after randomization. **Einschlusskriterien:** 1. Confirmation of chronic obstructive pulmonary disease (COPD): postbronchodilator forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) <0.7. 2. Hospital admission because COPD exacerbation without initial clinical suspicion of pulmonary embolism (PE) in the emergency department[a] (according by the emergency department physician evaluation). [a] No suspicion of PE was defined as a patient in whom the physician-in-charge would not have examined for a PE outside the study. **Ausschlusskriterien:** - Pregnancy - contraindication to CTPA - diagnosis of pneumonia, pneumothorax, or lower respiratory tract infection - needed invasive mechanical ven-tilation at the time of hospital admission **Studienzeitraum:** 09/2014 to 07/2020 (follow-up 11/2020) D-Dimer Cut-Off: siehe Suppl. 3, eTable3	Exazerbationen, Schwere der COPD, FEV1 nach Albuterolgabe, medikamentö-ser Vorbehandlung, klinischer Symptomatik, Risi-kofaktoren für VTE, Wells score weitestgehend ausgeglichen **primärer Endpunkt** (composite of nonfatal symp-tomatic venous thromboembolism (VTE), read-mission for COPD, or death within 90 days after randomization) - occurred in 110/370 patients (29.7%) in the intervention group and 107/367 patients (29.2%) in the control group - relative risk: 1.02 [95%CI, 0.82-1.28] **sekundäre Endpunkte:** <u>Nonfatal new or recurrent VTE</u> - not significantly different in the 2 groups (0.5%vs 2.5%; - relatives Risiko: 0.22 (95%CI 0.05 to 1.01) <u>Readmission for exacerbation of COPD by day 90:</u> - total of 94 patients (25.4%) in the intervention group and 84 (22.9%) in the control group had been readmitted for exacerbation of COPD - relatives Risiko: 1.11 (0.86 to 1.43) <u>Death from any cause</u> - occurred in 23 patients (6.2%) in the intervention group and 29 (7.9%) in the control group - relatives Risiko: 0.79 (0.46 to 1.43) <u>Major bleeding</u> - occurred in 3 patients (0.8%) in the intervention group and 3 patients (0.8%) in the control group - relatives Risiko: 0.99 (0.20 to 4.88) **authors conclusion** Among patients hospitalized for an exacerbation of COPD, the addition of an active strategy for the diagnosis of PE to usual care, compared with usual care alone, did not significantly improve a composite health outcome. The study may not have had adequate power to assess individual components of the composite outcome.	Performance bias (Verblindung von Teilnehmern und Personal). High Kommentar: Aufgrund des Studienaufbaus Verblindung nicht möglich (Although the patients and clinicians could not be blinded, the trial used central, blind adjudication of outcomes.) Detection bias (Verblindung der Ergebnisevaluation): low Attrition bias Verlust von Studienteilnehmern/ fehlende Daten: low ITT-Analyse: ja Reporting bias (selektive Ergebnisdarstellung): low andere Biasursachen Baseline imbalance: low Interessenkonflikte/ Sponsoring: <u>Evidenzqualität:</u> Qualität der Evidenz: moderat (composite EP) Ausgangsniveau: hoch (RCT) 1)Verzerrungsrisiko: moderat (keine Verblindung möglich) 2) Präzision: ok 3) Direktheit/Übertragbarkeit: gut 4) Konsistenz: n.a.	

3.4 CRP, Sputum oder Procalcitonin

3.4.1 CRP

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit der Evidenz	Kommentar
Butler CC. C-Reactive Protein Testing to Guide Antibiotic Prescribing for COPD Exacerbations. N Engl J Med 2019; 381(2):111–20. https://www.ncbi.nlm.nih.gov/pubmed/31291514.	**Studiendesign:** multicenter, open-label, RCT **Population:** patients with COPD presenting with an acute exacerbation in primary care; n = 653 **Intervention:** usual care guided by CRP point-of-care testing (CRP-guided group); at the initial consultation and at any further consultations **Vergleich:** usual care alone (usual-care group) **Follow-up:** week 1,2,4; 6 month **Ausschlusskriterien:** required urgent hospital admission; had severe illness (e.g. suspected pneumonia, tachypnea >30 breaths per minute); had a concurrent infection at another site (e.g. urinary tract infection); had a past history of respiratory failure or mechanical ventilation; were currently taking antibiotics or had already taken antibiotics for this AECOPD; had an active inflammatory condition; had cystic fibrosis, tracheostomy or bronchiectasis; were immunocompromised; were pregnant, or; had previously participated in the study **Studienzeitraum:** 01/2015 - 09/2017 **Ort:** 86 general medical practices in the UK Clinicians were provided with **guidance** on the interpretation of CRP test results: - CRP level < 20 mg per liter, antibiotics are unlikely to be beneficial and usually should not be prescribed; - CRP level from 20 to 40 mg per liter, antibiotics may be beneficial, mainly if purulent sputum is present; - CRP level > 40 mg per liter, antibiotics are likely to be beneficial.	**Baseline-Patientencharakteristika** - hinsichtlich Alter, Geschlecht, Rauchstatus, Komorbiditäten, Anzahl der Tage mit Symptomen vor der Konsultation; Vormedikation weitestgehend ausgeglichen - leichte Unterschiede in den verschiedenen GOLD-Stadien CRP-guided group: - n = 317: median CRP value was 6 mg per liter (interquartile range, 5.0 to 18.5) **primary outcomes** - patient-reported antibiotic use for an acute exacerbation of COPD within 4 weeks after randomization: 150/ 263 (57.0%) vs. 212/274 (77.4%); adjusted OR 0.31; 95% CI 0.20 to 0.47 - COPD-related health status (Clinical COPD Questionnaire at 2 weeks after randomization): adjusted MD −0.19 points (two-sided 90% CI, −0.33 to −0.05) in favor of the CRP-guided group **secondary outcomes:** - antibiotic prescriptions at the initial consultation: 47.7% (CRP-guided) vs. 69.7% (usual care); adjusted OR, 0.31; 95% CI, 0.21 to 0.45. - antibiotic prescriptions at the initial consultation in the CRP-guided group: -- 79/241 (32.8%) with CRP< 20 mg/l -- 32/38 (84.2%) with a CRP value between 20 and 40 mg per liter -- 36/38 (94.7%) with a CRP value > 40 mg/l During the first 4 weeks of follow- up, antibiotics were prescribed for 185 of 313 patients (59.1%) in the CRP-guided group and for 252 of 316 patients (79.7%) in the usualcare group (adjusted odds ratio, 0.30; 95% CI, 0.20 to 0.46). We found no evidence of any between- group difference in the use of other treatments for COPD (including oral glucocorticoids) during the first 4 weeks of follow-up (adjusted odds ratio, 0.79; 95% CI, 0.43 to 1.46). **authors conclusion:** CRP-guided prescribing of antibiotics for exacerbations of COPD in primary care clinics resulted in a lower	**Selection bias** Randomisierung: **unklar** Kommentar: keine weiteren Angaben Allocation concealment: **unklar** Kommentar: keine weiteren Angaben **Performance bias** Verblindung von Teilnehmern und Personal: **n.a.** **Detection bias** Verblindung der Ergebnisevaluation: **unklar** **Attrition bias** Verlust von Studienteilnehmern/ fehlende Daten: **hoch** Kommentar: Drop out kaum beschrieben, Gründe nicht dokumentiert **ITT-Analyse:** durchgeführt Kommentar: modified intention-to-treat population, which included all the patients who had undergone randomization and had available outcome data; full-ITT-Daten im Supplement dargestellt; keine wesentlichen Ergebnisunterschiede zur modifizierten ITT **Reporting bias** selektive Ergebnisdarstellung: **gering** Kommentar: published protocol, Sekundäre Endpunkte im Supplement dargestellt; Protokoll jedoch erst nach Studienende publiziert **Andere Biasursachen** Baseline imbalance: **gering** Interessenkonflikte/ Sponsoring: angegeben Evidenzqualität: moderat (primäre Endpunkte Antibiotikaverbrauch sowie Gesundheitszustand) Ausgangsniveau: hoch (RCT) 1)Verzerrungsrisiko: unklar 2) Präzision: ok 3) Direktheit/Übertragbarkeit: gut 4) Konsistenz: n.a.	

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit der Evidenz	Kommentar
		percentage of patients who reported antibiotic use and who received antibiotic prescriptions from clinicians, with no evidence of harm.		
Zou Y. Significance of serum procalcitonin combined with C-reactive protein in diagnosis of acute exacerbation of chronic obstructive pulmonary disease and guidance of antibiotics therapy. International journal of clinical and experimental medicine 2018; 11(10):11070–8. www.ijcem.com/files/ijcem0080681.pdf.	**Studiendesign:** diagnostic accuracy (1. Teil der Studie); RCT (2. Teil der Studie) **Population:** Patients with COPD admitted to hospital (n = 182) Part 1: patients divided into AECOPD group (n=60) and stable COPD group (n=62): - detection of Serum PCT, CRP values and white blood cell count (WBC) - sensitivity, specificity and the area under receiver operating characteristic (ROC) curves of the markers in judging AECOPD calculated Part 2: patients with AECOPD (n = 60): randomly divided into PCT-CRP guided treatment group and usual care group **Intervention:** PCT-CRP guided treatment group - same treatment as usual care group - Antibiotic drugs were given when PCT ≥ 0.25 ng/ml or CRP > 8 mg/L (it was considered to be the presence of bacterial infection); - antibiotic drugs were discontinued when PCT < 0.25 ng/ml and CRP < 8 ng/ml **Vergleich:** usual care group: received conventional treatment including bronchodilators, corticosteroids, expelling phlegm, antibiotic therapy, and mechanical ventilation when necessary **Studienzeitraum:** 01/2016 - 12/2016 & 01/2017 - 06/2017 **Ort:** Shanghai (China) **Definitionen**: - Stable COPD was defined as the stability or mild symptoms of the patient's cough, sputum production, and shortness of breath, with the condition basically restored to the state before	**Baseline-Patientencharakteristika** - für Part 2 der Studie: keine statistisch signifikanten Unterschiede hinsichtlich Alter, Geschlecht, Rauchstatus, Komorbiditäten; Abweichungen in absoluten Zahlen aufgrund geringerer Patientenzahl **Results:** Diagnostic accuracy The PCT level was highest (0.45±0.39 ng/ml) in AECOPD patients with positive sputum culture, followed by 0.27±0.26 ng/ml in sputum culture-negative AECOPD patients, and lowest (0.08±0.09 ng/ml) in stable COPD patients, and there was significant difference in pairwise comparison (all P<0.001). The CRP and WBC levels were remarkably higher in the acute exacerbation phase than in the stable phase of COPD, but they were insignificantly different between AECOPD patients with negative sputum culture and those with positive sputum culture. The sensitivity and specificity of PCT in diagnosis of AECOPD were 70.0% and 74.2%, respectively. The sensitivity and specificity of CRP and WBC were 46.7%, 41.7%, 66.1%, and 64.5%, respectively. The area under the ROC curve for PCT was 0.721 (95% CI: 0.633-0.798), significantly higher than that (0.564, 95% CI: 0.471-0.654) for CRP and that (0.531, 95% confidence interval (CI): 0.438-0.622) for WBC (all P<0.001). The sensitivity and specificity of PCT-CRP combination were 91.7% and 59.7%, respectively, and the area under the ROC curve was 0.757 (95% CI: 0.671-0.831). PCT-CRP guided treatment Among patients with PCT-CRP parallel guided antibiotic treatment, no significant difference was seen in expectorant drugs, hormones, bronchodilators, and other drugs, as well as the number of patients with antibiotics use. The days of antibiotics use were significantly fewer (P=0.037); hospital stay was also considerably shorter (P=0.048). However, the deaths during hospitalization differed insignificantly.	**Selection bias** Randomisierung: **unklar** Kommentar:keine weiteren Informationen, kein Protokoll Allocation concealment: **unklar** Kommentar:keine weiteren Informationen, kein Protokoll **Performance bias** Verblindung von Teilnehmern und Personal: **unklar** Kommentar:keine weiteren Informationen, kein Protokoll **Detection bias** Verblindung der Ergebnisevaluation: **unklar** Kommentar:keine weiteren Informationen, kein Protokoll **Attrition bias** Verlust von Studienteilnehmern/ fehlende Daten: **unklar** Kommentar:keine weiteren Informationen, kein Protokoll **ITT-Analyse:** nein **Reporting bias** selektive Ergebnisdarstellung: **unklar** Kommentar: keine weiteren Informationen, kein Protokoll **Andere Biasursachen** Baseline imbalance: **gering** Kommentar: wenige Patienten je Gruppe (je n = 30) Interessenkonflikte/ Sponsoring: CoI: none. Keine weiteren Angaben **weiteres:** Endpunkte hinsichtlich PCT-CRP guided treatment nicht detailliert beschrieben (nur: Signifikanz anhand P-Wert) Evidenzqualität: sehr niedrig Ausgangsniveau: hoch (RCT)	`- schwache methodische Qualität - Endpunkte zu "PCT-CRP guided treatment": nicht detailliert beschrieben (nur: Signifikanz anhand P-Wert) --> Aussagekraft fraglich

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit der Evidenz	Kommentar
	the acute exacerbation - AECOPD was defined as a continuous exacerbation of the patients' respiratory symptoms that is beyond the normal daily variations and leads to a change in medication.		1)Verzerrungsrisiko: unklar -1 2) Präzision: unklar - 2 (nur Signifikanzen angegeben) 3) Direktheit/Übertragbarkeit: gut 4) Konsistenz: n.a.	
Prins HJ. CRP-guided antibiotic treatment in acute exacerbations of COPD in hospital admissions. Eur Respir J 2019; 53(5). https://www.ncbi.nlm.nih.gov/pubmed/30880285 .	**Studiendesign:** investigator-initiated, multicentre, randomised, controlled open intervention clinical trial **Population:** patients hospitalised with acute exacerbations of COPD (n = 220) **Intervention:** C-reactive protein (CRP)-guided antibiotic treatment: - treated with amoxicillin/clavulanic acid (625 mg, 3x/ day for 7 days) if CRP levels on admission were ⩾50 mg·L^{-1}. - CRP levels <50 mg·L^{-1} no antibiotic was prescribed; however, CRP levels were re-evaluated within 24 h and, if they had risen to ⩾50 mg·L^{-1}, patients were also treated with amoxicillin/clavulanic acid. **Vergleich**: patient reported symptoms in accordance with the GOLD strategy: - treated with amoxicillin/clavulanic acid for 7 days (625 mg, 3x/ day) if they reported increased sputum purulence in combination with increased dyspnoea and/or increased sputum volume, or if this was observed by the attending physician in the first 24 h after admission - If patients were not able to expectorate sputum and remained unable to do so for the first 24 h after admission: considered to be non-purulent. **>>** receive antibiotics based either on the GOLD strategy or according to the CRP strategy (CRP ≥ 50 mg·L^{-1}). **Follow-Up:** monitored over 1 year, with scheduled visits at 1 month and 6 months.	**Baseline-Patientencharakteristika** - hinsichtlich Alter, Rauchstatus, Gewicht, Lungenfunktion, Komorbiditäten weitestgehend ausgeglichen; leichte Dysbalancen hinsichtlich Geschlechterverteilung und Vormedikation (CRP-Gruppe: mehr Frauen + größerer Anteil mit AB vorbehandelt) - In addition, all patients were treated with corticosteroids (oral prednisolone (60 mg) for 3 days, followed by 30 mg for 7 days) and bronchodilators. Supplemental oxygen and physiotherapy were added at the discretion of the attending physician. **Primärer Endpunkt** - Fewer patients in the CRP group were treated with antibiotics compared to the GOLD group (31.7% versus 46.2%, p=0.028; adjusted OR 0.178, 95% CI 0.077–0.411, p=0.029). **Sekundäre Endpunkte** - 30-day treatment failure rate: 44.5% in the CRP group versus 45.5% in the GOLD-group, p=0.881; adjusted OR 1.146, 95% CI 0.649–1.187, p=0.630 - time to next exacerbation: 32 days in the CRP group versus 28 days in the GOLD group, p=0.713; adjusted hazard ratio 0.878, 95% CI 0.649–1.187, p=0.398) - Length of stay: 7 days in the CRP group versus 6 days in the GOLD group, p=0.206 - On day 30: no difference in symptom score, quality of life or serious adverse events was detected.	**Selection bias** Randomisierung: **gering** Kommentar: Randomisation was performed with block sizes of fifty. Allocation concealment: **gering** Kommentar: Treatment allocation was concealed with a pre-specified computer-generated randomisation list by an independent statistician.; sealed, opaque envelops. **Performance bias** Verblindung von Teilnehmern und Personal: **gering** Kommentar: Medical staff treating subjects allocated to GOLD-guided treatment were blinded to the CRP results for the first 24 h. **Detection bias** Verblindung der Ergebnisevaluation: **unklar** Kommentar:keine weiteren Informationen **Attrition bias** Verlust von Studienteilnehmern/ fehlende Daten: **gering** Kommentar: Drop out beschrieben, Gründe dokumentiert **ITT-Analyse:** durchgeführt **Reporting bias** selektive Ergebnisdarstellung: **gering** Kommentar: alle in clinicaltrials.gov (Protokoll) angegebenen Endpunkte wurden dargestellt **Andere Biasursachen** Baseline imbalance: **gering** Kommentar: leichte Unterschiede hinsichtlich Geschlechterverteilung und Vormedikation mit Antibiotika; Signifikanz nicht darstellbar Interessenkonflikte/ Sponsoring: angegeben; funders had no role in the design and conduct of the study, in the collection, management, analysis and interpretation of the data [...]	

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit der Evidenz	Kommentar
	Studienzeitraum: 07/2011 - 02/2015 **Ort:** the Netherlands		Evidenzqualität: moderat/hoch Ausgangsniveau: hoch (RCT) 1)Verzerrungsrisiko: gering 2) Präzision: ausreichend 3) Direktheit/Übertragbarkeit: gut 4) Konsistenz: n.a.	

3.4.2 Sputum

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit der Evidenz	Kommentar
Chen K. A Systematic Review and Meta-Analysis of Sputum Purulence to Predict Bacterial Infection in COPD Exacerbations. COPD 2020; 17(3):311–7. https://www.ncbi.nlm.nih.gov/pubmed/32456479.	• **Fragestellung:** to evaluate the strength of literature supporting inclusion of sputum purulence in criteria utilized to evaluate if antimicrobials are indicated in acute COPD exacerbation. • **Suchzeitraum:** 29.02.2020 • **Population:** Patienten mit AECOPD • **Einschlusskriterien:** - evaluation of relationship between sputum purulence and culture results in COPD exacerbations • **Interventionen (Definition):** - Sputum purulence was defined by visual assessment of color, either subjectively by providers and/or patients or by a colored chart (green or yellow= considered purulent) • **Endpunkt:** presence of potentially pathogenic bacteria (PPB) on bacterial culture • **eingeschlossene Studien:** 6 observational studies • **quality assessment:** New Castle-Ottawa scale (NOS); GRADE	• **Setting:** - n=4 studies: hospitalized patients - n=1 study: emergency department - n=1 study: primary care setting • **sputum samples:** - n=5: expectorated sputum; n=1: bronchoscopy • **Effektivität:** purulent vs. mucoid sputum (probability of positive bacterial culture results): - RR 2,14 (95% CI 1,25; 3,67); 6 studies; n=1092; I²=88%; GRADE: moderate quality; 670/771 vs. 164/321 • **Sensitivitätsanalyse:** - after removal of studies losing 2 or more points from the NOS, the effect value remained statistically significant: RR 1,69 (95% CI 1,09; 2,63)	• Qualität des Reviews: -low Evidenzqualität siehe endpunktspezifische GRADE-Bewertung des Reviews	• ausschließlich Beobachtungsstudien eingeschlossen; kein Protokoll angegeben • hohe Heterogenität: Gewichtung nach Studiengröße; random effects Modell genutzt

3.4.3 Procalcitonin

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
Chen K. Procalcitonin for Antibiotic Prescription in Chronic Obstructive Pulmonary Disease Exacerbations: Systematic Review, Meta-Analysis, and Clinical Perspective. Pulm Ther 2020. https://www.ncbi.nlm.nih.gov/pubmed/32676981.	• **Fragestellung:** to investigate the impact of a PCT-based protocol on antibiotic prescription and clinical outcomes in patients with COPD exacerbations. • **Suchzeitraum:** 29.02.2020 • **Population:** Patienten mit AECOPD • **Intervention:** PCT-based protocols for guiding antibiotic use in patients with COPD exacerbations • **Vergleich:** standard-of-care-based • **primary study outcome:** length of antibiotics therapy • **secondary outcomes:** hospital length of stay (LOS), treatment failure, all-cause and respiratory-related mortality, and all-cause and respiratory-related readmission • **eingeschlossene Studien**: n=14 (RCTs + observational studies) • **quality assessment:** Cochrane risk of bias tool (for RCTs); Newcastle- Ottawa scale (NOS; for observational studies); Grading of Recommendations Assessment, Development and Evaluation (GRADE)	• **Setting:** - hospital (n=10 studies); emergency department (n=2 studies); ICU (n=2 studies) • **Target threshold PCT blood levels:** - n=9 studies: 0,25 µg L^{-1} (consistent with US FDA recommendations) - n=2 studies: used lower PCT level cutoffs (0,1 and 0,1–0,25 µg L^{-1}) • **mean PCT blood levels in COPD exacerbation** (n=14 studies): - wide variance ranging from 0,06 to 1,44 µg L^{-1}; some of this variation is related to higher PCT levels reported with pneumonia. • **Results:** PCT was found to decrease <u>overall antibiotic exposure in COPD exacerbations</u>: - MD -2.01 days (95% CI [-3.89, -0.14]; 6 RCT, n = 1334; p = 0.04; **GRADE: moderate**, - MD -1.64 [-2.91, -0.36]; 2 observational studies; n = 405; **GRADE: very low** No apparent effects were found on clinical outcomes: <u>length of hospital stay</u> - MD 0.06 [-0.71, 0.83]; 9 RCT, n = 1824, **GRADE: low** - MD -0.17 [-1.62, 1.28]; 3 observational studies, n = 650; **GRADE: very low** <u>treatment failure</u> (included worsening symptoms, ICU admission, death, and readmission within 72 h to 30 days of admission) - 152/734 vs. 160/732; RR 0.97 [0.77, 1.22]; 7 RCT, n = 1466; **GRADE: low** - 18/157 vs. 28/188; RR 0.83 [0.47, 1.45], 2 observational studies; n = 345; **GRADE: very low** <u>all-cause mortality</u> - 57/906 vs. 48/904; RR 1.19 [0.83, 1.71]; 9 RCT, n = 1810; **GRADE: low** - 16/337 vs. 13/406; RR 1.47 [0.73, 2.96]; 4 observational studies; n = 743; **GRADE: very low** <u>Respiratory-related mortality</u> - 21/156 vs. 3/153; RR 0.65 [0.11, 3.82]; 3 RCT, n = 310; **GRADE: moderate** The majority of blood PCT levels in COPD exacerbations were below the manufacturer-recommended cutoff for antibiotics, and the use of this marker was associated with worse outcomes in the intensive care setting.	• Qualität des Reviews: - low <u>Evidenzqualität</u> siehe endpunktspezifische GRADE- Bewertung des Reviews	• eingeschlossene Studien: **Christ-Crain 2004** **Corti 2006** **Daubin 2018** Huang 2018 Liu 2015 Nangia 2012 **Schuetz 2009** **Stolz 2007** **Verduri 2015**

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
		• **Additional sensitivity analysis** - effect of PCT on antibiotic duration in RCTs was no longer significant excluding studies with: -- high risk of bias: MD = -1.88 days, 95% CI [-3.95, 0.19] days, p = 0.08 -- converted outcome value: MD = -1.72 days, 95% CI [-4.28, 0.83] days, p = 0.19 - excluding RCTs with one or more high-risk-of-bias items (except blinding for outcome assessment) and application of a fixed effects model, --- PCT group had a significantly longer hospital LOS compared with the standard therapy group (MD = 0.56 days, 95% CI [0.06, 1.05] days, p = 0.03), I^2 was reduced from 65 to 45%. - For observational studies, after removal of Townsend et al., which had a lower NOS score and a converted outcome value, and application of a fixed effects model; -- PCT group had a significant 1-day shorter hospital LOS (MD = -1.01 days, 95% CI [-1.62, -0.40] days, p = 0.001) compared with the standard therapy group, I^2 was reduced from 84 to 37% **Author´s conclusion:** Our review and analysis does not support the use of PCT to guide antibiotic prescription in COPD exacerbations.		
Li Z. Procalcitonin-guided antibiotic therapy in acute exacerbation of chronic obstructive pulmonary disease: An updated meta-analysis. Medicine (Baltimore) 2019; 98(32):e16775. https://www.ncbi.nlm.nih.gov/pubmed/31393400.	• **Fragestellung:** we conducted an updated meta-analysis to comprehensively reevaluate the role of PCT-guided antibiotic strategies in the treatment of patients with AECOPD. • **Suchzeitraum:** 01.02.2019 • **Population:** Patienten mit AECOPD • **Interventionen:** PCT-guided antibiotic strategies • **Vergleich:** standard antibiotic therapy • **primary outcomes:** - antibiotic exposure (antibiotic prescription, antibiotic exposure duration, and antibiotic use after discharge) • **secondary outcomes:** - clinical success, all-cause mortality, exacerbation at follow-up, readmission at follow-up, length of hospital stay, and adverse events • **eingeschlossene Studien**: 8 RCTs (n = 1376 participants)	• **Baseline-Charakteristika** - n = 681 patients were allocated to a PCT-guided antibiotic strategy group and n = 695 patients to a standard antibiotic therapy group - n = 4 studies initiated antibiotics when PCT was above 0.25mg/L, - n = 3 studies initiated antibiotics when PCT was above 0.25mg/L or 0.1 to 0.25mg/L if the patient's clinical condition was unstable - n = 1 study initiated antibiotics when PCT was below 0.1mg/L if the patient's clinical condition was unstable. • **Effektivität:** - PCT-guided antibiotic strategy reduced antibiotic prescriptions (RR: 0.55; 95% CI: 0.39–0.76; p=0.0003), I^2 = 93%; 7 RCTs, n = 1287 - similar in both groups: -- antibiotic exposure duration (MD 1.34; 95% CI: 2.83–0.16; p=0.08), I^2 = 74%; 4 RCTs, n = 710 -- antibiotic use after discharge (RR 1.61; 95% CI: 0.61–4.23; p=0.34), I^2 = 86%; 3 RCTs, n = 577 -- clinical success (RR 1.02; 95% CI: 0.96–1.08; p=0.47),I^2 = 0%; 3 RCTs, n = 577 -- all-cause mortality (RR 1.05; 95% CI: 0.72–1.55; p=0.79), I^2 = 0%; 7 RCTs, n = 1470	• Qualität des Reviews: - critically low - nichterfüllte kritische Kriterien: -- Protocol a priori -- list of excluded studies -- account for RoB in individual studies when interpreting/discussing the results of the review	• eingeschlossene Studien: n= 8 RCTs **Christ Crain 2004** **Stolz 2007** Kristoffersen 2009 **Schuetz 2009** **Verduri 215** **Corti 2016** Wang 2016 **Daubin 2018** • hohe Heterogenitäten; random effects Modell genutzt

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
	• RoB der eingeschlossenen Studien: Christ Crain 2004 (RoB 5x low/1x unclear/1x high) Stolz 2007 (RoB 2x low/5x unclear) Kristoffersen 2009 (RoB 5x low/2x unclear) Schuetz 2009 (RoB 2x low/4x unclear/1x high) Verduri 215 (RoB 3x low/4x unclear) Corti 2016 (RoB 3x low/3x unclear/1x high) Wang 2016 (RoB 6x low/1x unclear) Daubin 2018 (RoB 4x low/3x unclear/)	-- exacerbation at follow-up (RR 0.97; 95% CI: 0.80– 1.18; p=0.78), I^2 = 30%; 6 RCTs, n = 975 -- readmission at follow-up (RR 1.12; 95% CI: 0.82–1.53; p=0.49), I^2 = 15%; 5 RCTs, n = 758 -- length of hospital stay (MD 0.36; 95% CI: 1.36– 0.64; p=0.48), I^2 = 52%; 7 RCTs, n = 1074 -- adverse events (RR 1.33; 95% CI: 0.79–2.23; p=0.28), I^2 = 0%; 2 RCTs, n = 298 **Sensitivity analysis** - Significant heterogeneity: among the studies reporting antibiotic prescriptions (I^2 =91%). - RR was not substantially altered when any single study was excluded, suggesting that the results of the current meta-analysis are robust - One trial by Wang et al was different from the others in the included population and antibiotic initiation strategy. Nevertheless, heterogeneity decreased from 91% to 81% after exclusion of this trial, and there was no significant change in the results (RR: 0.65; 95% CI: 0.52–0.83; P=.0004; 1; I^2=81%).		
Mathioudakis AG. Procalcitonin to guide antibiotic administration in COPD exacerbations: A meta-analysis. Eur Respir Rev 2017; 26(143):160073. https://www.ncbi.nlm.nih.gov/pubmed/28143877	• UK, Griechenland, Moldau • Metaanalyse, nur RCT • **Suchzeitraum:** inception - 19/07/2016 • **Population:** Patienten mit AECOPD • **Interventionen:** procalcitoninbased versus standard protocols to guide the initiation or discontinuation of antibiotics • **Einschlusskriterien:** trials focusing on patients with lower respiratory tract infections or respiratory tract infections in general; included subgroups of patients with AECOPD (studies included ⩾30 patients); procalcitonin-based protocols included recommendation to initiate or continue antibiotics for serum procalcitonin levels above a prespecified cut-point and to discontinue or not to initiate for lower levels; comparator: any other protocol used in clinical practice (clinicians were unaware of the participants' procalcitonin levels); previous clinical diagnosis of COPD was considered adequate; AECOPD was defined as a deterioration of the patients' respiratory symptoms that is beyond the normal day-to-day variations and leads to a change in medication; only studies in a primary care facility or hospital emergency, respiratory or internal medicine department were accepted. • **Ausschlusskriterien:** - Studies focusing on hospital-acquired infections or performed in the intensive care unit (ICU)	• none of the included trials was blinded • The procalcitonin-based protocols used in all included trials were similar. - n=7/8 studies: **Antibiotics were recommended for procalcitonin levels >0.25 µg·L−1 and discouraged for levels <0.25 µg·L−1** - n=1 study used a different cut-point: recommended antibiotics for procalcitonin levels >0.5 µg·L−1) - in some of the studies antibiotics were strongly discouraged for levels <0.1 µg·L−1 and/or strongly recommended for levels >0.5 µg·L−1. • **Effektivität** of procalcitonin-based protocols to initiate or discontinue antibiotics in patients presenting with AECOPD: - Treatment failure for the index exacerbation: n=834 (5 RCTs), RR 0.81 (0.62–1.06), Risk with standard care: 206 per 1000, Risk difference with procalcitonin-guided protocols: 39 fewer failures per 1000 (78 fewer to 12 more), **GRADE: LOW** - Length of hospital stay for the index exacerbation: n=1062 (8 RCTs), MD −0.76 (−1.95–0.43), Risk with standard care: Mean length of hospital stay was 8.55 days, Risk difference with procalcitonin-guided protocols:MD 0.76 fewer days (1.95 fewer to 0.43 more), **GRADE: MODERATE** - Proportion of patients who were prescribed antibiotics on admission: n=984 (7 RCTs), RR 0.56 (0.43–0.73), Risk with standard care: 791 per 1000, Risk difference with procalcitonin-guided protocols: 348 fewer prescriptions per 1000 (451 fewer to 214 fewer), **GRADE: MODERATE** - Duration of the course of antibiotics: n= 776 (6 RCTs), MD −3.83 (−4.32–−3.35), Risk with standard care: Mean	y-y-y-y-n-y-y-y-y-y-n AMSTAR Score: 9/11 Evidenzqualität siehe endpunktspezifische GRADE- Bewertung des Reviews	Nicht zitiert

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
	- patients with immunodeficiencies or receiving immune-suppressants (apart from corticosteroids administered for the management of COPD), patients with chronic infections requiring chronic antibiotic therapy and patients with medullary thyroid carcinoma • **primäre Endpunkte:** 1) treatment failure for the index exacerbation, defined as deterioration of symptoms, non-improvement or death (within 1–4 weeks) 2) length of hospitalisation for the index exacerbation • **Sekundäre Endpunkte**: 1) antibiotic exposure for the index exacerbation (including the proportion of patients who were prescribed antibiotics and the duration of the course of antibiotics) and at longest follow-up 2) antibiotic prescription after an opposite initial decision 3) re-exacerbation rate at longest follow-up 4) re-admission rate at longest follow-up 5) mortality at longest follow-up • **Body of Evidence:** n=8 RCTs, n=1062 Patienten	duration of course of antibiotics was 8.27 days, Risk difference with procalcitonin-guided protocols: MD 3.83 fewer days (4.32 fewer to 3.35 fewer), **GRADE: MODERATE** - Exacerbation recurrence rate at longest follow-up: n=496 (3 RCTs), RR 0.96 (0.69–1.35), Risk with standard care: 205 per 1000, Risk difference with procalcitonin-guided protocols: 8 fewer recurrences per 1000 (63 fewer to 72 more), **GRADE: LOW** - Re-hospitalisation rate at longest follow-up: n=398 (3 RCTs), RR 1.45 (0.92–2.29), Risk with standard care: 116 per 1000, Risk difference with procalcitonin-guided protocols: 52 more admissions per 1000 (9 fewer to 150 more), **GRADE: LOW** - Rate of re-hospitalisation due to an exacerbation at longest follow-up: n=298 (2 RCTs), RR 1.22 (0.71–2.09), Risk with standard care: 135 per 1000, Risk difference with procalcitonin-guided protocols: 30 more admissions per 1000 (39 fewer to 147 more), **GRADE: LOW** - Overall mortality at longest follow-up: n=1062 (8 RCTs), RR 0.99 (0.58–1.69), Risk with standard care: 41 per 1000, Risk difference with procalcitonin-guided protocols: 0 fewer deaths per 1000 (18 fewer to 29 more), **GRADE: MODERATE**		
Schuetz P. Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections. Cochrane Database Syst Rev 2017; 10(10):CD007498. https://www.ncbi.nlm.nih.gov/pubmed/29025194	• **Objectives:** to assess the safety and efficacy of using procalcitonin for starting or stopping antibiotics over a large range of patients with varying severity of ARIs and from different clinical settings. • Metaanalysen, nur prospektive RCT • **Suchzeitraum:** Inception - 10/02/2017 • **Population:** patients with varying severity of acute respiratory infections (ARIs): 1 Subgruppe: exacerbation of chronic obstructive pulmonary disease (COPD) • **Interventionen:** Strategies to initiate or discontinue antibiotic therapy based on PCT levels compared with usual care • **Einschlusskriterien:** adult participants with clinical diagnoses of ARIs: either a lower ARI including community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), acute bronchitis, exacerbation of asthma, or exacerbation of chronic obstructive pulmonary disease (COPD); or an upper ARI including common cold, rhino-sinusitis, pharyngitis, tonsillitis, or otitis media. We also included people with sepsis and suspected ARIs in the analyses.	• **PCT-Cut-Offs für COPD-Subgruppen aus** "Studiencharakteristika" extrahiert: AECOPD-Studien: (R= recommendation for or against antibiotics) Corti 2016 (ARI 120/120) Initiation and duration; R against AB < 0.25 (0.15)/ 80% decrease; R for AB > 0.25 Verduri 2015 (ARI 178/183) Initiation; R against AB: < 0.1; R for AB: > 0.25 Wang 2016 (ARI 191/194) All participants had initial PCT< 0. 1; AB group treated with AB for at least 3 days, control group noAB in the first 10 days Stolz 2007 (ARI 208/226) Initiation and duration; R against AB: < 0.25 (< 0. 1); R for AB: > 0.25 (> 0. 5) ***--> Sind auch im eingeschlossenen Mathioudakis-Metaanalyse 2017 betrachtet (Wang 2016 in der Diskussion)*** • **Allgemeine Endpunkte in diesem Review für Patienten mit exazerbierter COPD** (control group n=631; PCT group n=621) - 30 days mortality, n (%): control 24 (3.8%), PCT 19 (3.1%), effect measures 0.8 (0.43 to 1.48), P = 0.472; p for interaction 0.847 - Treatment failure, n (%): control 110 (17.4%); PCT 104 (16.7%), effect measures 0.94 (0.70 to 1.27), P = 0.704, p for interaction 0.676	y-n-y-y-y-y-y-y-y-y-y AMSTAR Score: 10/11	Nicht zitiert

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
	• **Ausschlusskriterien:** trials focusing exclusively on children or used PCT to escalate antibiotic therapy • **primäre Endpunkte:** 1. All-cause mortality following randomisation up to a follow up time of 30 days. 2. Setting-specific treatment failure within 30 days of inclusion. • **sekundäre Endpunkte:** 1. Antibiotic use (initiation of antibiotics, duration of antibiotics, and total exposure to antibiotics (total amount of antibiotic days divided by total number of participants)). 2. Length of hospital stay for hospitalised participants. 3. Length of ICU stay for critically ill participants. 4. Number of days with restricted activities within 14 days after randomisation for primary care participants. 5. Antibiotic-related side effects. • **Body of Evidence insgesamt:** n=26 RCTs, n=6708 eingeschlossene Patienten	- Length of hospital stay, mean (±SD): control 9.3 ± 13.9; PCT 8.4 ± 7.2, effect measures -0.60 (-1.84 to 0.64), P = 0.342, p for interaction 0.658 - Antibiotic-related side effects, n (%): control 30 (10.9%), PCT 29 (10.5%), effect measures 0.93 (0.53 to 1.63), P = 0.805, p for interaction 0.198 GRADE nicht speziell für COPD-Subgruppen		

3.5 Opioide

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
Ekström M. Effects of opioids on breathlessness and exercise capacity in chronic obstructive pulmonary disease. A systematic review. Ann Am Thorac Soc 2015; 12(7):1079–92. https://www.ncbi.nlm.nih.gov/pubmed/25803110.	**Fragestellung:** We aimed to estimate the efficacy and safety of opioids on refractory breathlessness, exercise capacity, and HRQL in COPD. **Suchzeitraum:** 9/2014 **Population:** patients with COPD (95% with severe COPD) **Einschlusskriterien:** randomized, double-blind, placebo-controlled trials of any opioid for breathlessness, exercise capacity, or HRQL that included at least one participant with COPD **Interventionen:** any opioid **Vergleich:** placebo controlled	Breathlessness - opioids overall: SMD -0.35 (95% CI -0.53 to -0.17); I²= 78.9%, 12 studies, n = 200 **(GRADE: nicht angegeben)** - systemic opioids: SMD, -0.34 (95% CI, -0.58 to -0.10); I², 0%; 8 studies, n = 118, **GRADE: moderat**e - nebulized opioids: SMD -0.39 (95% CI -0.71 to -0.07); I²= 78.9%; 4 studies, n = 82, **GRADE: low** exercise capacity - opioids overall: SMD 0.06 (95% CI -0.15 to 0.28); I² = 70.7%; 13 studies, n = 149; **GRADE: low** - systemic opioids: SMD 0.11 (95% CI -0.17 to 0.39); I²= 63.3%; 8 studies, n = 92; **GRADE: low** - nebulized opioids: SMD -0.01 (95% CI -0.36 to 0.34); I²= 78.5%; 6 studies, n = 69; **GRADE: low** - HRQL could not be analyzed. - Risk of study bias was low or unclear.	Qualität des Reviews: - low Evidenzqualität siehe endpunktspezifische GRADE- Bewertung des Reviews	

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
	eingeschlossene Studien: 16 studies (15 crossover trials and 1 parallel-group study, 271 participants)	**Sicherheit:** There were no serious adverse effects.		
Barnes H. Opioids for the palliation of refractory breathlessness in adults with advanced disease and terminal illness. Cochrane Database of Systematic Reviews 2016;(3).	**Fragestellung:** To determine the effectiveness of opioid drugs in relieving the symptom of breathlessness in people with advanced disease due to malignancy, respiratory or cardiovascular disease, or receiving palliative care for any other disease. **Suchzeitraum:** 10/2015 **Population:** people with advanced disease due to malignancy, respiratory or cardiovascular disease, or receiving palliative care for any other disease. **Interventionen:** use of any opioid drug **Vergleich:** placebo or any other intervention for the relief of breathlessness **eingeschlossene Studien:** 26 studies (n = 526 participants); Subgruppe Patienten mit COPD: 14 studies	**Subgruppe COPD** Breathlessness (Borg and the modified Borg scale, verbal categorical scales of breathlessness, and visual analogue scales (VAS) of breathlessness) - change from baseline: SMD −0.49 (95% CI −1.08 to 0.10); I² = 0%; p = 0.1; 2 studies, n =46 participants, - post-treatment scores: SMD −0.24 (95% CI −0.48 to 0.01); I² = 0%; p = 0.1; 8 studies, n =262 participants **RoB der eingeschlossenen Studie**n (GRADE nicht für Subgrupppe COPD durchgeführt; 8. RoB-Punkt: Size bias) - Abernethy 2003: 7x low / 1x high - Bar-Or: 1982 3x low / 4x unclear / 1x high - Light 1996: 3x low / 4x unclear / 1x high - Poole 1998: 6x low / 1x unclear / 1x high - Eiser 1991: 2x low / 4x unclear / 2x high - Jankleson 1997: 2x low / 5x unclear / 1x high - Jensen 2012: 6x low / 1x unclear / 1x high - Johnson 1983: 4x low / 3x unclear / 1x high - Leung 1996: 3x low / 4x unclear / 1x high - Masood 1995: 3x low / 4x unclear / 1x high - Noseda 1997: 3x low / 4x unclear / 1x high - Rice 1987: 3x low / 4x unclear / 1x high - Woodcock 1981: 3x low / 4x unclear / 1x high - Young 1989: 2x low / 5x unclear / 1x high	Qualität des Reviews: - moderate	Analysen vorhanden für Gesamtgruppe (ohne differenzierte Daten speziell für Patienten mit COPD) - Breathlessness: change from baseline - Breathlessness: post-treatment score - Exercise tolerance - Adverse events - QoL --> ggf. Übertragbarkeit diskutieren weitere Ananlysen für - Type of opioid - Condition (other diseases) - Opioids versus other interventions
Viglino D. Opioid drug use in emergency and adverse outcomes among pa-tients with chronic obstructive pulmonary disease: A multicenter observatio-nal study. Sci Rep 2020;	**Fragestellung:** addressing real-life punctual non-palliative opioid administration to patients with COPD in an acute care setting, and not uniquely for sedation for a respiratory intervention. **Studiendesign:** multicenter observational study (database extraction) **Population:** All patients > 40 presenting at two university hospital emergency departments with dyspnea, abdominal pain or trauma were retrieved, and COPD patients **Einschlusskriterien:**	**Baseline-Patientencharakteristika:** - A total of 83,119 emergency visits for dyspnea, abdominal pain or trauma were screened of which 7799 ED visits by COPD patients (corresponding to 4173 unique patients) were identified. - In 1317 (16,5%) of these visits, an opioid was prescribed. **Ergebnisse:** - opioid administration to patients with COPD was significantly associated with the principal composite endpoint (Hazard ratio (HR) = 4.73 (2.94; 7.61), p < 0.01,). - association between opioid use and -- ICU admission (HR = 1.81 (1.23; 2.67), p < 0.01), -- death (HR = 5.09 (2.81; 9.23), p < 0.01), and -- invasive ventilation (HR = 3.41 (1.66; 7.01), p < 0.01), but not with	**Manual Bewertung des Biasrisikos in Interventionsstudien** nicht-vergleichende Studien • prospektive Planung mit Protokoll, in dem Einschlusskriterien und Interventionen sowie interessierende Endpunkte hinterlegt sind: **unklar** (Protokoll erwähnt, jedoch nicht einsehbar) • konsekutiver Patient*innen-einschluss: **ja** • transparentes, nicht-selektives Berichten in Bezug auf	Nicht zitiert Gabe von Opioiden in einem Akutsetting, jedoch nicht aufgrund von Exazerbationen im Speziellen. Einschluss zur Diskussion von Sicherheitsaspekten im akuten Setting

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
10(1):5038. https://www.ncbi.nlm.nih.	- considered as opioids: morphine, hydromorphone, oxycodone, meperidine, fentanyl, and sufentanil **Ausschlusskriterien:** Patients with a decision for palliative care **Studienzeitraum:** 03/2008 - 09/2014 **Ort:** Frankreich, Kanada **primärer Endpunkt:** composite criterion including invasive ventilation and death **Statistik**: To estimate the effect of opioid administration on the composite outcome, a multivariate survival Cox model using an inverse probability of treatment and censoring weight (IPTCW) estimator with a robust estimation of the variance was used. - IPTW = inverse probability of treatment weights - IPCW = inverse probability of censoring weights	-- NIV (HR = 1.06 (0.82; 1.36), p = 0.65). - considered only patients treated by a parenteral route, they presented more composite criteria events than patients not treated with opioids (HR = 5.61 (3.25; 9.67), p < 0.01). The enteral route also remained associated with poor outcomes (HR = 5.95 (2.60; 13.58), p < 0.01). - For the 5267 visits when patients presented dyspnea an association with poor clinical outcomes was observed (HR = 7.08 (3.67; 13.64), p < 0.01). - No association was found when the main complaint was abdominal pain or trauma. **author´s conclusions** After analysis of the data from a large retrospective multicenter cohort, we found that non-palliative short term opioid use in an acute care context was associated with poor clinical outcomes. However, given the observed variety in the use of morphine in our cohort, in various different situations and for different purposes, prospective studies are needed to assess its safety in a well-defined population.	Patient*innencharakteristika, Intervention und Ergebnis: **ja** **Interessenkonflikte/Sponsoring:** This study was funded by the endowment fund “Agir pour les maladies chroniques”, and supported by the E-health and trajectories medicine (MIAI) chairs for integrated care in chronic diseases (Grenoble-Alpes University). J.L.P. and S.B. are supported by a research grant from the French National Research Agency (ANR-12-TECS-0010), in the framework of the “Investissements d’avenir” program (ANR-15 IDEX-02). The funders had no role in study design, data collection, analysis, manuscript writing or decision to submit to publication.	

3.6 Selektiv eingebrachte Literatur:

3.6.1 Auslöser von Exazerbationen

Zitat
Wedzicha, Jadwiga A.; Seemungal, Terence A. R. (2007): COPD exacerbations: defining their cause and prevention. In: Lancet 370 (9589), S. 786–796. DOI: 10.1016/S0140-6736(07)61382-8.
Werchan, Chelsey A.; Steele, Ashton M.; Janssens, Thomas; Millard, Mark W.; Ritz, Thomas (2019): Towards an assessment of perceived COPD exacerbation triggers: Initial development and validation of a questionnaire. In: Respirology 24 (1), S. 48–54. DOI: 10.1111/resp.13368.

3.6.2 Atemphysiotherapie

Zitat	Studiencharakteristika	Studienergebnisse	Aussagesicherheit	Kommentar
Huang H-P, Chen K-H, Tsai C-L, et al. Effects of High-Frequency Chest Wall Oscillation on Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Int J Chron Obstruct Pulmon Dis 2022; 17:2857–69. DOI: 10.2147/COPD.S378642. http://www.ncbi.nlm.nih.gov/pubmed/36381994.	**Fragestellung:** to evaluate the efficacy of high-frequency chest wall oscillation (HFCWO) for sputum expectoration and hospital length of stay in patients with acute exacerbations of chronic obstructive pulmonary disease. **Suchzeitraum:** to March 31, 2022 **Population:** AECOPD **Interventionen:** HFCWO **Vergleich:** - 7 studies: conventional therapies (eg, clapping percussion, postural drainage) in the control group. - 4 studies: mechanical percussion. - one article: about oscillatory positive expiratory pressure (OPEP) - one article used sham HFCWO as the control group **Primäre Endpunkte:** - sputum expectoration - length of hospital stay	Overall included: 13 studies (with 756 patients) HFCWO Compared to other airway clearance techniques: **expectorated sputum volume (alle ATCs gepoolt)**: 6.18 mL (95% CI: 1.71 to 10.64), I² = 87%, 6 studies, n = 407) - HFCWO vs. mechanical vibration (4 studies) 6.31 mL (95% CI: 0.31 to 12.30),I² = 87%, n = 156 - when compared to conventional therapy (1study) 10.59 mL (95% CI: 7.58 to 13.60), n = 84 - when compared to OPEP (1study) 0,87(95% CI: −3.49 to 5.23), n = 69 >> […]The heterogeneity among the subgroups in this meta-analysis was high, so it is possible that the introductiion of various devices into the control group had an impact. Additionally, **only one study was conducted in the included study to measure the patients' baseline sputum volume for comparison**, but this could have an impact on the experiment's outcomes.. **hospital stay**: -4.37 days (95% CI: −7.7; −1.05); I² = 84%, 4 studies, n = 179)	Methodische Qualität AMSTAR II: critically low AMSTAR-Score gesamt: **5/16** (PY: 2; N: 9) AMSTAR-Score kritische Kriterien: **1/7** (N: 5; PY: 1) **Endpunkt: hospital stay** Aussagesicherheit der Evidenz (in Anlehnung an GRADE)**: sehr niedrig** Ausgangsniviau: hoch (RCT) [1]Verzerrungsrisiko (RoB-Bewertung aus Review): -0,5 2) Präzision (kleine Fallzahl, kleine Eventzahl, weite KI): -1 3) Direktheit/Übertragbarkeit auf Fragestellung: ok (auf dt. Versorgungskontext übertragbar??) 4) Konsistenz/Heterogenität der eingeschlossenen Studien auf PICO-Ebene: u.a. verschiedene Kontrollgruppen /Verfahren (3x conventional therapy, 1x mechanical percussion): -1 5) publication bias (nicht erhoben): -1	Nicht zitiert Selektiv eingebracht Deutliche Heterogenität! Sehr schwache methodische Qualität; daher nicht in Evidenzbeschreibung zur nicht-medikamentösen Therapie bei Exazerbation aufgenommen

3.6.3 Körperliche Aktivität bei Exazerbation

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
Lai, Yuin; Cavalheri, Vinicius; Sawyer, Abbey; Hill, Kylie (2024): Exercise training initiated early during	**Fragestellung:** in adults hospitalised with an exacerbation of COPD, does initiating exercise training early during an admission versus not initiating exercise training during admission, change outcomes measured at discharge?	**Primary outcomes at discharge** - exercise capacity: SMD 0.58 (95 % CI 0,32 to 0.83); I² = 31%, 5 RCT, moderate effect, low certainty evidence) - To estimate the magnitude of effect in absolute units, studies that used 6MWD were combined and demonstrated a mean difference of 48 m (95 % CI 16 to 80; I² = 0 %; n = 166) in favour of the experimental group	AMSTAR II: Critically low AMSTAR-Score kritische Kriterien:	Berichtsqualität eingeschränkt

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
hospitalisation in individuals with chronic obstructive pulmonary disease is safe and improves exercise capacity and physical function at hospital discharge: A systematic review and meta-analysis. In: Respir Med 223, S. 107554. DOI: 10.1016/j.rmed.2024.107554 https://pubmed.ncbi.nlm.nih.gov/38307320/	**Suchzeitraum:** 01/2024 **Population:** adults hospitalised with an exacerbation of COPD; 10 studies (423 participants) **Ausschlusskriterien:** intervention: neuromuscular electrical stimulation in isolation **Interventionen:** one group that was prescribed exercise training within 48 h of hospital admission **Vergleich:** one group that received usual care which did not include prescribed exercise training **Primary outcomes: at discharge** - exercise capacity, physical function, adverse events **Additional outcome** - uptake of outpatient pulmonary rehabilitation programs.	- no clear evidence of any difference on the effect on exercise capacity with studies grouped as either resistance exercise alone versus combined aerobic and resistance exercise (Fig. 3) - physical function: SMD -0.54 (95 % CI -0.86 to − 0.22); I^2 = 42%, 4 RCT, moderate effect, low certainty evidence). No observed serious adverse events were reported. **Additional outcome** None of the studies reported uptake of pulmonary rehabilitation following discharge.	5/7 N=2 Keine Liste der ausgeschlossenen Studien Publication Bias nicht adäquat untersucht Evidenzqualität Siehe endpunktspezifische Bewertung des Reviews	

3.7 Gezielte Recherche: Häufigkeit von Exazerbationen

Zitat	Kommentar
Akmatov 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, abgerufen am 02.09.2019.	Auswertungen des Zi von bundesweiten vertragsärztlichen Abrechnungsdaten
Karch, Annika; Vogelmeier, Claus; Welte, Tobias; Bals, Robert; Kauczor, Hans-Ulrich; Biederer, Jürgen et al. (2016): The German COPD cohort COSYCONET. Aims, methods and descriptive analysis of the study population at baseline. In: Respir Med 114, S. 27–37. DOI: 10.1016/j.rmed.2016.03.008.	Cosyconet (German COPD and Systemic Consequences - Comorbidities Network)
Kardos, Peter; Vogelmeier, Claus; Worth, Heinrich; Buhl, Roland; Lossi, Nadine S.; Mailänder, Claudia; Criée, Carl-Peter (2017): A two-year evaluation of the 'real life' impact of COPD on patients in Germany. The DACCORD observational study. In: Respir Med 124, S. 57–64. DOI: 10.1016/j.rmed.2017.02.007.	longitudinale Beobachtungsstudie DACCORD (Die ambulante Versorgung mit langwirksamen Bronchodilatatoren: COPD-Register in Deutschland)
Kassenärztliche Bundesvereinigung (KBV) (2024): Disease-Management-Programm COPD - Qualitätszielerreichung 2022. Online verfügbar unter https://www.kbv.de/media/sp/DMP_COPD_Ergebnisse_QS.pdf, abgerufen am 18.09.2024.	bundesweite Daten zur Qualitätszielerreichung des DMP COPD 2022

3.8 AWMF-Leitlinien

Zitat
Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin (DGAI); Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin (DIVI); Schweizerische Gesellschaft für Intensivmedizin (SGI) (2017): S3-Leitlinie Invasive Beatmung und Einsatz extrakorporaler Verfahren bei akuter respiratorischer Insuffizienz. Registernummer 001-021, Version 2017-12. Online verfügbar unter https://register.awmf.org/de/leitlinien/detail/001-021, abgerufen am 08.08.2019.
Deutsche Gesellschaft für Angiologie - Gesellschaft für Gefäßmedizin (DGA); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2023): S2k-Leitlinie Diagnostik und Therapie der Venenthrombose und Lungenembolie. Registernummer 065 - 002, Version 5.5. Online verfügbar unter https://register.awmf.org/de/leitlinien/detail/065-002, abgerufen am 26.06.2024.
Deutsche Gesellschaft für Neurologie (DGN); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2020): S1-Leitlinie Neurogene Dysphagie. Registernummer 030 - 111, Version 4.0. Online verfügbar unter https://register.awmf.org/de/leitlinien/detail/030-111, zuletzt geprüft am 26.06.2024.
Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin (DGP); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2021): S3 Leitlinie Sauerstoff in der Akuttherapie beim Erwachsenen. Registernummer 020-021, Version 2021-06. Online verfügbar unter https://register.awmf.org/de/leitlinien/detail/020-021, abgerufen am 22.06.2021.
Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin (DGP); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2021): S3-Leitlinie Behandlung von erwachsenen Patienten mit ambulant erworbener Pneumonie. Registernummer 020-020, Version 4.0. Online verfügbar unter https://register.awmf.org/de/leitlinien/detail/020-020, abgerufen am 27.06.2024.
Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin (DGP); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2024): S3-Leitlinie Epidemiologie, Diagnostik und Therapie erwachsener Patienten mit nosokomialer Pneumonie. Registernummer 020 - 013, Version 3.0. Online verfügbar unter https://register.awmf.org/de/leitlinien/detail/020-013, abgerufen am 26.06.2024.
Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin (DGP); Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin (DGAI); Deutsche Gesellschaft für Chirurgie (DGCH) (2023): S2k-Leitlinie Nichtinvasive Beatmung als Therapie der akuten respiratorischen Insuffizienz. Registernummer 020-004. Version 2024-01. Online verfügbar unter https://register.awmf.org/de/leitlinien/detail/020-004, abgerufen am 21.03.2024.
Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin (DGP); Deutsche Krebsgesellschaft (DKG); Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF) (2024): S3-Leitlinie Prävention, Diagnostik, Therapie und Nachsorge des Lungenkarzinoms - Living Guideline. Registernummer 020 - 007OL, Version 3.0. Online verfügbar unter https://register.awmf.org/de/leitlinien/detail/020-007OL, abgerufen am 26.06.2024.
Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin (DGP) et al.: S2k-Leitlinie Fachärztliche Diagnostik, Prävention und Therapie der chronisch obstruktiven Lungenerkrankung (https://register.awmf.org/de/leitlinien/detail/020-006); aktuell in Erarbeitung, Stand 09/2024.

3.9 Weitere Literatur

Zitat	Charakteristika des SR	Ergebnisse	Aussagesicherheit	Kommentar
Ni H. Magnesium sulfate for acute exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2022; 5(5):CD013506. dx.doi.org/10.1002/14651858.CD013506.pub2. https://www.ncbi.nlm.nih.gov/pubmed/35616126.	**Fragestellung**: To assess the effects of magnesium sulfate for acute exacerbations of chronic obstructive pulmonary disease in adults. **Suchzeitraum:** 08/2021 **Population:** adults with COPD exacerbations **Intervention:** magnesium sulfate (i.v. or nebulised) **Control:** placebo or ipratropium bromide (1 study) **Body of Evidence:** 11 RCTs (10 double-blind and 1 single-blind) with a total 762 participants	**Intravenous magnesium sulfate versus placebo** hospital admission - Fewer people may require hospital admission with magnesium infusion compared to placebo - OR 0.45 (95% CI 0.23; 0.88); number needed to treat for an additional beneficial outcome (NNTB) = 7; 3 studies, n =170 ; **low-certainty evidence**). requirement for non-invasive ventilation - Intravenous magnesium may result in little to no difference in the requirement for non-invasive ventilation OR 0.74 (95% CI 0.31; 1.75); **very low-certainty evidence**). - There were no reported cases of endotracheal intubation (2 studies, 107 participants) or serious adverse events (1 study, 77 participants) in either group. length of hospital stay Magnesium infusion may reduce the length of hospital stay by a mean difference (MD) of 2.7 days (95% CI 4.73 days to 0.66 days; 2 studies, 54 participants; **low-certainty evidence**) and improve dyspnoea score by a standardised mean difference of -1.40 (95% CI -1.83 to -0.96; 2 studies, 101 participants; **low-certainty evidence**). lung function or oxygen saturation We were uncertain about the effect of magnesium infusion on improving lung function or oxygen saturation. AEs For all adverse events, the Peto OR was 0.14 (95% CI 0.02 to 1.00; 102 participants); however, the event rate was too low to reach a robust conclusion. **Nebulised magnesium sulfate versus placebo** hospital admission Magnesium inhalation may have little to no impact on hospital admission - OR 0.77, 95% CI 0.21 to 2.82; **very low-certainty evidence**) need for ventilatory support (NIV or mechanical ventilation)	AMSTAR 2: Qualität des Re-views: - high AMSTAR-Score kritische Kriterien: - 7/7 Evidenzqualität siehe endpunktspezifische GRADE- Bewertung des Reviews	Nicht zitiert; zu speziell für NVL?

Zitat	Charakteristika des SR	Ergebnisse	Aussagesicherheit	Kommentar
		Magnesium inhalation may have little to no impact on need for ventilatory support - OR 0.33, 95% CI 0.01 to 8.20; **very low-certainty evidence**). ICU admissions It may result in fewer ICU admissions compared to placebo - OR 0.39 (95% CI 0.15; 1.00); **very lowcertainty evidence**) dyspnoea It may result in fewer improvement in dyspnoea - MD -14.37, 95% CI -26.00 to -2.74; 1 study, 20 participants; **very low-certainty evidence**). SAEs There were no serious adverse events reported in either group. There was one reported death in the placebo arm in one trial, but the number of participants was too small for a conclusion. There was limited evidence about the effect of magnesium inhalation on length of hospital stay, lung function outcomes or oxygen saturation. Included studies did not report adverse events. **Magnesium sulfate vs. ipratropium bromide** - n=1 study with 124 participants assessed nebulised magnesium sulfate plus intravenous magnesium infusion vs. nebulised ipratropium plus intravenous normal saline. - little to no difference between these groups in terms of hospital admission (OR 1.62, 95% CI 0.78 to 3.37), endotracheal intubation (OR 1.69, 95% CI 0.61 to 4.71) and length of hospital stay (MD 1.10 days, 95% CI -0.22 to 2.42), **all with very low-certainty evidence.** There were no data available for non-invasive ventilation, ICU admission and serious adverse events. Adverse events were not reported		

4 Evidenztabellen Operative und interventionelle Verfahren

4.1 Cochrane Reviews

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
van Agteren JE, Carson KV, Tiong LU, et al. Lung volume reduction surgery for diffuse emphysema. Cochrane Database Syst Rev 2016; 10:CD001001. DOI: 10.1002/14651858.CD001001.pub3. http://www.ncbi.nlm.nih.gov/pubmed/27739074.	**Fragestellung:** to gather all available evidence from randomised controlled trials comparing the effectiveness of lung volume reduction surgery (LVRS) versus non surgical standard therapy in improving health outcomes for patients with severe diffuse emphysema. **Secondary objectives:** - determining which subgroup of patients benefit from LVRS and for which patients LVRS is contraindicated - establish the postoperative complications of LVRS and its morbidity and mortality - determine which surgical approaches for LVRS are most effective - calculate the cost-effectiveness of LVRS. **Suchzeitraum:** 04/2016 **Population:** participants with diffuse emphysema **Ausschlusskriterien:** - excluded studies that investigated giant or bullous emphysema **Interventionen**: lung volume reduction surgery (LVRS) **Vergleich:** non-surgical standard therapy **eingeschlossene Studien:** 11 RCT (1760 participants)	Participants completed a mandatory course of pulmonary rehabilitation/physical training before the procedure commenced (in all but 1 study) **Early mortality (90 days)** - 77/1000 (LVRS) vs. 13/1000 (control); OR 6.16 (95%CI 3.22; 11.79);I²=0%, 5 RCT, n=1489; GRADE: **moderate** **Long-term mortality (> 36 months)** - 478/1000 (LVRS) vs. 547/1000 (control); OR 0.76 (95%CI 0.61; 0.95); I²=0%; 2 RCT, n=1280; GRADE: **moderate** **Change in total scores SGRQ (end of follow-up)** - Mean SGRQ score in the LVRS group was -13.78 units lower (95%CI -15.75 to -11.78); I²=0% , 2 RCT, n=1326, GRADE: **moderate** **Walking distance (end of follow-up)** - Standardised mean walking distance in the LVRS group was 0.70 standard deviations higher (95%CI 0.42 to 0.98); I²=51%; 5 RCT, n=215, GRADE: **low** **Sicherheit** Adverse events were more common with LVRS than with control, specifically the occurrence of (persistent) air leaks, pulmonary morbidity (e.g. pneumonia) and cardiovascular morbidity. <u>high risk of death</u> Participants identified post hoc as being at high risk of death from surgery were those with - particularly impaired lung function - poor diffusing capacity and/or - homogenous emphysema. <u>most favourable outcomes</u> Participants with - upper lobe-predominant emphysema and - low baseline exercise capacity showed the most favourable outcomes related to mortality > no significant differences in early mortality between participants treated with LVRS and those in the control group: OR 0.87, 95% CI 0.23; 3.29; 1 RCT, n=290, **kein GRADE** durchgeführt	Qualität des Reviews: low	Nicht zitiert; Detaillierte Darstellung in S2k COPD Kritisches Kriterium: Protokoll nicht auffindbar/nicht zur Verfügung in Cochrane library > Erster Review wurde 1999 durchgeführt; Vorhandensein des Protokolls ggf. dadurch beeinträchtigt, daher Einschluss trotz AMSTAR-2: low > Unterschiede zwischen Protokoll und Review im CR sind aufgeführt --> Annahme: Methodenteil des Reviews entspricht dem Protokoll

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
		> significantly lower mortality at the end of follow-up for LVRS compared with control: OR 0.45, 95%CI 0.26; 0.78; 1 RCT, n= 290, **kein GRADE** durchgeführt		
van Agteren JE, Hnin K, Grosser D, et al. Bronchoscopic lung volume reduction procedures for chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2017; 2:CD012158. DOI: 10.1002/14651858.CD012158.pub2. http://www.ncbi.nlm.nih.gov/pubmed/28230230.	**Fragestellung**:To assess the effects of BLVR on the short- and long-term health outcomes in participants with moderate to severe COPD and determine the effectiveness and cost-effectiveness of each individual technique. **Suchzeitraum:** until 07 December 2016 **Population:** participants with moderate to severe COPD **Interventionen:** - Endobronchial valves + optimal medical care vs. optimal medical care - Intrabronchial valves + optimal medical care vs. sham bronchoscopy + optimal medical care - Vapour ablation + optimal medical care vs. optimal medical care - Endobronchial coils+ optimal medical care vs. optimal medical care - AeriSeal + optimal medical care vs. optimal medical care - Airway bypass stents + optimal medical care vs. sham bronchoscopy + optimal medical care **eingeschlossene Studien:** 14 RCTs; n=1979 participants	**· Endobronchial valves + optimal medical care vs. optimal medical care** - SGRQ -7.29 units fewer (95% CI -11.12 to -3.45 units), I²=67% ,5 RCTs, n=695, **GRADE: low** - Mortality (at end of follow- up): 35/1000 vs. 30/1000; OR 1.07 (95% CI 0.47;2.43), I²=0% , 5 RCTs, n=703, **GRADE: moderate** - Adverse events (at end of follow- up): 387/1000 vs. 97/1000, OR 5.85 (95% CI 2.16;15.84), I²=63% , 3 RCTs, n=482, **GRADE: high** - 6MWD: 38.12 meters more (8.68 more to 67.56 more) for intervention, I²=78% , 4 RCTs, n=379, **GRADE: low** --> Participant selection plays an important role as absence of collateral ventilation was associated with superior clinically significant improvements in health outcomes (Analysis 3.6.; 3.9) **· Intrabronchial valves + optimal medical care vs. sham bronchoscopy + optimal medical care** bilateral: - SGRQ scores: no significant differences: MD 2.64 units (95% CI -0.28; 5.56 units), I²=28%, 2 RCTs, n=350, **GRADE: high** - Mortality (at end of follow- up): 28/1000 vs. 6/1000; OR 4.95 (95% CI 0.85; 28.94); I²=0%, 2 RCTs, n=350; **GRADE: moderate** - Adverse events: 143/1000 vs. 47/1000; OR 3.41 (95% CI 1.48; 7.84), I²=0% , 2 RCTs, n=350; **GRADE: high** - 6MWD: 19.54 meters less (-37.11 less to -1.98 less) for intervention; I²=0% , 2 RCTs, n=316, **GRADE: moderate** -->The lack of functional benefits may be explained by the procedural strategy used, as another study (22 participants) compared unilateral versus partial bilateral placement, finding significant improvements in FEV1 and SGRQ when using the unilateral approach. **· Vapour ablation + optimal medical care vs. optimal medical care** - SGRQ: 9.70 units fewer favouring vapour ablation over control (95% CI -15.62; -3.78); 1 RCT, n=65; **GRADE: low** - Mortality (at end of follow- up): 44/1000 vs. 0/1000; OR 2.82 (95% CI 0.13; 61.06); 1 RCT, n=69, **GRADE: low** - Adverse events (at end of follow- up): 355/1000 vs. 125/1000; OR 3.86 (95% CI 1.00;14.97), 1 RCT, n=69, **GRADE: moderate**	Methodische Qualität des Reviews: moderate	Nicht zitiert; Detaillierte Darstellung in S2k COPD

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
		- 6MWD: The absolute between group difference 6MWD in meters at end of follow-up was 30.5 m (95% CI -1.5 to 62.4), 1 RCT, n=69, **GRADE: low** **· AeriSeal + optimal medical care vs. optimal medical care** - quality of life: =higher SGRQ -12 units (IQR -22 to -5 units) vs. -3 units (IQR -5 to 1 units), 1 RCT, n=34 participants; **GRADE: low** - Mortality(at end of follow- up): 21/1000 vs. 0/1000; OR 2.90 (95% CI 0.14;62.15), 1 RCT, n=95, **GRADE: low** - Adverse events: 443/1000 vs. 176 vs. 1000; OR 3.71 (95% CI 1.34;10.24), 1 RCT, n=95; **GRADE: moderate** -- Most common respiratory events: pneumonia, COPD exacerbations, postacute inflammatory response and pneumothorax. The postprocedure adverse event rate requiring hospitalization was significantly higher in the treatment condition (44%) compared to the control (18%) condition - 6MWD: + 31m (IQR 0 - 41.3m) vs. -22m (IQR -41.3 - 9.3m), 1 RCT, n=34, **GRADE: low** **· Airway bypass stents + optimal medical care vs. sham bronchoscopy + optimal medical care** - SGRQ -2.00 units fewer (95% CI -5.58 to 1.58 units),1 RCT, n= 350, **GRADE: high** - Mortality(at end of follow- up): 29/1000 vs. 37/1000; OR 0.76 (95% CI 0.21; 2.77), 1 RCT, n=350, **GRADE: moderate** - Adverse events: 144/1000 vs. 112/1000; OR 1.33 (95% CI 0.65; 2.73), 1 RCT, n=315, **GRADE: moderate** -- SAEs were reported in 3.4% (n = 7) participants in the treatment group compared to none in the sham control group. -- Pneumothorax (3 in treatment versus 1 in control), haemoptysis (1 in treatment versus 0 in control) and COPD exacerbations (33 in treatment versus 9 in control) were more frequent in treatment versus sham control. - 6 MWD: -16m fewer (95% CI -39.17; 7.17m) for intervention, 1 RCT, n=350, **GRADE: moderate** **· Endobronchial coils+ optimal medical care vs. optimal medical care** - SGRQ -9.14 units fewer (95% CI -11.59 to -6.70 units), I^2=0% , 3 RCTs, n=461, **GRADE: moderate** - Mortality(at end of follow- up): 70/1000 vs. 48/1000; OR 1.49 (95% CI 0.67; 3.29), I^2=0% , 3 RCTs, n=461, GRADE: moderate - Adverse events: 391/1000 vs. 230/1000; OR 2.14 (95% CI 1.41; 3.23), I^2=0% , 3 RCTs, n=461, **GRADE: high** - 6MWD: 30.85 meters more (-1.05 to 62.76 more) for intervention, I^2=69%, 3 RCTs, n=461, **GRADE: low**		

4.2 Prärehabilitation

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
Li X. Impact of preoperative exercise therapy on surgical outcomes in lung cancer patients with or without COPD: A systematic review and meta-analysis. Cancer Manag Res 2019; 11:1765–77. https://www.ncbi.nlm.nih.gov/pubmed/30858729.	**Fragestellung:** This meta-analysis aimed to demonstrate the impact of preoperative exercise therapy on surgical outcomes in patients with lung cancer and COPD. Pulmonary function and muscle capacity were investigated to explore their potential links with outcome improvements after exercise. **Suchzeitraum:** 06/2017 **Population:** lung cancer patients with or without COPD **Einschlusskriterien:** After preoperative interventions and basic therapy, patients received video-assisted thoracoscopic surgery or open thoracotomy, as scheduled. Types of surgery included wedge resection, segmentectomy, lobectomy, and pneumonectomy. Patients received similar clinical monitoring after surgery, and PCs were clearly recorded. **Interventionen:** preoperative exercise training - varied in terms of exercise type, frequency, and intensity, ranging from 3x/day for 1 week to 5x/week fo 4 weeks - 2 types of investigation after exercise were involved in the included studies: muscle capacity and pulmonary function analysis - Exercise programs contained aerobic exercise, resistance training, inspiratory muscle training, and education. In some studies, patients were advised to undertake a warm-up before exercise (after a 5-minute warm-up period, 50% of peak work rate was achieved). **Vergleich**: usual care with no exercise training **eingeschlossene Studien:** n= 7 (RCTs + prospective trials)	>> Es wurden 2 Subgruppenanalysen für Pat. mit COPD durchgeführt: **postoperative pulmonary complications of COPD patients** - 9/55 (16.4%) vs. 27/92 (29.3%); OR 0.44 (0.18–1.08); I²=0%; 3 studies, n=147, **GRADE: Moderate** **Length of hospital stay in patients with COPD** - MD –6.73 (–9.88, –3.58), I²= 14%, 2 studies, n=99; **GRADE: very low** >> Ergebnisse für Metaanalysen mit gemischter Population (Pat. mit und ohne COPD): **Risk of developing postoperative pulmonary complicatio**n - OR 0.44 (0.27, 0.71); I²=0% , 6 studies, n=382, **GRADE: high** **incidence of postoperative pneumonia** - OR 0.0.47 (0.24, 0.95); I²=0% , 5 studies, n=228, **GRADE: low** **postoperative length of hospital stay** - MD –4.23 (–6.14, –2.32); I²=66%, 5 studies; n=231; **GRADE: low** **duration of chest drainage** - MD -3.28 lower (-5.21;-1.36), I²=0%, 2 studies, n=38, **GRADE: moderate**	**Qualität des Reviews:** - critically low AMSTAR-Score kritische Kriterien: 4/7 PY=2 N=1 <u>Evidenzqualität</u> Siehe endpunktspezifische Bewertung des Reviews	Vertauenswürdigkeit diskutieren; methodische Qualität im Vergleich zum Cochrane Review (Cavalheri) beachten Heterogenität in einzelnen Analysen errechnet, jedoch unklarer Umgang (teilweise fixed effects Modell trotz Heterogenität): + keine zusätzliche Untersuchung der Ursachen Direktheit: Subgruppe mit Patienten mit COPD + LungenCa; Operation ist Therapie hinsichtlich Krebserkrankung; nicht COPD: dennoch Ergebnisse übertragbar? Differenzen in den dargestellten Ergebnisse (Text und Forest plots differieren zur Summary of Findings Tabelle: insbesondere für Darstellung der Resultate für die gesamte (gemischte) Population) --> Vertrauenswürdigkeit?

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
Cavalheri V, Granger C. Preoperative exercise training for patients with non-small cell lung cancer. Cochrane Database Syst Rev 2017; 6:CD012020. DOI: 10.1002/14651858.CD012020.pub2. http://www.ncbi.nlm.nih.gov/pubmed/28589547.	**Fragestellung:** The primary aims of this study were to determine the effect of preoperative exercise training on postoperative outcomes, such as risk of developing a postoperative pulmonary complication, and postoperative duration of intercostal catheter use in adults scheduled to undergo lung resection for NSCLC. The secondary aims of this study were to determine the effect of preoperative exercise training on length of hospital stay, fatigue, dyspnoea, exercise capacity, lung function, and postoperative mortality. **Suchzeitraum:** 28/11/2016 **Population:** patients with non-small cell lung cancer (NSCLC) with or without COPD **Einschlusskriterien**: - lung resection of any extent, (wedge resection, segmentectomy, lobectomy, bilobectomy, or pneumonectomy) - also included studies with patients who underwent both VATS and open thoracotomy - intervention group received a minimum of seven exercise sessions completed over a minimum of one week in the preoperative setting **Interventionen:** Exercise training (includes aerobic training, resistance training, or respiratory muscle training) **Vergleich:** usual care with no exercise training **eingeschlossene Studien:** n=5 RCT (167 participants)	>> Ergebnisse für Metaanalysen mit gemischter Population (Pat. mit und ohne COPD): **Number of patients who developed postoperative pulmonary complications** - RR 0.33 (0.17 to 0.61); I² =0% , 4 RCTs, n=158, **GRADE: low** - It is expected that one less person will develop a postoperative pulmonary complication for every four participants receiving preoperative exercise training rather than usual care (RD -0.25, 95% CI -0.37, -0.13; NNTB = 4). **Number of days patients needed an intercostal catheter** - intervention group (IG): - 3.33 fewer days (95% CI -5.35; -1.3) - I² =0%, 2 RCTs, n=38; **GRADE: low** **Postoperative length of hospital stay** - IG: - 4.34 fewer days (95% CI -5.65; -3.03) - I² =0%, 4 RCTs, n=158; **GRADE: low** **Post-intervention exercise capacity assessed with: 6- minute walk distance (6MWD)** - IG: 18.23 metres more (95% CI 8.5; 27.96) - I² =0%, 2 RCTs, n=81, **GRADE: low** >> Two studies specifically included participants with NSCLC and a diagnosis of chronic obstructive pulmonary disease (COPD; Benzo 2011; Stefanelli 2013). <u>Einzelergebnisse Benzo 2011</u> **Number of patients who developed a postoperative pulmonary complicatio**n: Intervention group (IG): 3 of 9 (33%) Control Group (CG): 5 of 8 (63%); p = 0.23 (between-group) **Number of days patients needed a chest tub**e: IG: 4.3 ± 2.1 days CG: 8.8 ± 5.3 days; p = 0.03 (between-group) **Postoperative length of hospital stay:** IG: 6.3 ± 3.0 days CG: 11.0 ± 6.3 days; p = 0.058 (between-group) <u>Einzelergebnisse Stefanelli 2013</u> **Exercise capacity:** Peak rate of oxygen uptake (VO2peak) Preoperative measurements: baseline and post-intervention: IG (n=20): 14.9 ± 2.3 ml/kg/min to 17.8 ± 2.1 ml/kg/min CG (n=20): 14.8 ± 1.4 ml/kg/min to 14.5 ± 1.2 ml/kg/min; p < 0.001 (between-group)	**Qualität des Reviews:** - moderate **Risk of bias** <u>Benzo 2011:</u> · Random sequence generation (selection bias): **unclear** · Allocation concealment (selection bias): **unclear** · Blinding of participants and personnel (performance bias): **high** · Blinding of outcome assessment (detection bias): **low** · Incomplete outcome data (attrition bias): **low** · Selective reporting (reporting bias): **high** · Other bias: **high** <u>Stefanelli 2013:</u> · Random sequence generation (selection bias): **unclear** · Allocation concealment (selection bias): **unclear** · Blinding of participants and personnel (performance bias): **high** · Blinding of outcome assessment (detection bias): **unclear** · Incomplete outcome data (attrition bias): **unclear** · Selective reporting (reporting bias): **unclear** · Other bias: **high**	Direktheit diskutieren: Übertragbarkeit von Ergebnissen aus Analysen, welche Studien mit Patienten auch ohne COPD eingeschlossen haben?

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
		Lung function: FEV1; % predicted Preoperative measurements: baseline and post-intervention: IG (n=20): 57.4 ± 19.1% to 59.8 ± 19.2% CG (n=20): 57.6 ± 16.9% to 57.5 ± 17.0%; p > 0.05 (between-group)	Evidenzqualität Siehe endpunktspezifische Bewertung des Reviews	
Bradley A. Pulmonary rehabilitation programme for patients undergoing curative lung cancer surgery. Eur J Cardiothorac Surg 2013; 44(4):e266-71. https://www.ncbi.nlm.nih.gov/pubmed/23959742.	**Studiendesign:** prospective cohort study **Population:** any patient who was considered fit for curative lung cancer surgery - Interventionsgruppe: 21/58 (36%) COPD - Vergleichsgruppe: 70/305 (23%) COPD **Intervention:** multistranded pragmatic rehabilitation programme pre- and post-surgery - Education and self-management - Exercise training - Smoking cessation - Nutritional intervention >> Surgery was not delayed for the purposes of the programme - Postoperatively: Between 4 and 6 weeks post-hospital discharge, the intervention group rejoined the rehabilitation programme **Vergleich:** standard care **In-hospital journey** - All operations were performed through a thoracotomy incision - Both groups were managed daily by a specialized thoracic team, and all received a daily physiotherapy programme from the first postoperative day (sitting out of bed, early mobilization, deep breathing exercises, assisted coughing augmented by nebulizers and humidified oxygen) **Follow-up intervention group**: 6-min walk test (6MWT), weight, urine cotinine and exhaled carbon monoxide levels were measured, prerehabilitation, post-rehabilitation, presurgery, 4 weeks post-surgery and then at 6 months.	**Baseline-Patientencharakteristika:** - mehr COPD-Pat. in der Interventionsgruppe (36% vs. 23%) - higher incidence of a confirmed pathology of cancer in the intervention group (97% vs. 87%), but similar patterns for the type of surgical resection and postoperative analgesia - keine anderen relevanten Unterschiede hinsichtlich Alter, BMI, FEV1, Smoking history, Geschlecht **6MWT** - significant improvement from pre- to postrehabilitation (presurgery): of 20 m (n = 30, range −73 to 195, p = 0.001). - In contrast, there was a drop of 41 m in the postoperative 6MWT compared with preoperative (post-rehabilitation) (n = 15, range −240 to 58, p = 0.005). **FEV1** - improvement from pre- to post-rehabilitation (presurgery): of 0.66 l (n = 43, range −1.85 to 1.11, p = 0.009). **smoking cessation** Of the 13 current smoking patients in the intervention group at baseline, 7 agreed to be referred to smoking cessation sessions and 6 of these patients stopped smoking, as confirmed by biochemical testing. **Nutrition** Nine (16%) patients were identified as being at risk of malnourishmen due to recent weight loss, although none had a BMI of <20. There were too little data to comment on the efficacy of the nutritional supplementation. **Postoperative pulmonary complication (PPC)** - intervention group experienced fewer PPC's (9% vs 16%, p = 0.21) **Readmissions** - intervention group: fewer readmissions (5% vs 14%, respectively, p = 0.12).	NOS RoB **Selektion der Studienteilnehmer*innen** 1) Ist die exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition? **Ja** 2) Ist die nicht-exponierte Kohorte repräsentativ, wurde sie adäquat ausgewählt? **Ja** 3) Erfolgte eine valide Erfassung der Exposition? **Ja** 4) Ist es wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war? **NA** **Vergleichbarkeit** 1) Ist die Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben? **Ja** **Endpunkterfassung** 1) Erfolgte eine valide Erfassung der Endpunkte? **Nein** 2) Konnte in der Beobachtungszeit der Endpunkt überhaupt auftreten? **NA** 3) Wurden fehlende Da-	Interventionsgruppe: 1/3 COPD Vergleichsgruppe: 1/4 COPD --> Direktheit? - deutlich kleinere Interventionsgruppe om Vergleich zur Kontrollgruppe (58 vs. 305 Teilnehmende) - Both groups were matched for age, lung function, comorbidity and type of surgery

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
	Matching: Patients from 3 of 12 referring hospitals were invited to be in the intervention group and join an existing COPD PRP. Patients from the remaining referring hospitals were in the control non-intervention group of the study.	**Factors for predicting PPC** A multivariate analysis identified COPD (P = 0.007) and smoking (P = 0.049) as significant factors for predicting PPC. Patients with COPD (OR 2.88, 95% CI 1.56–5.31) and smokers (OR = 1.90, 95% CI = 1.00–3.59) were at a higher risk of developing a PPC. After adjusting for COPD and smoking, having the intervention tended to reduce the risk of developing a PPC (OR = 0.40, 95% CI 0.13–1.01, P = 0.07).	ten adäquat berücksichtigt? **Ja**	
Saito H. Impact of pulmonary rehabilitation on postoperative complications in patients with lung cancer and chronic obstructive pulmonary disease. Thorac Cancer 2017; 8(5):451–60. https://www.ncbi.nlm.nih.gov/pubmed/28696575 .	**Ziel der Studie:** to assess the contribution of preoperative pulmonary rehabilitation (PR) for reducing the incidence of postoperative pulmonary complications in non-small cell lung cancer (NSCLC) patients with chronic obstructive pulmonary disease (COPD). **Studiendesign:** retrospective analysis (medical records of 589 consecutive patients with NSCLC who underwent pulmonary lobectomy) **Population:** patients with COPD (n=116 initial) - None of the patients had received preoperative chemotherapy or radiation **surgical procedure**: videoassisted thoracoscopic surgery (VATS) or open thoracotomy **Intervention:** preoperative PR - breathing and coughing techniques and peripheral muscle exercise training including a cycle ergometer for 2-4 weeks (five days a week) under physiotherapist supervision - patients themselves continued the training involving breathing and coughing techniques until the morning of the day of surgery **postoperativ:** - PR started as early as postoperative day 1. (diaphragmatic breathing exercises, peripheral circulation exercises, aerosol therapy with bronchodilators, and exercises for chest expansion and shoulder girdle mobilization) **Vergleich:** keine PR	Propensity score analysis generated well-matched pairs of 31 patients **Baseline-Patientencharakteristika:** - no significant differences in observed preoperative variables such as age, gender, height, Brinkman Index, and all predicted postoperative pulmonary function parameters between the groups after matching - duration of PR: 18.7 ± 12.7 days <u>Effektivität:</u> **Preoperative pulmonary function** - significantly improved after PR (VC 5.3%, FEV1 5.5%, both p < 0.05) **Postoperative pulmonary function** (performed at 1 month + 6 months) - recovery rate of VC one month after surgery was not significantly different between the groups - recovery rate of FEV1 one month after surgery was significantly better in the PR group (101.6%; p < 0.001) compared to the non-PR group (93.9%). - no significant difference between the groups regarding the recovery rate of postoperative VC/FEV1 at six months. **independent factors related to postoperative pulmonary complications after pulmonary lobectomy** (logistic regression analysis; p < 0.05): - age: OR 1.53 (95% CI 1.27–78.4) - predicted postoperative FEV1 (<1500 mL): OR 7.10 (95% CI 1.33–439.2) - predicted postoperative % FEV1 (≤60%): OR 6.80 (95% CI 1.425–235.0) - no preoperative pulmonary rehabilitation: OR 6.42 (95% CI 1.69–589.1)	NOS RoB **Selektion der Studienteilnehmer*innen** 1) Ist die exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition? **Ja** 2) Ist die nicht-exponierte Kohorte repräsentativ, wurde sie adäquat ausgewählt? **Ja** 3) Erfolgte eine valide Erfassung der Exposition? **Ja** 4) Ist es wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war? **NA** **Vergleichbarkeit** 1) Ist die Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben? **Ja** **Endpunkterfassung** 1) Erfolgte eine valide Erfassung der Endpunkte? **Ja** 2) Konnte in der Beobachtungszeit der Endpunkt überhaupt auftreten? **NA** 3) Wurden fehlende Daten adäquat berücksichtigt? **Nein**	Übertragbarkeit (chrirugische Prozedur?, Krebserkrankung?) auf die Beantwortung unserer Fragestellung sehr breite Konfidenzintervalle in der logistischen Regressionsanalyse

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	Follow-up: After discharge, patients were followed-up clinically, and spirometry was performed one and six months after surgery. **Ausschlusskriterien:** - lost to follow-up - with complications that prevented postoperative pulmonary function testing - Cases of sublobar resection, pneumonectomy, or concomitant resection with the thoracic chest wall . **Studienzeitraum:** 09/2005 - 01/2016 Japan **Matching:** propensity score matching method			
Mujovic N. Influence of Pulmonary Rehabilitation on Lung Function Changes After the Lung Resection for Primary Lung Cancer in Patients with Chronic Obstructive Pulmonary Disease. Aging Dis 2015; 6(6):466–77. https://www.ncbi.nlm.nih.gov/pubmed/26618048 .	**Ziel der Studie**: to assess the influence of physiotherapy program on postoperative lung function and effort tolerance in lung cancer patients with chronic obstructive pulmonary disease (COPD) that are undergoing lobectomy or pneumonectomy **Studiendesign:** prospective study **Population:** COPD patients who underwent lung resection for primary non small-cell lung cancer **Intervention:** preoperative Physiotherapy - intravenous bronchodilators (Theophylline derivatives 12.5mg or 25mg twice a day, without corticosteroids; - pulmonary physiotherapy - general physiotherapy - patient education **Vergleich**: no physiotherapy - iv bronchodilators (Theophylline derivatives 12.5mg or 25mg 2x/ day), as well as bronchodilator aerosols (Salbutamol) in concentration of 0.5ml/3ml in 0.9% NaCl solution Serbien	relevante Unterschiede der Baseline-Charakteristika hinsichtlich Komorbiditäten; COPD-Schweregrad, verschiedene LuFu-Parameter **Total complications** (Interventionsgruppe (IG) vs. Kontrollgruppe (CG)) IG: 20/56 (26%) ; CG: 21/47 (45%) **pulmonary complications** IG: 17/56 (30%); CG: 20/47 (43%) **Comparison between IG + CG in relation to lung function changes after the lung resection:** Although the preoperative FEV1 and VC were significantly lower in the Group A, both parameters reached similar values after performed physiotherapy. No significant difference existed between the groups in relation to the postoperative loss either in FEV1. Although the postoperative loss in the small airways function followed the similar trend in both groups, the small airways function in the Group B was evidently better postoperatively.	NOS RoB **Selektion der Studienteilnehmer*innen** 1) Ist die exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition? **Ja** 2) Ist die nicht-exponierte Kohorte repräsentativ, wurde sie adäquat ausgewählt? **Unklar** 3) Erfolgte eine valide Erfassung der Exposition? **Ja** 4) Ist es wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war? **NA** **Vergleichbarkeit** 1) Ist die Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben? **Nein** **Endpunkterfassung**	>> didn't take into account an influence of other factors on incidence of pulmonary complications after surgery - "keine Randomisierung"; kein adäquates Matching der Gruppen - aufgrund technischer Gründe erfolgte keine direkte Messung von TLC, FRC und RV - keine adäquate Darstellung der aufgetretenen Komplikationen >> methodische Qualität beachten (vertrauenswürdig?)

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
			1) Erfolgte eine valide Erfassung der Endpunkte? **Unklar** 2) Konnte in der Beobachtungszeit der Endpunkt überhaupt auftreten? **NA** 3) Wurden fehlende Daten adäquat berücksichtigt? **Unklar**	
Zhou K. Comprehensive Pulmonary Rehabilitation is an Effective Way for Better Postoperative Outcomes in Surgical Lung Cancer Patients with Risk Factors: A Propensity Score-Matched Retrospective Cohort Study. Cancer Manag Res 2020; 12:8903–12. https://www.ncbi.nlm.nih.gov/pubmed/33061586.	**Ziel der Studie:** To investigate the effectiveness and cost minimization of comprehensive pulmonary rehabilitation (CPR) in lung cancer patients who underwent surgery. **Studiendesign:** A Propensity Score-Matched Retrospective Cohort Study **Population:** surgical lung cancer patients with/without COPD **Intervention:** comprehensive pulmonary rehabilitation (CPR) - inspiratory muscle training (IMT), aerobic endurance training, and pharmacotherapy. **Vergleich**: Without CPR **relevante Einschlusskriterien:** - Patients enrolled in the rehabilitation program need to meet at least one of the following criterion: age > 70 yr, a ≥ 20 pack-year smoking history, chronic obstructive pulmonary disease (COPD) or airway hyperresponsiveness, and postoperative predicted percentage forced expiratory volume in 1 s (ppoFEV1%) < 60%. - patients underwent video-assisted thoracoscopic surgery (VATS) or thoracotomy. **Studienzeitraum:** 01/01/2012 - 31/12/2017 China	**Baseline-Patientencharakteristika:** - ratio of matched patients = 1:4 - COPD-Pat. in der Interventionsgruppe (IG): 52/205 (25.4%) - COPD-Patienten in der Kontrollgruppe (CG): 194/820 (23.7%) >> keine relevanten Unterschiede hinsichtlich Alter, Geschlecht, BMI, LuFu-Parametern, Rauchstatus, Komorbiditäten;Tumorklassifikationen; operativem Eingriff **length of postoperative hospital stay** - in the IG lower vs CG: median 5 days (4–7) vs 7 days (4–8), p < 0.001 **postoperative pulmonary complications** (PPCs; IG vs. CG) - overall incidence of PPC: 26.8% vs 36.7%, p = 0.008 - incidence of pneumonia: 10.7% vs 16.8%, p = 0.035 - incidence of atelectasis: 8.8% vs 14.0%, p = 0.046 >> keine signifikanten Unterschiede zwischen den Gruppen hinsichtlich - Air leak > 5 d; Pulmonary embolism; ARDS; Ventilator support >48 h; Empyema; Bronchopleural fistula; Reintubation; Unexpected admission to ICU **factors related to postoperative pulmonary complications** Multivariable analysis showed that - CPR intervention: OR = 0.655, 95% CI: 0.430–0.865, p = 0.006 - age ≥70 yr: OR = 1.919, 95% CI: 1.342–2.744, p < 0.001 - smoking: OR = 2.048, 95% CI: 1.552–2.704, p < 0.001 and - COPD: OR= 1.158, 95% CI: 1.160–2.152, p = 0.004 were related to PPCs.	NOS RoB **Selektion der Studienteilnehmer*innen** 1) Ist die exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition? **Ja** 2) Ist die nicht-exponierte Kohorte repräsentativ, wurde sie adäquat ausgewählt? **Ja** 3) Erfolgte eine valide Erfassung der Exposition? **Ja** 4) Ist es wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war? **NA** **Vergleichbarkeit** 1) Ist die Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben? Ja **Endpunkterfassung** 1) Erfolgte eine valide Erfassung der Endpunkte? **Ja** 2) Konnte in der Beobachtungszeit der Endpunkt überhaupt auftreten? **Ja** 3) Wurden fehlende Daten	Anteil an COPD-Patienten in Interventions- und Kontrollgruppe ausreichend für Beantwortung unserer Fragestellung (gematcht: 25% vs. 24%)? --> Direktheit - IG und CG wurden 1:4 gematcht (Surgical approach, Histologic subtypes, Comorbidities, Smoking status, Smoking status, Age, BMI, Pathological stage)

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
			adäquat berücksichtigt? **Unklar**	
Yusen RD. A prospective evaluation of lung volume reduction surgery in 200 consecutive patients. Chest 2003; 123(4):1026–37. https://www.ncbi.nlm.nih.gov/pubmed/12684290.	**Ziel der Studie:** to assess long-term health-related quality of life, satisfaction, physiologic status, and survival of patients following LVRS. **Studiendesign:** prospective cohort study **Population:** pstients with emphysema; first 200 patients undergoing bilateral LVRS **Intervention:** Each patient served as his own control - Preoperative postrehabilitation data + bilateral stapling LVRS **Vergleich:** - postoperative data **relevante Ausschlusskriterien:** - predominance of airways disease, an inadequate amount of lung spared from severe emphysema as demonstrated on CT scan, or the presence of major comorbidity - systolic pulmonary artery pressure > 45 mm Hg or a mean pulmonary artery pressure > 35 mm Hg - Patients accepted for unilateral LVRS or giant bullectomy **Studienzeitraum:** **-** from 1993 to 1998,with follow-up through the year 2000 - assessment: 6 months, 3 years, and 5 years after surgery	**Effects of LVRS on dyspnea (modified Medical Research Council dyspnea sale)** - dyspnea scores were improved in 81% (6 months), 52% (3 years), and 40% (5 years) of patients G**eneral health-related quality of life (Medical Outcomes Study 36-Item Short-Form Health Survey [SF-36])** - SF-36 physical functioning were improved in 93% (6 months), 78% (3 years), and 69% (5 years) of patients P**atient satisfaction** - Good-to-excellent satisfaction with the outcomes was reported by 96% (6 months), 89% (3 years), and 77% (5 years) of patients S**urvival** The 90-day postoperative mortality was 4.5%. Annual Kaplan-Meier survival through 5 years after surgery was 93%, 88%, 83%, 74%, and 63%, respectively. During follow-up, 15 patients underwent subsequent lung transplantation. CONCLUSIONS: In stringently selected patients, LVRS resulted in substantial beneficial effects over and above those achieved with optimized medical therapy. The duration of improvement was at least 5 years in the majority of survivors.	NOS RoB **Selektion der Studienteilnehmer*innen** 1) Ist die exponierte Kohorte repräsentativ für die zu untersuchende Intervention/Exposition? Ja 2) Ist die nicht-exponierte Kohorte repräsentativ, wurde sie adäquat ausgewählt? n.a. (keine nicht-exponierte Kontrollgruppe) 3) Erfolgte eine valide Erfassung der Exposition? Ja 4) Ist es wahrscheinlich, dass der gemessene Endpunkt nicht zu Studienbeginn vorhanden war? Ja **Vergleichbarkeit** 1) Ist die Vergleichbarkeit der exponierten und nicht-exponierten Kohorte gegeben? na (keine nicht-exponierte Kontrollgruppe) **Endpunkterfassung** 1) Erfolgte eine valide Erfassung der Endpunkte? Ja 2) Konnte in der Beobachtungszeit der Endpunkt überhaupt auftreten? Ja 3) Wurden fehlende Daten adäquat berücksichtigt? Ja	Keine Kontrollgruppe, potentieller Einfluss der Präreha nicht quantifizierbar
Pehlivan E. A comparative study of the effectiveness of	**Fragestellung:** compare between hospital-based and home-based Pulmonary rehabilitation (PR) programms in terms of effectiveness on BLVR candidates	Baselinecharakteristika weitestgehend ausgeglichen **Exercise capacity (in-group change before/after PR; Auszug)** 6MWD	**Confounding (Baseline): unclear** (Allocation nach: Vorhandenen Transferproblemen	einzige Studie mit Population: Pat. mit COPD und Prärehabilitation vor BLVR, daher Einschluss, obwohl kein

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
hospital-based versus home-based pulmonary rehabilitation in candidates for bronchoscopic lung volume reduction. Heart Lung 2020; 49(6):959–64. https://www.ncbi.nlm.nih.gov/pubmed/32709500 .	**Studiendesign:** prospective, controlled, nonrandomized clinical trial **Population:** stable COPD patients, reffered to PR clinic prior to BLVR; n=67 with advanced emphysema **Interventionen** Group 1: hospital-based pulmonary rehabilitation: 8-weeks; including education, breathing exercises, treadmill walking, cycle ergometer, arm ergometer training and strengthening trainning with free weights at hospital. Group 2: home-based pulmonary rehabilitation 8-weeks; including education, breathing exercises, free-walking (at least 4 days/week), and strengthening training with free weights (3x/week) at home **Studienzeitraum:** 05 - 10/2018	- group 1: 68 m (-92 min; 253 max); p<0,001 - group 2: 18 m (-126 min; 153 max); p=0,074 **Pulmonary functions (in-group change before/after PR; Auszug)** FEV1 - group 1: 1,25% (-11 min; 22 max); p=0,686 - group 2: 1,11% (-8 min; 11 max); p=0,144 **authors conclusion:** This study, demonstrated that both home-based and hospital-based PR provided significant and similar improvements in the mMRC and CAT scores but 6MWD was only significantly increased in the hospital-based PR. Since 6MWD after PR plays a major role in BLVR eligibility, our findings suggest that hospital-based PR may be the most appropriate method for BLVR candidates.	zum Krankenhaus? Selbsteinschätzung, ob Teilnehmende die Übungen regelmäßig selbst zu Hause durchführen würden? Möchten nicht 2x/Woche ins Krankenhaus fahren? --> schwer einzuschätzen, ob diese Punkte (Motivation?) Einfluss auf Resultate haben; + Einfluss der Supervision vor Ort vs. keine Supervision auf Resultate nicht abzuschätzen) **Selection Bias: low** (aber: 4/71 wurden ausgeschlossen aufgrund Nichteinhaltung des vorgegebenen Rehaprogramms) **Measurement Bias: low** **Detection Bias: unclear** (keine Informationen) **Reporting bias: low** Kleine Studiengröße; geringer Anteil an Frauen Interessen erklärt **Evidenzqualität** 1) Verzerrungsrisiko (RoB-Bewertung): unclear -0,5 2) Präzision (geringe Fallzahl, KI nicht angegeben):-1 3) Direktheit/Übertragbarkeit auf Fragestellung: -0,5, da keine Kontrollgruppe ohne Rehabilitationsmaßnahme	RCT Direktheit: Fragestellung nicht exakt beantwortet (PräReha vs. keine PräReha) keine Kontrollgruppe ohne Reha

4.3 Gezielte Lungendenervierung

4.3.1 IQWiG-Berichte

Zitat	Berichtcharakteristika	Ergebnisse	Kommentar
IQWiG-Berichte – Nr. 479/ H16-01 Gezielte Lungendenervierung durch Katheterablation bei chronisch obstruktiver Lungenerkrankung 2017 https://www.iqwig.de/download/H16-01_Gezielte-Lungendenervierung-bei-COPD_Bewertung-137h-SGB-V.pdf	IQWiG Bewertung gemäß § 137h SGB V **Fragestellung:** Gezielte Lungendenervierung durch Katheterablation bei COPD **eingereichte Studien:** 4, davon gingen 2 in die Beurteilung mit ein (AIRFLOW-1 und AIRFLOW-1-Extension)	**Baseline-Charakteristika** AIRFLOW-1 (RCT, Pilotstudie): - n=30 Teilnehmer*innen; TLD bei 2 verschiedenen Energiedosen (32 Watt vs. 29 Watt), 2014 - 2015 - Ziel: optimale Energiedosis zu ermitteln und das in AIRFLOW-2 anzuwendende Verfahren zu optimieren - mehrere Modifikation der Prozedur im Verlauf der Studie; Grund u.a.: Auftreten von Gastroparesen --> Änderung: standardmäßige Bildgebung des Ösophagus + angepasste Energiedosis je nach Abstand zwischen Ösophagus und Elektrode AIRFLOW-1-Extension: Abstände zwischen Elektrode und Ösophagus modifiziert (> 12 mm: 32 Watt; 9 bis 12 mm: 26 Watt; ≤ 9 mm: keine Behandlung). In der anterioren Position wird regelhaft die volle Energiedosis von 32 Watt angewendet. In der medialen Position wird regelhaft die verminderte Energiedosis von 26 Watt angewendet, auch wenn der Abstand über 12 mm ist. Bei der in AIRFLOW-1-Extension angewendeten TLD-Variante handelt es sich um die aktuelle zu bewertende TLD-Variante. - Nachbeobachtungsphasen beider Studien liefen zum Zeitpunkt der Bewertung durch das IQWiG noch **Beurteilung IQWiG:** Die Gesamtschau der Unterlagen zeigt, dass die übermittelten Studienergebnisse unvollständig und möglicherweise selektiv ausgewählt wurden, sodass hiermit eine Bewertung der TLD nicht möglich ist. Daher lässt sich für die TLD weder ein Nutzen noch ein Potenzial einer erforderlichen Behandlungsalternative ableiten. Aus diesem Grund werden für die Methode keine Eckpunkte einer Erprobungsstudie konkretisiert.	- keine eigens durchgeführte RoB-Bewertung der eingereichten Unterlagen - Bewertung IQWiG: Verzerrung durch fehlende Daten wahrscheinlich
IQWiG-Berichte – Nr. 622/ H18-02 Gezielte Lungendenervierung durch Katheterablation bei chronisch obstruk-	Addendum zum Auftrag H16-01 **Fragestellung:** Gezielte Lungendenervierung durch Katheterablation bei COPD **Patient*innen:** Laut Hersteller ist die TLD für solche Patientinnen und Patienten mit mittelgradiger bis schwerer COPD vorgesehen, die trotz optimaler medizinischer Versorgung symptomatisch bleiben.	**Baseline-Charakteristika** AIRFLOW-2 (RCT, doppelt verblindet): - Gezielte Lungendenervierung + Tiotropium vs. Scheinbehandlung + Tiotropium (Anwendung des TLD-Systems ohne Energieaktivierung) - Einschlusskriterien: Alter: 40 - 75 Jahre; Rauchervorgeschichte von mindestens 10 Packungsjahren und einer mindestens 2-monatigen Raucherabstinenz vor Studieneinschluss. - zunächste beide Studienarme: ergänzende standardisierte Medikation mit Tiotropium als alleiniges LAMA für 6 Monate; dann 1-wöchige Unterbrechung für Datenerhebung ohne Tiotropium **primärer Endunkt:** Rate an respiratorischen UE: (Auswertungszeitpunkt 6,5 Monate nach Therapie)	- keine direkt gekennzeichnete RoB-Bewertung abgebildet; Ergebnissicherheit jedoch eingeschätzt (siehe Charakteristika des IQWiG-Berichtes) - Aus den ursprünglich übermittelten Bewertungsunterlagen [für die Bewertung H16-1; 2017] ließ sich für die TLD weder ein Nut-

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tiver Lungenerkrankung Addendum zum Auftrag H16-01 2018 https://www.iqwig.de/download/H18-02_Gezielte-Lungendenervierung-bei-COPD_Addendum-zum-Auftrag_H16-01_V1-0.pdf	**eingereichte Unterlagen:** Zusammenfassung der 6-Monats-Daten der AIRFLOW-2-Studie, ergänzt durch die Angabe der 6,5-Monats-Daten, die der Hersteller für den G-BA erstellt hat **Einschätzung der Ergebnissicherheit durch IQWiG:** AIRFLOW-2 = RCT; damit der Evidenzstufe I gemäß Verfahrensordnung (VerfO) des G-BA zuzuordnen. Die vorliegenden Unterlagen enthalten keine Angaben zur Erzeugung der Randomisierungssequenz und der Verdeckung der Gruppenzuteilung. Schon deshalb kann die Ergebnissicherheit auf Basis der vorliegenden Unterlagen höchstens als mäßig eingestuft werden	- relatives Risiko (RR): 0,45 (95 %-KI 0,27; 0,73) (eigene IQWiG-Berechnung) zugunsten der Intervention - Rate von Patient*innen mit mindestens 1 respiratorischen UE: Interventionsgruppe: 32 % / Kontrollgruppe: 71 % Der beobachtete Effekt zeigte sich auch grundsätzlich in allen einzeln aufgeführten Kategorien von respiratorischen UEs. **sekundäre Endpunkte:** <u>- Dyspnoe-Schwere (TDI):</u> Mittelwertdifferenz (MWD) 1,76 (95 %-KI 0,16; 3,36) (MWD und 95 %-KI eigene IQWiG-Berechnung) - keine statistisch signifikanten Unterschiede zwischen Behandlungsgruppen für Dyspnoe-Schwere (mMRC), gesundheitsbezogene Lebensqualität und körperliche Belastbarkeit (Fahrradergometrie) Die Ergebnisse zur gesundheitsbezogenen Lebensqualität, körperlichen Belastbarkeit und Dyspnoe-Schwere zum Zeitpunkt 6,5 Monate nach Behandlung sind für die vorliegende Bewertung nicht relevant, da in der Kontrollgruppe aufgrund fehlender LAMA-Medikation (Tiotropium) gegebenenfalls keine individuell optimierte medikamentöse Therapie vorlag. **Beurteilung IQWiG**: Auf Basis der eingereichten Unterlagen lässt sich somit ein Potenzial der ergänzenden TLD (TLD + LAMA) bei chronisch obstruktiver Lungenerkrankung im Vergleich zur LAMA-Medikation ableiten, das insbesondere auf den vorhandenen Erkenntnissen zu den Endpunkten respiratorische UEs und Dyspnoe-Schwere (gemessen mittels Übergangs-Dyspnoe-Index, TDI) beruht. Eine Erprobungsstudie, die geeignet ist, die notwendigen Erkenntnisse für die Bewertung des Nutzens der Methode zu gewinnen, ist grundsätzlich möglich.	zen noch ein Potenzial einer erforderlichen Behandlungsalternative ableiten. - Addendum schließt Ergebnisse der AIRFLOW-2-Studie mit ein - lediglich Feststellung, dass eine Erprobungsstudie für die Bewertung des Nutzens der Methode zu gewinnen, grundsätzlich möglich ist

4.3.2 RCT

Es konnten keine neuen RCTs anderer Studiengruppen zum Thema gezielte Lungendenervierung identifiziert werden. Follow up-Publikationen der AIRFLOW-1 und AIRFLOW-2 Studie werden hier aufgeführt.

AIRFLOW-1 Follow up

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
Valipour A. Safety and Dose Study of Targeted Lung Denervation in Moderate/Severe COPD Patients. Respiration 2019; 98(4):329–39. https://www.ncbi.nlm.nih.gov/pubmed/31220851.	**Studiendesign:** randomized dose evaluation study; safety study **Population:** patients with moderate to severe COPD **Interventionen:** Targeted lung denervation (TLD) with 29 vs. 32 Watt; TLD to both lungs in a single procedure under general anesthesia **Follow-up:** 3 Monate, 1 Jahr **Studienzeitraum:** 08/2014 - 07/2015	´- n=30 (randomized part) - n=16 in confirmation phase study to confirm safety improvements after procedural enhancements following gastrointestinal adverse events during the randomized part of the trial --> new: fluoroscopic visualization and active measurement of the distance between the electrode and the outer wall of the esophagus + low power (26 W) for treatment positions close to the main carina (siehe IQWiG-Bericht H16-01) **Ergebnisse primärer Endpunkt:** <u>rate of TLD associated adverse airway effects that required treatment through 3 months posttreatment</u> - Four subjects, 1 in the 29 W group (6.6%; nodule) and 3 in the 32 W group (20%; 1x nodule, 1x whitish mucosal blanching immediately posttreatment (treated with steroids and antibiotics), 1x pneumonia poorly responsive to antibiotics) met the primary safety endpoint. (0 in confirmation group) **sekundäre Endpunkte (**At 1 year during the bronchodilator washout study visit): <u>32 W group compared to baseline:</u> - SGRQ-C –7.5 ± 10.3 - CAT –2.9 ± 6.1 - mMRC 0.1 ± 0.9 - Exercise endurance (Performed at 75% of Wmax), min –2.7 ± 8 <u>29W group compared to baseline:</u> - SGRQ-C –1.9 ± 12.5 - CAT 0.3 ± 7.8 - mMRC 0.0 ± 0.7 - Exercise endurance, min –0.3 ± 4.7 --> The difference between groups did not reach statistical significance 32 W confirmation group compared to baseline: (n=16) - SGRQ-C –6.1±21 - CAT –6.1±21 - mMRC –0.2±0.7 - Exercise endurance, min –2.1±9.3	Randomisierung: **low** Allocation concealment**: low** Verblindung von Teilnehmern und Personal: **low** Verblindung der Ergebnisevaluation: **low** Verlust von Studienteilnehmern/ fehlende Daten: **low** **ITT-Analyse: nein** Kommentar: keine Angaben selektive Ergebnisdarstellung: **low** Baseline imbalance: **unclear** **weiteres**: geringe Patientenzahl (n=30)	1-Jahres-Follow up der AIRFLOW-1-Studie geringe Patientenzahl; keine Poweranalyse durchgeführt

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
Pison C. Safety of denervation following targeted lung denervation therapy for COPD: AIRFLOW-1 3-year outcomes. Respir Res 2021; 22(1):62. https://www.ncbi.nlm.nih.gov/pubmed/33608007.	> siehe Valipour et. al 2019 **Interventionen:** TLD delivered via a dual-cooled radiofrequency (RF) catheter (Nuvaira, Minneapolis, Minnesota, USA) - 32 Watt vs. 29 Watt **Follow-up:** 1,2,3 Jahre	> siehe Valipour et. al 2019 **Results:** Three-year follow-up data were available for 73.9% of patients (**n = 34**: n=11 in 29 Watt group; n=12 in 32 Watt group; n=11 in confirmation group). The percentage of patients having at least one moderate or severe COPD exacerbation was 70% (31/44), 61% (23/38), and 46% (16/35) at the 1, 2 and 3-year followup respectively. The annualized rate of moderate to severe COPD exacerbations remained stable over the duration of the study. Lung function (FEV1, FVC, RV, and TLC) and quality of life (SGRQ-C and CAT) remained stable over 3 years of follow-up. **Sicherheit** Over the 2nd and 3rd years of follow-up, there were no new gastrointestinal serious adverse events related to the procedure or device + no unexpected serious adverse events were observed.	> siehe Valipour et. al 2019 beziehen sich auf methodische Details in o.g. Publikation **RoB: unclear** bspw unklar, ob nach 3 Jahren noch Verblindung bei Datenerhebung gegeben	3-Jahres-Follow up der AIRFLOW-1-Studie geringe Patientenzahl

AIRFLOW-2 Follow up

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
Slebos D-J. Safety and Adverse Events after Targeted Lung Denervation for Symptomatic Moderate to Severe Chronic Obstructive Pulmonary Disease (AIRFLOW). A Multicenter Randomized Controlled Clinical Trial. Am J Respir Crit Care Med 2019;	**Studiendesign:** multicenter, randomized, prospective, sham bronchoscopy–controlled, double-blind trial **Population:** patients with symptomatic (mMRC >2; or CAT >10) COPD (FEV1, 30–60% predicted). **Haupt-Ausschlusskriterien:** - more than two respiratory system–related hospitalizations within the past year - Gastroparesis Cardinal Symptom Index ≥ 18 - previous lung or chest procedure **Intervention:** TLD (Nuvaira lung denervation therapy) + optimal pharmacotherapy **Vergleich**: Sham bronchoscopy (without energy activation) Washout: LAMA 7 days; ultra LABA 72h, LABA	**Baseline-Patientencharakteristika:** - 82 patients (50% female; mean ± SD: age, 63.7 ± 6.8 yr; FEV1, 41.6 ± 7.3% predicted; mMRC , 2.2 ± 0.7; CAT 18.4 ± 6.1) - hinsichtlich Medikation, Alter, Geschlecht, Gewicht, Emphysemscore weitestgehend ausgeglichen **Effektivität:** respiratory adverse events During the predefined 3- to 6.5-monthwindow, patients in the TLD group experienced significantly fewer respiratory adverse events than those in the sham group: - 32% vs. 71%, - OR 0.19 (95% CI 0.0750–0.4923) Between 0 and 12.5 months, these findings were not different (83% vs. 90%) The risk of COPD exacerbation requiring hospitalization in the 0- to 12.5-month window was significantly lower in the TLD group	Randomisierung: **low**	AIRFLOW-2: 12-Monate Follow up; in IQWiG-Addendum waren nur 6,5-Monate Follow-Up verfügbar n=82 Patient*innen: Poweranalyse wurde vorab durchgeführt

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
200(12):1477–86. https://www.ncbi.nlm.nih.gov/pubmed/31404499.	24h After washout: all patients inhaled tiotropium 18 mg/d + other medication at the discretion of their physician **Follow-up:** 6,5 months;12.5 months **Informationen zu Aufhebung der Verblindung und Crossover:** Blinding was maintained through 12.5 months when control subjects were offered the opportunity to undergo TLD **Studienzeitraum:** July 2016 and May 2017 **Definition primärer Endpunkt**: - rate of respiratory adverse events between 3 and 6.5 months after randomization (defined as COPD exacerbation, tachypnea, wheezing, worsening bronchitis, worsening dyspnea, influenza, pneumonia, other respiratory infections, respiratory failure, or airway effects requiring therapeutic intervention - time window: set to evaluate the effect of TLD on respiratory safety in isolation from the effects of bronchoscopy	than in the sham group - HR 0.35 (95% CI 0.13–0.99; P = 0.039). There was no statistical difference in the time to first moderate or severe COPD exacerbation, patientreported symptoms, or other physiologic measures over the 12.5 months of follow-up. **Sicherheit** (Secondary overall safety) The overall number of serious adverse events was similar between groups, except for differences in respiratory adverse events. Although there was no statistical difference in gastrointestinal adverse events, there was a trend for increased gastrointestinal events in the TLD arm (Supplemental Appendix 4). There were five patients with gastrointestinal serious adverse events.	Allocation concealment: **low** Verblindung von Teilnehmern und Personal: **low** Verblindung der Ergebnisevaluation: **low** Verlust von Studienteilnehmern/ fehlende Daten: **low** ITT-Analyse: nein selektive Ergebnisdarstellung: **low** Baseline imbalance: **low:**	
Valipour A. Two-Year Outcomes for the Double-Blind, Randomized, Sham-Controlled Study of Targeted Lung Denervation in Patients with Moderate to Severe COPD: AIRFLOW-2. Int J Chron Obstruct Pulmon Dis 2020; 15:2807–16. https://www.ncbi.nlm.nih.gov/pu	> siehe Slebos 2019 **Follow-up** after 2 years: A time-to-first-event analysis on moderate and severe and severe exacerbations of COPD was performed. **Cross-over** could occur at any timepoint during follow-up after the 12.5-month follow-up visit.	**Baselinecharakteristika:** > siehe Slebos 2019; n=82 Patient*innen randomisiert - TLD group: retention of 88% at 2 years (n=36) - control group: reduced (n=14) as 49% of control subjects (n=20) underwent an optional cross-over procedure and 5 subjects voluntarily exited due to crossover ineligibility or other reasons - Control patients who underwent a cross-over procedure were censored from the adverse event annualized rate and time-to-event analysis at the time of cross-over and are not included in other variable analysis as they did not complete a full 2-year follow-up time period. **Ergebnisse:** Time-to-first severe COPD exacerbation - significantly lengthened in the TLD arm: HR=0.38 (95% CI 0.15–0.99).) at 2 years post-TLD therapy - no statistical difference in risk of first moderate or severe COPD exacerbation from baseline to 2 years: HR=0.71 (95% CI 0.42–	> siehe Slebos 2019 beziehen sich auf methodische Details in o.g. Publikation **RoB: unclear** keine Verblindung mehr nach 2 Jahren - bei Datenerhebung gegeben - bei Teilnehmern und Untersuchern	2-Jahres Follow-Up Airflow-2 - durch Crossover nach Entblindung sehr wenige Patienten in Kontrollgruppe für Auswertung (n=14) --> which likely resulted in a healthier group, ie, subjects who had a higher symptomatic disease characteristic were more likely to undergo TLD

Zitat	Studiencharakteristika	Ergebnisse	Aussagesicherheit	Kommentar
bmed/33177818 .		1.18) No significant changes in lung function or SGRQC were found 2 years post randomization between groups. Long-Term Safety Assessment: All Adverse Events In the second year of follow-up, 11.1% of TLD subjects (n=4) experienced a respiratory-related hospitalization, compared to 28.6% of control subjects (n=4). These events resolved.		

4.4 AWMF-Leitlinien

Zitat
Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin (DGP) et al.: S2k-Leitlinie Fachärztliche Diagnostik, Prävention und Therapie der chronisch obstruktiven Lungenerkrankung (https://register.awmf.org/de/leitlinien/detail/020-006); aktuell in Erarbeitung, Stand 09/2024.
Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin (DGP) et al.: DACH-Leitlinie: Nachsorge von Erwachsenen nach Lungentransplantation (https://register.awmf.org/de/leitlinien/detail/020-033); aktuell in Erarbeitung, Stand 09/2024.

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1. Bundesärztekammer (BÄK), Kassenärztliche Bundesvereinigung (KBV), Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF). Nationale VersorgungsLeitlinie COPD – Langfassung, 2. Auflage. Version 1. 2021 [cited: 2021-08-17]. DOI: 10.6101/AZQ/000477. http://doi.org/10.6101/AZQ/000477.
2. Bundesärztekammer (BÄK), Kassenärztliche Bundesvereinigung (KBV), Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF). Nationale VersorgungsLeitlinie COPD – Leitlinienreport, 2. Auflage. Version 1. 2021 [cited: 2021-06-07]. DOI: 10.6101/AZQ/000478. http://doi.org/10.6101/AZQ/000478.