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Keywords:	Chronic obstructive pulmonary disease, pharmacological interventions, non-pharmacological interventions, umbrella review, evidence map, knowledge translation

Treatment of stable chronic obstructive pulmonary disease: a protocol for a systematic review and evidence map

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Abstract

Introduction: Chronic obstructive pulmonary (COPD) disease is a progressive lung disease, usually caused by tobacco smoking, but other important risk factors include exposures to combustion products of biomass fuels and environmental pollution. The introduction of several new (combination) inhaler therapies, increasing uncertainty about the role of inhaled corticosteroids and a rapid proliferation of the literature on management of stable COPD in general, call for novel ways of evidence synthesis in this area. A systematic review and evidence map can provide the basis for shared decision-making tools and help establish a future research agenda.

Methods and analysis: This systematic review will follow an umbrella systematic review design (also called overview of reviews). We plan to conduct a comprehensive literature search of six databases. We will include systematic reviews that assessed the effectiveness of any pharmacological or non-pharmacological intervention on one or more patient-important outcomes and/or lung function in patients with stable COPD. For every intervention/outcome pair one systematic review will be included. An a priori protocol will guide which systematic reviews will be chosen, how their credibility will be evaluated, and how the quality of the body of evidence will be rated. Data will be synthesized into an evidence map that will present a matrix that depicts each available treatment for stable COPD with a quantitative estimate on symptoms/outcomes from the patient perspective, along with an indication of the size and certainty in the evidence.

Ethics and dissemination: Approval by a research ethics committee is not required since the review will only include published and publicly accessible data. The systematic review will be published in a peer-reviewed journal and will provide various stakeholders with an evidence map.

Systematic review registration: PROSPERO registration number CRD42018095079

Keywords

Chronic obstructive pulmonary disease, pharmacological interventions, non-pharmacological interventions, umbrella review, evidence map, knowledge translation, decision aid

Article Summary

Strengths and limitations of this study

- The planned evidence synthesis will summarise a very large body of literature on pharmacological and non-pharmacological interventions thus making research evidence more accessible for stakeholders
- The systematic review will be the first to use an evidence map to identify evidence gaps and to facilitate evidence communication in clinical encounters for COPD.
- For patients and clinicians, the map will facilitate the production of decision aids. For policymakers and researchers, the map helps in establishing a future research agenda.
- The systematic review uses an a priori protocol to identify the most up-to-date systematic reviews of the highest possible quality, and the level of evidence for many intervention/outcome pairs will therefore likely be high
- As we will only include one systematic review per intervention/outcome pair, it is possible that some studies will not have been captured in included systematic reviews

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive lung disease characterized by chronic obstruction of airflow and permanent damage to the air sacs that leads to breathing problems. COPD is mainly a consequence of tobacco smoking, but other important risk factors include exposures to combustion products of biomass fuels and environmental pollution.[1] COPD is the fourth most common cause of death globally and is predicted to be the third by 2030.[2] In 2010, the number of COPD cases was estimated at 384 million, which corresponded to a global prevalence of 11.7% (95% confidence interval [CI] 8.4%–15.0%).[2] COPD was responsible for about 5% of global disability–adjusted life years (76.7 million) and 5% of total deaths (2.9 million) based on data from the 2010 Global Burden of Disease study.[3 4] In some low- and middle income countries COPD has become a growing, but often neglected, epidemic, with a recent study showing a prevalence of COPD of 13.7% (95% CI 12.1–15.5) in Chinese people aged 40 years or older.[5] Patients with COPD are frequent users of the health care system and often need to be admitted to hospital repeatedly, often within short intervals.[6]

Recently, there has been a rapid increase in inhaler therapies available for the management of COPD. In particular, several new inhalers including fixed-dose combinations (containing bronchodilator(s) with or without inhaled corticosteroids) have been introduced. Concurrently, the literature on pharmacological and non-pharmacological interventions for COPD has proliferated substantially. Multiple systematic reviews have been conducted to synthesise the evidence on inhalation treatments in COPD.[7-16]

The role of inhaled corticosteroids for the treatment of stable COPD is increasingly questioned, including in patients with severe disease, driven by the growing evidence of an increased risk of pneumonia associated with inhaled corticosteroids,[17 18] and the introduction of combined dual long acting bronchodilator inhalation therapy as a plausible treatment alternative.[19 20]

A search of the Cochrane Database of Systematic Reviews (Issue 5 of 12, May 2018) with the keyword “chronic obstructive pulmonary disease” yielded 132 unique records, indicating that keeping track not just

of original studies, but also evidence syntheses, has become a daunting task for decision makers in this area.

The implementation of evidence-based practice in the management of patients with COPD is challenging for medical practitioners due to the rapidly growing body of evidence. Additionally, non-adherence of patients with COPD to prescribed treatments is an ongoing challenge, with many patients being overburdened with the treatment work they need to do for their COPD care.[21-24] Patients' beliefs and concerns about the safety and benefits of their treatment and complex treatment regimens all impact on adherence. Non-pharmacological interventions such as pulmonary rehabilitation are persistently underutilised despite scientific evidence of their effectiveness.[25]

Faced with these challenges, novel tools of evidence synthesis and evidence communication in CODP for the patient-clinician encounter are needed that will allow collaborative deliberation of treatment options between patients and clinicians to make health care decisions together, taking into account the best scientific evidence available, as well as the patient's values and preferences.[26-29] Further, given the rapidly growing body of evidence on treatments for stable COPD, it is timely to identify current knowledge gaps to inform future research needs.

Consequently, the aim of our systematic review is 1) to synthesise the evidence on pharmacological and non-pharmacological treatments for stable COPD, 2) produce an evidence map that identifies evidence gaps in order to inform future research, and that provides information that can be incorporated into a decision/communication aid for use during clinical encounters between patients and clinicians.

Methods and analysis

This protocol adheres to the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols (PRISMA-P) (see "Additional file 1 PRISMA-P checklist.pdf").[30]

Patient and Public Involvement

No patients or the public were involved in this systematic review of the literature.

Review question

What are the impacts of pharmacological and non-pharmacological interventions in patients with COPD on patient-important outcomes (including dyspnea and other symptoms such as anxiety, functional/exercise capacity, frequency of acute exacerbations, health-related quality of life, hospitalizations, emergency department visits) and lung function parameters?

Eligibility criteria

Types of studies

We will include systematic reviews that assessed the effectiveness of any pharmacological or non-pharmacological intervention on one or more relevant outcomes (see below) in patients with stable COPD. For every intervention/outcome pair (e.g. effectiveness of pulmonary rehabilitation to improve dyspnea) one systematic review will be included. The following a priori protocol will guide which systematic reviews will be chosen, how their credibility will be evaluated, and how the quality of the body of evidence will be rated.

Systematic reviews will be excluded if:

- they were not published in English (included studies, however, could have been in any language)
- their pooled estimates were (partially) derived from studies that had not been published in the peer-reviewed literature (e.g. abstracts, studies only published on pharmaceutical company websites)
- they only contained indirect or mixed indirect and direct comparisons (network meta-analysis)
- they were umbrella reviews (reviews of reviews)
- they included patient populations other than patients with COPD and did not report outcomes separately for COPD patients

We will derive a single pooled estimate per outcome per intervention. If multiple systematic reviews provided multiple estimates for the same intervention and outcome, we will choose a systematic review based on the following a priori defined scoring system:

a. Availability of one or more meta-analyses (as opposed to narrative data synthesis only)
b. Year of publication, date of literature search
c. Size based on a) Number of studies included, b) Number of participants included
d. Type of studies: randomized controlled trials (RCTs) generally provide stronger evidence than observational studies
e. Synthesis of data from drug classes rather than specific drugs

If we encounter the scenario in which despite the above mentioned criteria we still have to choose between two or more systematic reviews, we will make this choice based on these additional criteria:

a. Consensus among two practicing pulmonologists
b. Credibility of the systematic reviews as judged using the "A Measurement Tool to Assess Systematic Reviews" (AMSTAR2) criteria.[31]

Types of participants

Studies that evaluated adults (aged 18 years and older) with stable COPD will be included. Studies conducted in patients with an acute exacerbation of COPD will be excluded.

Types of interventions

We will include any pharmacological or non-pharmacological intervention. Interventions that we are expecting are the following: inhaled and other medications, smoking cessation, vaccinations, exercise and pulmonary rehabilitation, airway clearance techniques, nutrition and dietary interventions, COPD action plans, psychological interventions, home oxygen therapy, home mechanical ventilation, interventional bronchoscopy, and surgery. Complex interventions with multiple components such as

exercise, smoking cessation advice, psychological support and home visits will be excluded. We will also exclude interventions only relevant during an acute exacerbation of COPD.

Comparators will include placebo or usual care. Comparisons between different (combinations of) inhaler treatments (focusing on different drug classes rather than different inhalation devices/ formulations) will also be included. We will exclude indirect comparisons between interventions or mixed direct and indirect comparisons (network meta-analyses).

Types of outcomes

The following outcomes will be included:

a. Dyspnea and other symptoms
b. Exercise capacity and functional capacity
c. COPD exacerbations
d. Health-related quality of life
e. Hospitalizations, emergency department visits
f. Mortality
g. Lung function parameters
h. Adverse events

There will be no restrictions based on measurement methods.

Information sources and search strategy

This systematic review will follow an umbrella systematic review design (also called overview of reviews). We plan to conduct a comprehensive literature search of six databases, including Ovid MEDLINE Epub Ahead of Print, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE, Ovid EMBASE, Ovid Cochrane Database of Systematic Reviews, and Scopus from database inception to the present. We have developed a preliminary database search strategy and found that these databases can adequately identify the relevant literature. Reference mining of relevant publications will be conducted. The search strategy will be designed and conducted by an experienced librarian with input from the

study's principle investigator. Controlled vocabulary supplemented with keywords will be used to search for systematic reviews and meta-analyses of pharmacological and non-pharmacological treatments for stable COPD. Search strategies are shown in Additional file 2.

All citations identified through the process will be imported to a reference management system (EndNote® Version X7 and X8; Thomson Reuters, Philadelphia, PA). We will use a web-based systematic review software, DistillerSR (Evidence Partners Incorporated, Ottawa, Canada), to facilitate the study selection process.

Data extraction

For every intervention/outcome pair one systematic review will be chosen following the priori protocol outlined above. At the beginning of data abstraction, we will develop a standardized data extraction form to extract study characteristics (author, study design, inclusion and exclusion criteria, patient characteristics, interventions, comparisons, outcomes, and related items for assessing study quality and applicability). The standardized form will be pilot-tested by all study team members. We will iteratively continue testing the form until no additional items or unresolved questions exist. All study details will be extracted by two independent reviewers. A third reviewer will review data extraction, and resolve conflicts.

Strategy for data synthesis

Data will be synthesized into an evidence map. An evidence map is defined as a systematic search of a broad field to identify gaps in knowledge and/or future research needs that presents results in a user-friendly format, often a visual figure or graph, or a searchable database.[32] The planned map will present a matrix that depicts each available treatment for stable COPD with a quantitative estimate on symptoms/outcomes from the patient perspective, along with an indication of the size and certainty in the evidence.

We will also provide a narrative synthesis of the findings from the included systematic reviews, structured around the type of intervention, target population characteristics (e.g. severity of COPD), type of outcome and intervention content.

Analysis of subgroups or subsets

Pre-determined characteristics for subgroup analysis are:

- Severity of COPD, e.g. based on GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria,[33] FEV1 (forced expiratory volume in one second) in % predicted
- COPD phenotypes, e.g. patients with frequent exacerbations, eosinophilic inflammation
- Duration of intervention
- Different study types (e.g. randomized controlled trials versus observational studies)

Credibility (methodological quality) assessment

We will use AMSTAR2[31] to assess the credibility of the included systematic reviews. The AMSTAR2 tool addresses the following 16 items:

- Use of the components of PICO (population, intervention, comparator, outcome) for research questions and inclusion criteria
- Protocol for the systematic review, justification of any significant protocol deviations
- Study selection
- Literature search strategy
- Study selection by two independent reviewers
- Data extraction by two independent reviewers
- Excluded studies
- Description of included studies
- Risk of bias assessment in individual studies
- Sources of funding
- Methods for meta-analysis
- Impact of risk of bias on the meta-analysis or other evidence synthesis

- Accounting for risk of bias in the interpretation/discussion of results
- Explanation for heterogeneity in the results
- Publication bias
- Conflicts of interest

Ethics and dissemination

This systematic review is registered with PROSPERO (registration number: CRD42018095079; http://www.crd.york.ac.uk/PROSPERO). Approval by a research ethics committee is not required since the review will only include published and publicly accessible data. The systematic review will be published in a peer-reviewed journal and will provide various stakeholders with an evidence map.

Discussion

The aim of this systematic review is to systematically identify, summarize and assess a large body of evidence on pharmacological and non-pharmacological interventions in stable COPD. The information will be used to produce an evidence map to identify knowledge gaps and to inform a decision/communication aid for the clinical encounter between patients and clinicians.

Strengths and limitations of this systematic review

We have not identified any systematic reviews that have provided an evidence map for the treatment of stable COPD, and this systematic review will therefore be the first to use an evidence map to identify evidence gaps and to facilitate evidence communication in clinical encounters for COPD. The systematic review uses an a priori protocol to identify the most up-to-date systematic reviews of the highest possible quality, and the level of evidence for many intervention/outcome pairs will therefore likely be high.

As we will only include one systematic review per intervention/outcome pair, it is possible that some studies will not have been captured in included systematic reviews.

Practical Implications

Evidence mapping is a relative novel method of evidence synthesis, which aims to identify gaps in knowledge and/or future research needs based on a comprehensive literature search and present results in an easy to understand format in a figure or graph.[32] Evidence presented in such a user-friendly way may facilitate knowledge dissemination and implementation among relevant stakeholder groups including policy makers.[34 35] In this proposed study, we are targeting two aims that address the needs of different stakeholders.

The first type of stakeholders is patients and clinicians. In the context of a clinical encounter, they require shared decision-making tools (decision aids) because the available treatments are numerous and the impact on the different symptoms varies by intervention. Traditional systematic reviews usually summarize evidence grouped around specific interventions. In clinical practice, however, discussions between patients and clinicians often focus on a problem that demands a solution (e.g. shortness of breath or limited functional capacity in patients with COPD). This requires that evidence is communicated from an outcome rather than an intervention perspective (e.g. which interventions can improve shortness of breath or functional capacity in patients with stable COPD?). We plan to present the results of our systematic review structured by outcomes to facilitate knowledge translation into a decision/communication aid (the COPD CHOICE decision aid project). This will hopefully contribute to patient-centred and transparent evidence communication in clinical encounters.

The second type of stakeholders is policymakers funding research and researchers. The presentation of results in the form of evidence map can quickly provide them with a snapshot of which symptoms (daily dilemmas that patients face) or which interventions are only supported by low quality evidence (or no evidence). Such areas are prime targets for future research.

The proposed approach (overview of reviews and evidence mapping) is ideal in the context of the very large volume of literature available on pharmacological and non-pharmacological interventions in stable COPD, and the need to synthesize and present summaries that cater to different stakeholders.

List of abbreviations

95% CI: 95% confidence interval; AMSTAR2: A Measurement Tool to Assess Systematic Reviews 2; COPD: Chronic obstructive pulmonary disease (COPD); FEV1: forced expiratory volume in one second; GOLD: Global Initiative for Chronic Obstructive Lung Disease; PICO: population, intervention, comparator, outcome; PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-analysis Protocols; RCT: randomized controlled trial

Authors' contributions

CCD drafted the manuscript. MHM made substantial contributions to the conception and design. Working with CCD, LJP designed the search strategy for the systematic review. All authors revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript.

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Competing interests statement

No conflict of interest to declare.

Word count

Abstract 283, Main text 2,328

References

1. Postma DS, Bush A, van den Berge M. Risk factors and early origins of chronic obstructive pulmonary disease. *Lancet (London, England)* 2015;385(9971):899-909. doi: 10.1016/s0140-6736(14)60446-3 [published Online First: 2014/08/16]
2. Adeloye D, Chua S, Lee C, et al. Global and regional estimates of COPD prevalence: Systematic review and meta-analysis. *Journal of global health* 2015;5(2):020415. doi: 10.7189/jogh.05-020415 [published Online First: 2016/01/13]
3. Murray CJ, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet (London, England)* 2012;380(9859):2197-223. doi: 10.1016/s0140-6736(12)61689-4 [published Online First: 2012/12/19]
4. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet (London, England)* 2012;380(9859):2095-128. doi: 10.1016/s0140-6736(12)61728-0 [published Online First: 2012/12/19]
5. Wang C, Xu J, Yang L, et al. Prevalence and risk factors of chronic obstructive pulmonary disease in China (the China Pulmonary Health [CPH] study): a national cross-sectional study. *Lancet (London, England)* 2018;391(10131):1706-17. doi: 10.1016/s0140-6736(18)30841-9 [published Online First: 2018/04/14]
6. Hakim MA, Garden FL, Jennings MD, et al. Performance of the LACE index to predict 30-day hospital readmissions in patients with chronic obstructive pulmonary disease. *Clinical epidemiology* 2018;10:51-59. doi: 10.2147/clep.s149574 [published Online First: 2018/01/19]
7. Horita N, Goto A, Shibata Y, et al. Long-acting muscarinic antagonist (LAMA) plus long-acting beta-agonist (LABA) versus LABA plus inhaled corticosteroid (ICS) for stable chronic obstructive pulmonary disease (COPD). *Cochrane Database Syst Rev* 2017;2:CD012066. doi: https://dx.doi.org/10.1002/14651858.CD012066.pub2

8. Calzetta L, Ora J, Cavalli F, et al. Impact of LABA/LAMA combination on exercise endurance and lung hyperinflation in COPD: A pair-wise and network meta-analysis. *Respir Med* 2017;129:189-98. doi: https://dx.doi.org/10.1016/j.rmed.2017.06.020
9. Farne HA, Cates CJ. Long-acting beta2-agonist in addition to tiotropium versus either tiotropium or long-acting beta2-agonist alone for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2015(10):CD008989. doi: https://dx.doi.org/10.1002/14651858.CD008989.pub3
10. Rodrigo GJ, Price D, Anzueto A, et al. LABA/LAMA combinations versus LAMA monotherapy or LABA/ICS in COPD: a systematic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2017;12:907-22. doi: https://dx.doi.org/10.2147/COPD.S130482
11. Karner C, Cates CJ. Combination inhaled steroid and long-acting beta(2)-agonist in addition to tiotropium versus tiotropium or combination alone for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2011(3):CD008532. doi: https://dx.doi.org/10.1002/14651858.CD008532.pub2
12. Kwak M-S, Kim E, Jang EJ, et al. The efficacy and safety of triple inhaled treatment in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis using Bayesian methods. *Int J Chron Obstruct Pulmon Dis* 2015;10:2365-76. doi: https://dx.doi.org/10.2147/COPD.S93191
13. Nannini LJ, Lasserson TJ, Poole P. Combined corticosteroid and long-acting beta(2)-agonist in one inhaler versus long-acting beta(2)-agonists for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2012(9):CD006829. doi: https://dx.doi.org/10.1002/14651858.CD006829.pub2
14. Nannini LJ, Poole P, Milan SJ, et al. Combined corticosteroid and long-acting beta(2)-agonist in one inhaler versus inhaled corticosteroids alone for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2013(8):CD006826. doi: https://dx.doi.org/10.1002/14651858.CD006826.pub2
15. Rojas-Reyes MX, Garcia Morales OM, Dennis RJ, et al. Combination inhaled steroid and long-acting beta2-agonist in addition to tiotropium versus tiotropium or combination alone

for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2016(6):CD008532. doi: https://dx.doi.org/10.1002/14651858.CD008532.pub3

16. Welsh EJ, Cates CJ, Poole P. Combination inhaled steroid and long-acting beta2-agonist versus tiotropium for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2013(5)
17. Singh S, Amin AV, Loke YK. Long-term use of inhaled corticosteroids and the risk of pneumonia in chronic obstructive pulmonary disease: a meta-analysis. *Arch Intern Med* 2009;169(3):219-29. doi: https://dx.doi.org/10.1001/archinternmed.2008.550
18. Kew KM, Seniukovich A. Inhaled steroids and risk of pneumonia for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2014(3):CD010115. doi: https://dx.doi.org/10.1002/14651858.CD010115.pub2
19. Wedzicha JA, Banerji D, Chapman KR, et al. Indacaterol-Glycopyrronium versus Salmeterol-Fluticasone for COPD. *The New England journal of medicine* 2016;374(23):2222-34. doi: 10.1056/NEJMoa1516385 [published Online First: 2016/05/18]
20. Magnussen H, Disse B, Rodriguez-Roisin R, et al. Withdrawal of inhaled glucocorticoids and exacerbations of COPD. *The New England journal of medicine* 2014;371(14):1285-94. doi: 10.1056/NEJMoa1407154 [published Online First: 2014/09/10]
21. Bourbeau J, Bartlett SJ. Patient adherence in COPD. *Thorax* 2008;63(9):831-8. doi: 10.1136/thx.2007.086041 [published Online First: 2008/08/30]
22. Agh T, Inotai A, Meszaros A. Factors associated with medication adherence in patients with chronic obstructive pulmonary disease. *Respiration; international review of thoracic diseases* 2011;82(4):328-34. doi: 10.1159/000324453 [published Online First: 2011/04/02]
23. Harb N, Foster JM, Dobler CC. Patient-perceived treatment burden of chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2017;12:1641-52. doi: 10.2147/copd.s130353 [published Online First: 2017/06/16]

24. Dobler CC, Harb N, Maguire CA, et al. Treatment burden should be included in clinical practice guidelines. *BMJ (Clinical research ed)* 2018;363:k4065. doi: 10.1136/bmj.k4065 [published Online First: 2018/10/14]
25. Safka KA, McIvor RA. Non-pharmacological management of chronic obstructive pulmonary disease. *The Ulster medical journal* 2015;84(1):13-21. [published Online First: 2015/05/13]
26. Stiggelbout AM, Van der Weijden T, De Wit MP, et al. Shared decision making: really putting patients at the centre of healthcare. *BMJ (Clinical research ed)* 2012;344:e256. doi: 10.1136/bmj.e256 [published Online First: 2012/01/31]
27. Elwyn G, Frosch D, Thomson R, et al. Shared decision making: a model for clinical practice. *Journal of general internal medicine* 2012;27(10):1361-7. doi: 10.1007/s11606-012-2077-6 [published Online First: 2012/05/24]
28. Dobler CC, Sanchez M, Gionfriddo MR, et al. Impact of decision aids used during clinical encounters on clinician outcomes and consultation length: a systematic review. *BMJ quality & safety* 2018 doi: 10.1136/bmjqs-2018-008022 [published Online First: 2018/10/12]
29. Dobler CC, Midthun DE, Montori VM. Quality of Shared Decision Making in Lung Cancer Screening: The Right Process, With the Right Partners, at the Right Time and Place. *Mayo Clinic proceedings* 2017;92(11):1612-16. doi: 10.1016/j.mayocp.2017.08.010 [published Online First: 2017/11/06]
30. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ (Clinical research ed)* 2015;350:g7647. doi: 10.1136/bmj.g7647 [published Online First: 2015/01/04]
31. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ (Clinical research ed)* 2017;358:j4008. doi: 10.1136/bmj.j4008 [published Online First: 2017/09/25]

32. Miake-Lye IM, Hempel S, Shanman R, et al. What is an evidence map? A systematic review of published evidence maps and their definitions, methods, and products. *Systematic reviews* 2016;5:28. doi: 10.1186/s13643-016-0204-x [published Online First: 2016/02/13]

33. Global Strategy for Prevention, Diagnosis and Management of COPD, 2018 reprt. Available at: http://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf Accessed May 15, 2018.

34. Bangerter LR, Griffin JM, Langer S, et al. The Effect of Psychosocial Interventions on Outcomes for Caregivers of Hematopoietic Cell Transplant Patients. *Current hematologic malignancy reports* 2018 doi: 10.1007/s11899-018-0445-y [published Online First: 2018/05/01]

35. Farah WH, Alsawas M, Mainou M, et al. Non-pharmacological treatment of depression: a systematic review and evidence map. *Evidence-based medicine* 2016;21(6):214-21. doi: 10.1136/ebmed-2016-110522 [published Online First: 2016/11/12]

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
METHODS		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review

Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

Literature search strategy for

Treatment of stable chronic obstructive pulmonary disease: a protocol for a systematic review and evidence map

Claudia C. Dobler,[1] Magdoleen H Farah,[1] Allison S. Morrow,[1] Mouaz Alsawas,[1] Raed Benkhadra[1] Bashar Hasan,[1] Larry J Prokop,[2] Zhen Wang,[1] M. Hassan Murad[1]

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2) Library Public Services, Mayo Clinic, Rochester, Minnesota, USA.

Ovid

Part 1

Database(s): Embase 1988 to 2018 Week 16, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 11, 2018, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search Strategy:

#	Searches	Results
1	exp Pulmonary Disease, Chronic Obstructive/dh, dt, px, rh, su, th [Diet Therapy, Drug Therapy, Psychology, Rehabilitation, Surgery, Therapy]	18829
2	exp chronic obstructive lung disease/dm, dt, rh, su, th [Disease Management, Drug Therapy, Rehabilitation, Surgery, Therapy]	27067
3	1 or 2	45896
4	("chronic airflow disease*" or "chronic airflow disorder*" or "chronic airflow limitation*" or "chronic airflow obstruction*" or "chronic airway disease*" or "chronic airway disorder*" or "chronic airway limitation*" or "chronic airway obstruction*" or "chronic bronchitis" or "chronic obstructive airflow disease*" or "chronic obstructive airflow disorder*" or "chronic obstructive airway disease*" or "chronic obstructive airway disorder*" or "chronic obstructive bronchitis" or "chronic obstructive bronchopulmonary disease*" or "chronic obstructive broncho-pulmonary disease*" or "chronic obstructive bronchopulmonary disorder*" or "chronic obstructive broncho-pulmonary disorder*" or "chronic obstructive lung disease*" or "chronic obstructive lung disorder*" or "chronic obstructive pulmonary disease*" or "chronic obstructive pulmonary disorder*" or "chronic obstructive respiratory disease*" or "chronic obstructive respiratory disorder*" or coad or copd or emphysema or "obstructive lung disease" or "obstructive lung disorder*" or "obstructive pulmonary disease*" or "obstructive pulmonary disorder*" or "obstructive pulmonary tract disease*" or "obstructive pulmonary tract disorder*" or "obstructive respiratory disease*" or "obstructive respiratory disorder*" or "obstructive respiratory tract disease*" or "obstructive respiratory tract disorder*").ti,ab,hw,kw.	248757

5	exp Bronchodilator Agents/	383398
6	(abediterol or acefylline or "acefylline clofibrol" or "acefylline piperazine" or "aclidinium bromide" or "adrenalin hydrogen tartrate" or Adrenomedullin or Albuterol or ambuphylline or Aminophylline or antibronchospastic or arformoterol or Atropine or bambuterol or bamifylline or baralgin or batefenterol or bitolterol or "bitolterol mesilate" or "bronchial dilating" or "bronchial-dilating" or bronchodilatant* or "broncho-dilatant*" or bronchodilatating or "broncho-dilatating" or bronchodilatator* or "broncho-dilatator*" or bronchodilating or "broncho-dilating" or bronchodilator* or "broncho-dilator*" or broncholytic* or broncholytica or bronchospasmolytic or broxaterol or Budesonide or carbuterol or carmoterol or "choline theophyllinate" or Clenbuterol or clorprenaline or Colforsin or Cromakalim or danirixin or "darotropium bromide" or dilator* or diprophylline or ditec or doxofylline or Dyphylline or elubrixin or enprofylline or ephedrine or "ephedrine sulfate" or Epinephrine or eprozinol or espatropate or etafedrine or etamiphyllin or "etamiphyllin camsilate" or etanterol or etofylline or Fenoterol or fenspiride or Fluticasone or "flutropium bromide" or formoterol or "Formoterol Fumarate" or furafylline or glycopyrronium or "gsk 159802" or "gsk 597901" or guaifylline or "gw 678007" or Hexoprenaline or Hyoscyamine or ibuterol or "ilmetropium iodide" or imoxiterol or indacaterol or inhaler* or Ipratropium or "ipratropium bromide" or isbufylline or isoetarine or "isoetarine mesylate" or Isoetharine or isoprenaline or Isoproterenol or Khellin or laprafylline or levalbuterol or mabuterol or marax or Metaproterenol or methoxyphenamine or milveterol or "n methylmequitazine" or naminterol or neobiphyllin or nestifylline or "Nitric Oxide" or olodaterol or orciprenaline or "oxitropium bromide" or "oxyphenonium bromide" or pibaxizine or pirbuterol or "pirbuterol acetate" or pneumodilator or Procaterol or protokylol or proxyphylline or Pseudoephedrine or racephedrine or Racepinephrine or reproterol or rimiterol or "ru 45703" or salbutamol or "salbutamol sulfate" or salmefamol or salmeterol or "Salmeterol Xinafoate" or sibenadet or "S-Nitrosoglutathione" or "S-Nitrosothiols" or soterenol or tazifylline or Terbutaline or Theobromine or Theophylline or "theophylline sodium glycinate" or thiazinamium or "thiazinamium metilsulfate" or Tiotropium or Tretoquinol or "tretoquinol derivative" or trimetaquinol or tulobuterol or "uk 432097" or Umeclidinium or vephylline or verofylline or vilanterol or "vilanterol trifenatate" or zindotrine).ti,ab,hw,kw.	860675
7	exp Adrenergic beta-2 Receptor Agonists/	82439
8	("adrenergic beta 2 agonist*" or "adrenergic beta 2 receptor agonist*" or "adrenergic beta2 agonist*" or "adrenergic beta-2 agonist*" or "adrenergic beta-2 receptor agonist*" or "adrenergic beta2-agonist*" or Albuterol or "beta 2 adrenergic agent*" or "beta 2 adrenergic agonist*" or "beta 2 adrenergic receptor agonist*" or "beta 2 adrenergic receptor stimulant*" or "beta 2 adrenergic receptor stimulat*" or "beta 2 adrenergic receptor stimulator*" or "beta 2 adrenergic stimulant*" or "beta 2 adrenergic stimulat*" or "beta 2 adrenergic stimulator*" or "beta 2 adrenoceptor agonist*" or "beta 2 adrenoceptor stimulant*" or "beta 2 adrenoceptor stimulat**" or "beta 2 adrenoceptor stimulator*" or "beta 2 agonist*" or "beta agonist*" or "beta receptor agonist*" or "beta receptor stimulant*" or "beta stimulant" or "beta2 adrenergic receptor stimulat*" or Fenoterol or formoterol or Hexoprenaline or indacaterol or Isoetharine or LABA or LABAs or Metaproterenol or Procaterol or Ritodrine or SABA or SABAs or salmeterol or "Salmeterol Xinafoate" or Terbutaline).ti,ab,hw,kw.	83917
9	exp Cholinergic Antagonists/	215195
10	("acetylcholine antagonist*" or "acetylcholine receptor block*" or "acetylcholine receptor inhibitor*" or "AChR inhibitor" or aclidinium or "aclidinium bromide" or acotiamide or adiphenine or afacifenacin or Alcuronium or "alpha conotoxin MII" or alvameline or alverine or "alverine citrate" or anisodamine or "anti cholinergics" or anticholinergic or anticholinergic* or "anti-cholinergic*" or antimuscarinic* or aprofene or aspaminol or Atracurium or Atropine or atropinic* or azaprophen or belladonna or bellergal or Benactyzine or benzetimide or benzilonium or "benzilylcholine mustard" or benzoquinonium or Benztropine or Biperiden or bornaprine or Butylscopolammonium or buzepide or catestatin or "central anticholinergic" or Chlorisondamine or chlorphenoxamine or cholinolytic* or cimetropium or clidinium or Curare or Cyclopentolate or cycrimine or darifenacin or darotropium or deptropine or desfesoterodine or Dexetimide or dexmecamylamine or "dibutoline sulfate" or Dicyclomine or	400683

	dicycloverine or diethazine or dimevamide or "diphemanil methylsulfate" or drofenine or elantrine or Emepronium or espatropate or Ethidium or "ethylcholine mustard aziridinium" or eucatropine or fenoverine or fenpipramide or fenpiverinium or fesoterodine or fluperlapine or flutropium or furtramine or "Gallamine Triethiodide" or ganglefene or Glycopyrrolate or glycopyrronium or "gsk 202405" or "h cholinoreactive cell*" or hemicholinium or hexahydrodifenidol or hexahydroprocyclidine or hexahydrosiladifenidol or Hexamethonium or hexbutinol or "hexbutinol methiodide" or "hexocyclium metilsulfate" or himbacine or homatropine or "homatropine methyl" or "homatropine terephthalate" or Hyoscyamine or imidafenacin or Ipratropium or isomylamine or "isopropamide iodide" or LAMA or LAMAs or levetimide or lophotoxin or mazaticol or Mecamylamine or mefurtramine or mepenzolate or meptazinol or "meta cholinoreactive cell*" or methantheline or methoctramine or methylatropine or methyllycaconitine or methylscopolamine or metixene or muscarinic* or muscarinolytic* or "nicotine tartrate" or nicotinic* or nuvenzepine or "octatropine methylbromide" or Orphenadrine or otenzepad or oxitropium or oxybutynin or oxyphencyclimine or Oxyphenonium or Pancuronium or "para fluorohexahydrosiladifenidol" or "para fluorohexbutinol" or parapenzolate or "parasympathetic block*" or "parasympathetic inhibitor*" or parasympathicolytic* or parasympatholytic* or parasympatolytic* or Pempidine or penthienate or "Pentolinium Tartrate" or phenglutarimide or Pipecuronium or pipenzolate or piperidolate or piperphenamine or pipethanate or Pirenzepine or piroheptine or "poldine methylsulfate" or pridinol or "pridinol mesilate" or "prifinium bromide" or Procyclidine or profenamine or proglumide or Propantheline or propiverine or "propylbenziloylcholine mustard" or "Propylbenzilylcholine Mustard" or pyrrinol or Quinidine or "Quinuclidinyl Benzilate" or revatropate or revefenacin or rispenzepine or SAMA or SAMAs or Scopolamine or secoverine or silahexocyclium or siltenzepine or sofpironium or solifenacin or "Solifenacin Succinate" or stramonium or sydnofen or tarafenacin or telenzepine or tematropium or temiverine or thiazinamium or "thiazinamium metilsulfate" or thihexinol or "tiemonium iodide" or "tiemonium methylsulfate" or tifenamil or timepidium or Tiotropium or tofenacin or tolterodine or "Tolterodine Tartrate" or tonopan or Toxiferine or tricyclamol or "tridihexethyl chloride" or Trihexyphenidyl or Trimethaphan or triperidene or tripitramine or tropacin or Tropicamide or tropine or "tropine benzoate" or "trospium chloride" or troventol or Tubocurarine or umeclidinium or valethamate or vamicamide or Vecuronium or vedaclidine or zamifenacin or zolenzepine).ti,ab,hw,kw.	
11	exp Phosphodiesterase 4 Inhibitors/	10642
12	(apremilast or arofylline or atizoram or benzafentrine or catramilast or cilomilast or cipamfylline or daxalipram or denbufylline or elbimilast or filaminast or ibudilast or indimilast or lavamilast or nitraquazone or oglemilast or "PDE 4 inhibitor*" or "PDE IV inhibitor*" or "PDE type 4 inhibitor*" or "PDE type IV inhibitor*" or "pde-4 inhibitor*" or "PDE4 inhibitor*" or "phosphodiesterase 4 inhibitor*" or "phosphodiesterase IV inhibitor*" or "phosphodiesterase type 4 inhibitor*" or "phosphodiesterase type IV inhibitor*" or piclamilast or pumafentrine or revamilast or roflumilast or Rolipram or tetomilast or tibenelast or tilivapram or tipelukast or tofimilast or tolafentrine or zardaverine).ti,ab,hw,kw.	12671
13	or/5-12	1192205
14	4 and 13	38943
15	3 or 14	67111
16	exp meta analysis/	229890
17	exp "systematic review"/	165306
18	((meta adj analys*) or (systematic* adj3 review*)).ti,ab,hw,kw,pt.	589817
19	16 or 17 or 18	589821
20	15 and 19	2911
21	limit 20 to (editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media	161

	or webcasts) [Limit not valid in Embase,CDSR,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	
22	20 not 21	2750
23	from 15 keep 41670-41728	59
24	22 or 23	2809
25	remove duplicates from 24	2077

Part 2

Database(s): Embase 1988 to 2018 Week 16, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 11, 2018, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search Strategy:

#	Searches	Results
1	("chronic airflow disease*" or "chronic airflow disorder*" or "chronic airflow limitation*" or "chronic airflow obstruction*" or "chronic airway disease*" or "chronic airway disorder*" or "chronic airway limitation*" or "chronic airway obstruction*" or "chronic bronchitis" or "chronic obstructive airflow disease*" or "chronic obstructive airflow disorder*" or "chronic obstructive airway disease*" or "chronic obstructive airway disorder*" or "chronic obstructive bronchitis" or "chronic obstructive bronchopulmonary disease*" or "chronic obstructive broncho-pulmonary disease*" or "chronic obstructive bronchopulmonary disorder*" or "chronic obstructive broncho-pulmonary disorder*" or "chronic obstructive lung disease*" or "chronic obstructive lung disorder*" or "chronic obstructive pulmonary disease*" or "chronic obstructive pulmonary disorder*" or "chronic obstructive respiratory disease*" or "chronic obstructive respiratory disorder*" or coad or copd or emphysema or "obstructive lung disease" or "obstructive lung disorder*" or "obstructive pulmonary disease*" or "obstructive pulmonary disorder*" or "obstructive pulmonary tract disease*" or "obstructive pulmonary tract disorder*" or "obstructive respiratory disease*" or "obstructive respiratory disorder*" or "obstructive respiratory tract disease*" or "obstructive respiratory tract disorder*").ti,ab,hw,kw.	248757
2	exp Antibiotic Prophylaxis/	39823
3	exp Anti-Bacterial Agents/	3061033
4	exp antibiotic agent/	986815
5	("1 methylmocimycin*" or "11 deoxydaunorubicin*" or "14 hydroxyclarithromycin*" or "19 deformyl 4 deoxydesmycosin*" or "19 deformyldesmycosin*" or "2 acetylerythromycin*" or "2 fluoroidarubicin*" or "2 n ethylnetilmicin*" or "2 pyrrolinodoxorubicin*" or "21 aminoepothilone B" or "3 3 cyanomorpholino 3 deaminodoxorubicin*" or "3 deamino 2 fluoro 3 hydroxydoxorubicin 14 pimelate" or "3 deamino 3 morpholinodoxorubicin*" or "3 deamino 3 morpholinooxaunomycin*" or "4 demethoxy 11 deoxydaunomycinone" or "4 demethoxydaunomycinone" or "4 demethoxydoxorubicin*" or "4 deoxydesmycosin*" or "4 iodoesorubicin*" or "5 iminodaunorubicin*" or "6 n ethylnetilmicin*" or "6beta iodopenicillanic acid" or "9 deacetyl 9 methylidarubicin*" or "9 deoxydoxorubicin*" or "9 dihydroerythronolide A" or "a 102395" or "a 10255" or "a 10947" or "a 130b" or "a 192411" or "a 63075" or abkhazomycin* or abyssomicin* or acetomycin* or acetylspiramycin* or aclacinomycin* or aclarubicin* or actagardin* or actaplanin* or actinorhodine or "aculeacin A" or aculeximycin* or adicillin* or aditoprim or adriamycinone or agglomerin* or aklavinone or alafosfalin* or Alamethicin* or albocycline or aldecalmycin* or aldoxorubicin* or alisamycin* or allicin* or almecillin* or "alpha defensin*" or ambruticin* or Amdinocillin* or amfomycin* or Amikacin* or aminoglycoside* or aminopenicillin* or "Aminosalicylic Acid" or Amoxicillin* or "Amphotericin B" or Ampicillin* or amrubicin* or "angucycline derivative" or anhydrochlortetracycline or anhydroepitetracycline or anhydrotetracycline or anidulafungin* or Anisomycin* or annamycin* or ansamitocin* or "ansamycin derivative" or anthracycline* or anthracyclinone* or antibacterial* or "anti-bacterial*" or antibiotic* or "anti-biotic*" or "antimicrobial cationic peptide*" or Antimycin* or antimycobacterial* or "anti-mycobacterial*" or Antitreponemal* or "Anti-treponemal*" or Antitubercular* or "Anti-tubercular*" or apalcillin* or aplasmomycin* or "aplysianin E" or apramycin* or aristeromycin* or Arsphenamine or aspoxicillin* or astromicin* or asukamycin* or "atpenin B" or auricularum or Aurodox or aurograb or avibactam or avilamycin* or avoparcin* or azidamfenicol or azidocillin* or Azithromycin* or Azlocillin* or Aztreonam or "aztreonam lysine" or azurocidin* or bacampicillin* or Bacitracin* or bacmecillinam or bactenecin* or bacteriocid* or Bacteriocin* or bafilomycin* or balhimycin* or "baliz 2" or Bambermycin* or baquiloprim or "barminomycin I" or baycuten or beauvericin*	2430080

or beroline or berubicin* or berythromycin* or "beta defensin*" or betafectin* or "beta-Lactam*" or "betaLactamase Inhibitor*" or "beta-Lactamase Inhibitor*" or betamipron or bialaphos or biapenem or bicozamycin* or "biphenomycin A" or bluensomycin* or bombinin* or "Bongkrekic Acid" or boromycin* or borrelidin* or "Brefeldin A" or brilacidin* or brobactam or butalactin* or butirosin* or cadazolid or Calcimycin* or Candicidin* or Capreomycin* or carbacephem or carbadox or carbapenem or "carbazomycin A" or Carbenicillin* or carbomycin* or Carfecillin* or carindacillin* or carubicin* or carumonam or caspofungin* or cathelicidin* or cecropin* or cefacetrile or Cefaclor or Cefadroxil or cefalexin* or cefaloglycin* or cefaloram or cefaloridine or cefalotin* or Cefamandole or cefapirin* or Cefatrizine or cefazaflur or cefazedone or Cefazolin* or cefbuperazone or cefcanel or cefcapene or cefclidin* or cefdaloxime or cefdinir or cefditoren or cefepime or cefetamet or cefetecol or cefilavancin* or Cefixime or cefluprenam or cefmatilen or Cefmenoxime or Cefmetazole or cefminox or cefodizime or Cefonicid or Cefoperazone or ceforanide or cefoselis or Cefotaxime or Cefotetan or Cefotiam or cefovecin* or Cefoxitin* or cefozopran or cefpimizole or cefpiramide or cefpirome or cefpodoxime or cefprozil or cefquinome or cefradine or cefroxadine or Cefsulodin* or ceftaroline or Ceftazidime or cefteram or ceftezole or ceftibuten or ceftiofur or Ceftizoxime or ceftobiprole or ceftolozane or Ceftriaxone or Cefuroxime or cefuzonam or Cephacetrile or Cephalexin* or Cephaloglycin* or Cephaloridine or cephalosporin* or Cephalothin* or cephamycin* or Cephapirin* or Cephradine or chalcomycin* or Chloramphenicol* or chloroorienticin* or chloropolysporin* or chlorothricin* or chlorothricolide or Chlortetracycline or "chymotrypsin trypsin*" or ciadox or "cilastatin plus imipenem" or "cinerubin A" or "cinerubin B" or cinoquidox or Ciprofloxacin* or cirramycin* or Citrinin* or Clarithromycin* or "clavulanate potassium" or "Clavulanic Acid*" or Clindamycin* or clomocycline or Cloxacillin* or colicin* or colistimethate or Colistin* or "concanamycin A" or coumamidine or coumamycin* or "cp 63956" or cryptosporin* or Cyclacillin* or cycloheximide or Cycloserine or cystargin* or "cytarabine plus daunorubicin*" or cytovaricin* or dactimicin* or Dactinomycin* or dalbaheptide or dalbavancin* or dalfopristin* or "damavaricin Fc pentyl ether" or Daptomycin* or daunomycinone or daunorubicin* or daunorubicinol or "deacetoxycephalosporin C" or deacetylcefotaxime or "deacetylcephalosporin C" or dealanylalahopcin* or decaplanin* or dechloroeremomycin* or decilorubicin* or defensin* or Demeclocycline or dermaseptin* or dermcidin* or dermostatin* or desmycosin* or detorubicin* or Diarylquinoline* or Dibekacin* or Dicloxacillin* or dihydrostreptomycin* or Diketopiperazines or dimethylchlortetracycline or dioxidine or dirithromycin* or Distamycin* or "ditrisarubicin B" or doripenem or doxorubicin* or doxorubicinol or Doxycycline or drosocin* or echinocandin* or Echinomycin* or Edeine or efepristin* or efrotomycin* or emimycin* or endusamycin* or enniatin* or Enoxacin* or Enviomycin* or eperezolid or epetraborole or epicillin* or epidermin* or epiderstatin* or epiroprim or epirubicin* or epirubicinol or epitetracycline or epothilone* or "epsilon rhodomycinone" or eravacycline or eremomycin* or ertapenem or Erythromycin* or erythromycylamine or erythronolide* or esorubicin* or Ethambutol or Ethionamide or ethylhydrocupreine or etimicin* or evernimicin* or everninomicin* or faeriefungin* or fidaxomicin* or Filipin* or "fleroxacin deacetylcefotaxime ester" or flomoxef or flopristin* or florfenicol or Floxacillin* or flucloxacillin* or flumoxil or Fluoroquinolone* or flurithromycin* or fomidacillin* or fortimicin* or Fosfomycin* or fosmidomycin* or Framycetin* or fropenem or fungichromin* or furaquinocin* or furazidin* or "furazolium chloride" or furbenicillin* or fusafungine or "fusidate sodium" or "Fusidic Acid" or fuzlocillin* or galarubicin* or gallidermin* or gamithromycin* or ganefromycin* or "ge 2270a" or gentamicin* or gepotidacin* or globomycin* or gloximonam or "glycylcycline derivative" or "gonadorelin6 dextro lysine 2 pyrrolinodoxorubicin*" or "goniodomin A" or Gramicidin* or granulysin* or grisein* or guamecycline or habekacin* or hamycin* or hatomamicin* or hedamycin* or heliomycin* or hepcidin* or hetacillin* or hexacycline or hidamicin* or "histatin 5" or histatin* or hygromycin* or hymeglusin* or hypothemycin* or iclaprim or idarubicin* or idarubicinol or ikarugamycin* or "imidacloprid plus moxidectin*" or Imipenem or indolicidin* or inostamycin* or iseganan or isepamicin* or Isoniazid or "isopenicillin N" or "isoswinholide A" or istamycin* or "iturin A" or ixabepilone or Josamycin* or "k 252a" or kalafungin* or Kanamycin* or kanendomycin* or kasugamycin* or kelfiprim or ketolide or kidamycin* or kinamycin* or Kitasamycin* or "l 156602" or "l 733560" or "l 786392" or lactacystin* or

Lactams or lactivicin* or "lactocin S" or lactococcin* or lactoferricin* or ladirubicin* or laidlomycin* or lancovutide or lankamycin* or lanopepden or lanthiopeptin* or lantibiotic or Lasalocid or latamoxef or lavanducyanin* or lefamulin* or lenampicillin* or lenapenem or lenoremycin* or Leprostatic* or "leucinostatin A" or "leucinostatin B" or Leucomycin* or leurubicin* or Levofloxacin* or lexithromycin* or "lff 571" or Lincomycin* or lincosamide* or Linezolid or linopristin* or lividomycin* or "lonomycin A" or loracarbef or lotilibcin* or Lucensomycin* or lydicamycin* or Lymecycline or lysobactin* or lysocellin* or lysostaphin* or macrolide or magainin* or malyngolide or manumycin* or maridomycin* or "mdl 62208" or "mdl 62211" or mecillinam or meclocycline or megacin* or megalomicin* or Mepartricin* or meropenem or mersacidin* or metacycline or metampicillin* or Methacycline or Methicillin* or "methylenomycin A" or "methylenomycin B" or methymycin* or methynolide or meticillin* or Mezlocillin* or "microcin b17" or "microcin J25" or micronomicin* or midecamycin* or mideplanin* or "mikamycin B" or Mikamycin* or "milbemycin oxime" or milbemycin* or Minocycline or Miocamycin* or miokamycin* or miporamicin* or miraxid or mocimycin* or "moenomycin A" or monensin* or "monobactam derivative" or Moxalactam or moxidectin* or "ms 8209" or Mupirocin* or mureidomycin* or murepavadin* or mycinamicin* or Mycobacillin* or mycolog or mycoticin* or myxothiazol or "n benzyldoxorubicin 14 valerate" or "n trifluoroacetyldoxorubicin*" or Nafcillin* or "Nalidixic Acid" or narasin* or Natamycin* or neamine or nebacetin* or Nebramycin* or negamycin* or nemadectin* or nemorubicin* or Neomycin* or neosporin* or Netilmicin* or Netropsin* or niddamycin* or Nigericin* or Nisin* or nitrocefin* or nitrosochloramphenicol or "nocardicin A" or "nocardicin E" or "nocardicinic acid derivative*" or Norfloxacin* or nosiheptide or nourseothricin* or Novobiocin* or "nvb 302" or nybomycin* or Nystatin* or "oasomycin A" or obelmycin* or Ofloxacin* or olaquindox or oleandolide or Oleandomycin* or oligomycin* or omadacycline or omiganan or optocillin* or "orienticin A" or orientiparcin* or oritavancin* or oropivalone or Oxacillin* or oxaunomycin* or "Oxolinic Acid" or Oxytetracycline or paldimycin* or panipenem or pardaxin* or Paromomycin* or patulin* or pediazole or pediocin* or Pefloxacin* or penamecillin* or penethamate or "Penicillanic Acid" or "Penicillic Acid" or penicillin* or "penicilloic acid" or pentalenolactone or pentisomicin* or peptaibol or pexiganan or "pf 708093" or phenelfamycin* or pheneticillin* or phleomycin* or pikromycin* or "Pipemidic Acid" or Piperacillin* or pirarubicin* or pirazmonam or pirlimycin* or Pivampicillin* or pivmecillinam or platensimycin* or plazomicin* or plectasin* or pleuromutilin* or pluramycin* or pneumocandin* or "polyactin A" or polyfungin* or polymyxin* or "polyoxin B" or "polyoxin D" or polysporin* or polytrim or posizolid or "pr 39" or Pristinamycin* or Prodigiosin* or prohepcidin* or propicillin* or protegrin* or Prothionamide or prothracarcin* or "pseudomonic acid" or Pyrazinamide or pyrromycinone or pyrroxamycin* or quinacillin* or quinomycin* or quinupristin* or radezolid or radicicol or ramoplanin* or ranalexin* or ranbezolid or razupenem or retacillin* or retapamulin* or "rhodomycin A" or Ribostamycin* or Rifabutin* or Rifampin* or Rifamycin* or rimocidin* or Ristocetin* or ritipenem or "ritipenem acoxil" or rodorubicin* or roflamycoin* or rokitamycin* or Rolitetracycline or rosaramicin* or Roxarsone or Roxithromycin* or ruboxyl or Rutamycin* or sabarubicin* or sagopilone or sanfetrinem or sarecycline or "simaomicin alpha" or "simocyclinone D8" or Sirolimus or "sisomicin sulfate" or Sisomicin* or "skf 104662" or sofradex or Spectinomycin* or "spinosyn A" or Spiramycin* or squalamine or stigmatellin* or streptoduocin* or Streptogramin* or streptolydigin* or Streptomycin* or streptothricin* or streptotriad or Streptovaricin* or streptovirudin* or "streptovitacin A" or stubomycin* or subtilin* or Sulbactam or Sulbenicillin* or Sulfamerazine or Sulfamethoxypyridazine or sulfazecin* or sulopenem or sultamicillin* or surfactin* or surotomycin* or "swinholide A" or "swinholide B" or tachyplesin* or Talampicillin* or tameticillin* or tazobactam or tebipenem or tedizolid or Teicoplanin* or teixobactin* or telavancin* or temocillin* or terdecamycin* or tetracyclin* or Tetracycline or tetramycin* or tetronasin* or tetronomycin* or tetroxoprim or Thiamphenicol or Thienamycin* or Thioacetazone or thiolactomycin* or "thionin peptide" or thiopeptin* or thiophenoxycefalotin* or Thiostrepton or tiamulin* or "tibezonium iodide" or Ticarcillin* or tigecycline or tigemonam or tildipirosin* or tilmicosin* or timentin* or tirandamycin* or tizoxanide or tobicillin* or Tobramycin* or tolramycin* or tomopenem or toyocamycin* or tresaderm or tribactam or trichomycin* or "trichostatic acid" or "trichostatin A" or trimethoprim* or "trinem derivative" or

	"triostin A" or triplopen or trisep or Troleandomycin* or trospectomycin* or tuftsin* or tulathromycin* or Tunicamycin* or tutofusin* or Tylosin* or tylvalosin* or Tyrocidine or Tyrothricin* or "u 78608" or "uk 69753" or unphenelfamycin* or "urdamycin C" or "urdamycin D" or "urdamycin H" or ureidopenicillin* or urobiotic or "vacidin A" or validamycin* or Valinomycin* or valnemulin* or valrubicin* or Vancomycin* or venturicidin* or vernamycin* or "violamycin B1" or Viomycin* or "virginiae butanolide A" or "virginiae butanolide C" or "virginiamycin M" or "virginiamycin S" or Virginiamycin* or "viriplanin A" or viscosin* or volpristin* or "ws 9659 b" or "zibrofusidic acid" or zineryt or "zoptarelin doxorubicin*" or zorbamycin* or zorubicin*).mp.	
6	or/2-5	3703559
7	1 and 6	28719
8	exp meta analysis/	229890
9	exp "systematic review"/	165306
10	((meta adj analys*) or (systematic* adj3 review*)).ti,ab,hw,kw,pt.	589817
11	8 or 9 or 10	589821
12	7 and 11	879
13	limit 12 to (editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,CDSR,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	64
14	12 not 13	815
15	from 7 keep 23035-23104	70
16	14 or 15	885
17	remove duplicates from 16	767

Part 3

Database(s): Embase 1988 to 2018 Week 16, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 11, 2018, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search Strategy:

#	Searches	Results
1	("chronic airflow disease*" or "chronic airflow disorder*" or "chronic airflow limitation*" or "chronic airflow obstruction*" or "chronic airway disease*" or "chronic airway disorder*" or "chronic airway limitation*" or "chronic airway obstruction*" or "chronic bronchitis" or "chronic obstructive airflow disease*" or "chronic obstructive airflow disorder*" or "chronic obstructive airway disease*" or "chronic obstructive airway disorder*" or "chronic obstructive bronchitis" or "chronic obstructive bronchopulmonary disease*" or "chronic obstructive broncho-pulmonary disease*" or "chronic obstructive bronchopulmonary disorder*" or "chronic obstructive broncho-pulmonary disorder*" or "chronic obstructive lung disease*" or "chronic obstructive lung disorder*" or "chronic obstructive pulmonary disease*" or "chronic obstructive pulmonary disorder*" or "chronic obstructive respiratory disease*" or "chronic obstructive respiratory disorder*" or coad or copd or emphysema or "obstructive lung disease" or "obstructive lung disorder*" or "obstructive pulmonary disease*" or "obstructive pulmonary disorder*" or "obstructive pulmonary tract disease*" or "obstructive pulmonary tract disorder*" or "obstructive respiratory disease*" or "obstructive respiratory disorder*" or "obstructive respiratory tract disease*" or "obstructive respiratory tract disorder*").ti,ab,hw,kw.	248757
2	exp Benzodiazepines/	223779
3	(Alprazolam or arfendazam or benzodiazepin or benzodiazepine* or Benzodiazepinone* or bromazepam or camazepam or Chlordiazepoxide or cinolazepam or clobazam or clonazepam or clorazepate or "Clorazepate Dipotassium" or "clorazepate potassium" or dealkylflurazepam or delorazepam or demoxepam or devazepide or diazepam or doxefazepam or Estazolam or fludiazepam or flunitrazepam or flurazepam or flutoprazepam or fosazepam or gidazepam or girisopam or halazepam or loflazepate or lorazepam or lormetazepam or lotrafiban or meclonazepam or Medazepam or metaclazepam or Midazolam or nastorazepide or nerisopam or netazepide or nimetazepam or nitrazepam or nitrosochlordiazepoxide or norchlordiazepoxide or norclobazam or nordazepam or norfludiazepam or norflunitrazepam or oxazepam or phenazepam or pinazepam or prazepam or quazepam or "ro 7 0213" or talampanel or tampramine or tarazepide or temazepam or tetrazepam or tibezonium or tifluadom or tofisopam or tomaymycin or Triazolam or tuclazepam or uxepam).ti,ab,hw,kw.	271678
4	exp Home Care Services/	101515
5	(((domestic or home or domiciliary) adj3 (residence or residences or setting or settings or care or nurs* or help or service* or treatment* or therap* or "respiratory care" or "respiratory treatment*" or "respiratory therap*" or "respiratory service*" or "respiratory assist*" or ventilat*)) or "assisted living" or homecare).ti,ab,hw,kw.	209664
6	"nursing home*".ti,ab,hw,kw.	90908
7	(4 or 5) not 6	151038
8	exp Respiration, Artificial/	225415
9	(((((respiration* or respiratory or breathing) adj3 (assist* or controlled or mechanical)) or (facial or face or nasal)) adj3 mask*) or "artificial respiration*" or BiPAP or CPAP or "Fluidic Breathing Assister" or HMV or IPPB or IPPV or NIAV or NIV or NPPV or "Oxygen Regulator*" or PAP or PAV or "Portable Oxygen" or "Positive Airway Pressure*" or "positive end-expiratory pressure*" or "positive pressure*" or respirator or respirators or "Respiratory insufficiency" or Tracheostom* or ventilation or ventilator*).ti,ab,hw,kw.	529399
10	8 or 9	549586
11	7 and 10	6909

12	2 or 3 or 11	280786
13	1 and 12	3036
14	exp meta analysis/	229890
15	exp "systematic review"/	165306
16	((meta adj analys*) or (systematic* adj3 review*)).ti,ab,hw,kw,pt.	589817
17	14 or 15 or 16	589821
18	13 and 17	119
19	limit 18 to (editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,CDSR,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	3
20	18 not 19	116
21	from 13 keep 2384	1
22	20 or 21	117
23	remove duplicates from 22	97

Part 4

Database(s): Embase 1988 to 2018 Week 16, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 11, 2018, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search Strategy:

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1	("chronic airflow disease*" or "chronic airflow disorder*" or "chronic airflow limitation*" or "chronic airflow obstruction*" or "chronic airway disease*" or "chronic airway disorder*" or "chronic airway limitation*" or "chronic airway obstruction*" or "chronic bronchitis" or "chronic obstructive airflow disease*" or "chronic obstructive airflow disorder*" or "chronic obstructive airway disease*" or "chronic obstructive airway disorder*" or "chronic obstructive bronchitis" or "chronic obstructive bronchopulmonary disease*" or "chronic obstructive broncho-pulmonary disease*" or "chronic obstructive bronchopulmonary disorder*" or "chronic obstructive broncho-pulmonary disorder*" or "chronic obstructive lung disease*" or "chronic obstructive lung disorder*" or "chronic obstructive pulmonary disease*" or "chronic obstructive pulmonary disorder*" or "chronic obstructive respiratory disease*" or "chronic obstructive respiratory disorder*" or coad or copd or emphysema or "obstructive lung disease" or "obstructive lung disorder*" or "obstructive pulmonary disease*" or "obstructive pulmonary disorder*" or "obstructive pulmonary tract disease*" or "obstructive pulmonary tract disorder*" or "obstructive respiratory disease*" or "obstructive respiratory disorder*" or "obstructive respiratory tract disease*" or "obstructive respiratory tract disorder*").ti,ab,hw,kw.	248757
2	exp Adrenal Cortex Hormones/	1085572
3	exp corticosteroid/	710384
4	exp corticosteroid therapy/	41274
5	("adrenal cortex hormone*" or "adrenal cortex steroid*" or "adrenal cortical hormone*" or "adrenal cortical steroid*" or "adrenal steroid*" or "adreno cortical steroid*" or "adreno corticosteroid*" or "adrenocortical hormone*" or "adrenocortical steroid*" or adrenocorticosteroid* or adreson or alclometasone or aldosterone or algestone or "algestone acetonide" or amcinonide or amelometasone or beclometasone or budesonide or butixocort or chloroprednisone or ciclesonide or ciprocinonide or clioquinol or clobetasol or clobetasone or clocortolone or cloprednol or "cortical steroid*" or corticalsteroid* or "cortico steroid*" or corticoid* or corticosteroid* or corticosterone or corticotherap* or cortifair or cortisol or cortisone or cortivazol or cortril or deflazacort or dehydrocorticosterone or dehydrocortisone or deoxycorticosterone or dermocorticosteroid* or dexamethasone or diflorasone or diflucortolone or difluprednate or domoprednate or drocinonide or dutimelan or epicortisol or "etiprednol dicloacetate" or fluclorolone or fludrocortisone or fludroxycortide or flumetasone or flumoxonide or flunisolide or fluocinolone or fluocinonide or fluocortin or fluocortolone or fluorometholone or fluprednidene or fluprednisolone or fluticasone or formocortal or "formoterol fumarate" or Glucocorticoid* or glucocorticoidsteroid* or glucocorticosteroid* or glucocortoid* or glycocorticoid* or glycocorticosteroid* or halcinonide or halometasone or halopredone or hydrocortisone or "hydroxy norcorticosterone" or hydroxycorticoid* or hydroxycorticosteroid* or hydroxycorticosterone or hydroxydeoxycorticosterone or hydroxyhydrocortisone or "icometasone enbutate" or isoflupredone or itrocinonide or "locicortolone dicibate" or "lorinden a" or "lorinden t" or loteprednol or mazipredone or medrysone or meprednisone or mineralcorticosteroid* or mineralocorticosteroid* or minerocorticoid* or mometasone or nicocortonide or nivacortol or nordeoxycorticosterone or oropivalone or oxohydrocortisone or oxycorticosteroid* or paramethasone or prednisolone or prednisone or pregnenolone or procinonide or promestriene or resocortol or rimexolone or rofleponide or steroid* or tetrahydrodeoxycorticosterone or ticabesone or timobesone or tipredane or tixocortol or	1707747

	triamcinolone or "ulobetasol propionate" or uniderm or zoticasone).ti,ab,hw,kw.	
6	exp Expectorants/	30553
7	(Acetylcysteine or Ambroxol or aminophylline or Bromhexine or bron or cafedrine or Carbocysteine or diprophylline or etofylline or eucalyptus or expectorant* or fudosteine or guaiacol or "guaiacol carbonate" or guaietolin or Guaifenesin or guaifylline or "iodinated glycerol" or ipecac or mucolytic* or "Potassium Citrate" or "primula flower" or stepronin or "stepronin lysine" or sulfoguaiacol or tipepidine or ulogesic).ti,ab,hw,kw.	91107
8	exp narcotic analgesic agent/	243598
9	exp Analgesics, Opioid/	347494
10	(acetorphine or acetylcodeine or acetylmethadol or Alfentanil or Alphaprodine or anileridine or apadoline or azidomorphine or benzhydrocodone or bezitramide or bremazocine or "Brompton mixture" or Buprenorphine or Butorphanol or ciramadol or cocodamol or Codeine or codydramol or conorfone or cyclazocine or Dextromoramide or Dextropropoxyphene or dextrorphan or dezocine or diamorphine or diconal or dihydrocodeine or dihydroetorphine or Dihydromorphine or dimethylthiambutene or Diphenoxylate or dipipanone or enadoline or eptazocine or ethylketazocine or Ethylketocyclazocine or Ethylmorphine or etonitazene or Etorphine or etoxeridine or faxeladol or Fentanyl or furethidine or gelonida or Heroin or Hydrocodone or isalmadol or isomethadone or ketazocine or ketobemidone or ketogan or kyotorphin or lefetamine or levacetylmethadol or levomethadone or Levorphanol or Meperidine or Meptazinol or metazocine or Methadone or "Methadyl Acetate" or methylsamidorphan or Morphine or "morphinomimetic agent*" or "morphinomimetic drug*" or morphinone or Nalbuphine or narcotic* or nicocodine or nicomorphine or noracymethadol or norbuprenorphine or nordextropropoxyphene or normorphine or norpethidine or norpropoxyphene or "o nortramadol" or oliceridine or opiate or Opiate* or opioid* or Opium or oripavine or Oxycodone or Oxymorphone or pentamorphone or Pentazocine or pethidine or phenadoxone or phenaridine or Phenazocine or phencyclidine or Phenoperidine or picenadol or piminodine or Pirinitramide or piritramide or profadol or Promedol or propiram or sameridine or samidorphan or semorphone or Sufentanil or tapentadol or thebaine or tifluadom or Tilidine or tonazocine or Tramadol or trimeperidine).ti,ab,hw,kw.	525567
11	exp Bronchoscopy/	68088
12	exp lung/su	8000
13	exp Pneumonectomy/	49308
14	("airflow clearance" or "airway clearance" or BLVR or bronchoscop* or ELVR or "lung clearance" or "lung denervation" or LVRS or pneumectom* or pneumonectom* or pneumoresection* or "pulmonary clearance" or "volume reducing" or "volume reduction*").ti,ab,hw,kw.	143837
15	exp Smoking Cessation/	76463
16	((smoking* or tobacco* or cigar* or cigarette* or cigaret*) and (quit* or discontinu* or ceas* or cessation*)).ti,ab,hw,kw.	110813
17	exp Respiratory Therapy/	107010
18	exp exercise/	423706
19	exp Exercise Therapy/	102223
20	exp Breathing Exercises/	8723
21	exp Exercise Movement Techniques/	66908
22	(aerobics or anaerobics or "artificial respiration*" or bicycling or biking or "Chest Wall Oscillation*" or dance or dancing or "endurance training" or exercis* or "Extracorporeal Membrane Oxygen*" or "fitness training" or "inhalation therap*" or isometrics or oxygen or "physical activit*" or "physical exertion" or "postural drain*" or rehab* or "resistance training" or "respiration care*" or "respiration therap*" or "respiratory care*" or "respiratory therap*" or running or "strength training" or swimming or "Tai Chi" or "Tai Ji" or walking or weightlifting	2620447

	or yoga).ti,ab,hw,kw.	
23	exp Nutrition Therapy/	384447
24	(diet or dietary or diets or nutrition* or supplementation or supplements).ti,ab,hw,kw.	1856949
25	exp Influenza Vaccines/	50514
26	exp Pneumococcal Vaccines/	22742
27	exp vaccination/	204458
28	(moniarix or "pcv 13" or pcv13 or "pneu immune" or "pneumo 23" or pneumopur or pneumovax or "pnu immune" or "pnu imune" or "polysaccharide vaccine pneumococcal" or prevenar or prevnar or "streptococcus pneumoniae vaccine" or streptopur or streptorix or synflorix or vaccin*).ti,ab,hw,kw.	702951
29	exp Psychotherapy/	367662
30	exp Cognitive Therapy/	66331
31	exp Cognitive Behavior Therapy/	28661
32	exp Mindfulness/	6317
33	exp Mind-Body Therapies/	90152
34	exp Mentoring/	1557
35	exp Health Promotion/	153501
36	(CBT or coach* or "Cognitive behavioral therap*" or "Cognitive therap*" or "health promotion*" or meditat* or mentor* or "mind body" or mindfulness or psychological or psychosocial or psychotherap*).ti,ab,hw,kw.	1535477
37	exp Self Care/	113331
38	exp Telemedicine/	53304
39	exp Therapy, Computer-Assisted/	67118
40	exp Mobile Applications/	8595
41	("action plan*" or android or app or apps or ehealth or "e-health" or internet or ipad* or iphone* or mhealth or "m-health" or "mobile app*" or "mobile health" or "mobile technolog*" or "portable computer*" or "portable electronic app*" or "portable software app*" or "remote consultation*" or "self care" or "self help" or "self management" or "self treatment" or "smart phone*" or smartphone* or "tablet computer*" or teleconsultation* or "tele-consultation*" or telehealth or "tele-health" or telemedicine or "tele-medicine" or teletherap* or "tele-therap*" or web).ti,ab,hw,kw.	603033
42	exp "Delivery of Health Care, Integrated"/	20570
43	exp Acupuncture/	38261
44	exp Complementary Therapies/	250389
45	exp Electric Stimulation Therapy/	260840
46	(acupuncture or agent* or "alternative medicine" or "care package*" or chemotherap* or "complementary medicine" or drug* or "electric stimulation*" or holistic or "integrated care" or "integrated health care" or "integrated healthcare" or intervention* or manag* or medication* or "muscle stimulation*" or operat* or pharmacotherap* or procedure* or reconstruction* or repair* or resect* or surg* or therap* or treat* or wellness).ti,ab,hw,kw.	26377389
47	or/2-46	30049403
48	1 and 47	182842
49	exp meta analysis/	229890
50	exp "systematic review"/	165306
51	((meta adj analys*) or (systematic* adj3 review*)).ti,ab,hw,kw,pt.	589817
52	49 or 50 or 51	589821
53	48 and 52	5613

54	limit 53 to (editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,CDSR,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	261
55	53 not 54	5352
56	from 48 keep 121215-121366	152
57	55 or 56	5504
58	remove duplicates from 57	3991

Scopus

Part 1

1 TITLE-ABS-KEY("chronic airflow disease*" OR "chronic airflow disorder*" OR "chronic airflow limitation*" OR "chronic airflow obstruction*" OR "chronic airway disease*" OR "chronic airway disorder*" OR "chronic airway limitation*" OR "chronic airway obstruction*" OR "chronic bronchitis" OR "chronic obstructive airflow disease*" OR "chronic obstructive airflow disorder*" OR "chronic obstructive airway disease*" OR "chronic obstructive airway disorder*" OR "chronic obstructive bronchitis" OR "chronic obstructive bronchopulmonary disease*" OR "chronic obstructive broncho-pulmonary disease*" OR "chronic obstructive bronchopulmonary disorder*" OR "chronic obstructive broncho-pulmonary disorder*" OR "chronic obstructive lung disease*" OR "chronic obstructive lung disorder*" OR "chronic obstructive pulmonary disease*" OR "chronic obstructive pulmonary disorder*" OR "chronic obstructive respiratory disease*" OR "chronic obstructive respiratory disorder*" OR coad OR copd OR emphysema OR "obstructive lung disease" OR "obstructive lung disorder*" OR "obstructive pulmonary disease*" OR "obstructive pulmonary disorder*" OR "obstructive pulmonary tract disease*" OR "obstructive pulmonary tract disorder*" OR "obstructive respiratory disease*" OR "obstructive respiratory disorder*" OR "obstructive respiratory tract disease*" OR "obstructive respiratory tract disorder*")

2 TITLE-ABS-KEY(abediterol OR acefylline OR "acefylline clofibrol" OR "acefylline piperazine" OR "aclidinium bromide" OR "adrenalin hydrogen tartrate" OR Adrenomedullin OR Albuterol OR ambuphylline OR Aminophylline OR antibronchospastic OR arformoterol OR Atropine OR bambuterol OR bamifylline OR baralgin OR batefenterol OR bitolterol OR "bitolterol mesilate" OR "bronchial dilating" OR "bronchial-dilating" OR bronchodilatant* OR "broncho-dilatant*" OR bronchodilatating OR "broncho-dilatating" OR bronchodilatator* OR "broncho-dilatator*" OR bronchodilating OR "broncho-dilating" OR bronchodilator* OR "broncho-dilator*" OR broncholytic* OR broncholytica OR bronchospasmolytic OR broxaterol OR Budesonide OR carbuterol OR carmoterol OR "choline theophyllinate" OR Clenbuterol OR clorprenaline OR Colforsin OR Cromakalim OR danirixin OR "darotropium bromide" OR dilator* OR diprophylline OR ditec OR doxofylline OR Dyphylline OR elubrixin OR enprofylline OR ephedrine OR "ephedrine sulfate" OR Epinephrine OR eprozinol OR espatropate OR etafedrine OR etamiphyllin OR "etamiphyllin camsilate" OR etanterol OR etofylline OR Fenoterol OR fenspiride OR Fluticasone OR "flutropium bromide" OR formoterol OR "Formoterol Fumarate" OR furafylline OR glycopyrronium OR "gsk 159802" OR "gsk 597901" OR guaifylline OR "gw 678007" OR Hexoprenaline OR Hyoscyamine OR ibuterol OR "ilmetropium iodide" OR imoxiterol OR indacaterol OR inhaler* OR Ipratropium OR "ipratropium bromide" OR isbufylline OR isoetarine OR "isoetarine mesylate" OR Isoetharine OR isoprenaline OR Isoproterenol OR Khellin OR laprafylline OR levalbuterol OR mabuterol OR marax OR Metaproterenol OR methoxyphenamine OR milveterol OR "n methylmequitazine" OR naminterol OR neobiphyllin OR nestifylline OR "Nitric Oxide" OR olodaterol OR orciprenaline OR "oxitropium bromide" OR "oxyphenonium bromide" OR pibaxizine OR pirbuterol OR "pirbuterol acetate" OR pneumodilator OR Procaterol OR protokylol OR proxyphylline OR Pseudoephedrine OR racephedrine OR Racepinephrine OR reproterol OR rimiterol OR "ru 45703" OR salbutamol OR "salbutamol sulfate" OR salmefamol OR salmeterol OR "Salmeterol Xinafoate" OR sibenadet OR "S-Nitrosoglutathione" OR "S-Nitrosothiols" OR soterenol OR tazifylline OR Terbutaline OR Theobromine OR Theophylline OR "theophylline sodium glycinate" OR thiazinamium OR "thiazinamium metilsulfate" OR Tiotropium OR Tretoquinol OR "tretoquinol derivative" OR trimetaquinol OR tulobuterol OR "uk 432097" OR Umeclidinium OR vephylline OR verofylline OR vilanterol OR "vilanterol trifenatate" OR zindotrine)

3 TITLE-ABS-KEY("adrenergic beta 2 agonist*" OR "adrenergic beta 2 receptor agonist*" OR "adrenergic beta2 agonist*" OR "adrenergic beta-2 agonist*" OR "adrenergic beta-2 receptor agonist*" OR "adrenergic beta2-agonist*" OR Albuterol OR "beta 2 adrenergic agent*" OR "beta 2 adrenergic agonist*" OR "beta 2 adrenergic receptor agonist*" OR "beta 2 adrenergic receptor stimulant*" OR "beta 2 adrenergic receptor stimulat*" OR "beta 2 adrenergic receptor stimulator*" OR "beta 2 adrenergic stimulant*" OR "beta 2 adrenergic stimulat*" OR "beta 2 adrenergic

stimulator*" OR "beta 2 adrenoceptor agonist*" OR "beta 2 adrenoceptor stimulant*" OR "beta 2 adrenoceptor stimulat**" OR "beta 2 adrenoceptor stimulator*" OR "beta 2 agonist*" OR "beta agonist*" OR "beta receptor agonist*" OR "beta receptor stimulant*" OR "beta stimulant" OR "beta2 adrenergic receptor stimulat*" OR Fenoterol OR formoterol OR Hexoprenaline OR indacaterol OR Isoetharine OR LABA OR LABAs OR Metaproterenol OR Procaterol OR Ritodrine OR SABA OR SABAs OR salmeterol OR "Salmeterol Xinafoate" OR Terbutaline)

4 TITLE-ABS-KEY("acetylcholine antagonist*" OR "acetylcholine receptor block*" OR "acetylcholine receptor inhibitor*" OR "AChR inhibitor" OR aclidinium OR "aclidinium bromide" OR acotiamide OR adiphenine OR afacifenacin OR Alcuronium OR "alpha conotoxin MII" OR alvameline OR alverine OR "alverine citrate" OR anisodamine OR "anti cholinergics" OR anticholinergic OR anticholinergic* OR "anti-cholinergic*" OR antimuscarinic* OR aprofene OR aspaminol OR Atracurium OR Atropine OR atropinic* OR azaprophen OR belladonna OR bellergal OR Benactyzine OR benzetimide OR benzilonium OR "benzilylcholine mustard" OR benzoquinonium OR Benztropine OR Biperiden OR bornaprine OR Butylscopolammonium OR buzepide OR catestatin OR "central anticholinergic" OR Chlorisondamine OR chlorphenoxamine OR cholinolytic* OR cimetropium OR clidinium OR Curare OR Cyclopentolate OR cycrimine OR darifenacin OR darotropium OR deptropine OR desfesoterodine OR Dexetimide OR dexmecamylamine OR "dibutoline sulfate" OR Dicyclomine OR dicycloverine OR diethazine OR dimevamide OR "diphemanil methylsulfate" OR drofenine OR elantrine OR Emepronium OR espatropate OR Ethidium OR "ethylcholine mustard aziridinium" OR eucatropine OR fenoverine OR fenpipramide OR fenpiverinium OR fesoterodine OR fluperlapine OR flutropium OR furtramine OR "Gallamine Triethiodide" OR ganglefene OR Glycopyrrolate OR glycopyrronium OR "gsk 202405" OR "h cholinoreactive cell*" OR hemicholinium OR hexahydrodifenidol OR hexahydroprocyclidine OR hexahydrosiladifenidol OR Hexamethonium OR hexbutinol OR "hexbutinol methiodide" OR "hexocyclium metilsulfate" OR himbacine OR homatropine OR "homatropine methyl" OR "homatropine terephthalate" OR Hyoscyamine OR imidafenacin OR Ipratropium OR isomylamine OR "isopropamide iodide" OR LAMA OR LAMAs OR levetimide OR lophotoxin OR mazaticol OR Mecamylamine OR mefurtramine OR mepenzolate OR meptazinol OR "meta cholinoreactive cell*" OR methantheline OR methoctramine OR methylatropine OR methyllycaconitine OR methylscopolamine OR metixene OR muscarinic* OR muscarinolytic* OR "nicotine tartrate" OR nicotinic* OR nuvenzepine OR "octatropine methylbromide" OR Orphenadrine OR otenzepad OR oxitropium OR oxybutynin OR oxyphencyclimine OR Oxyphenonium OR Pancuronium OR "para fluorohexahydrosiladifenidol" OR "para fluorohexbutinol" OR parapenzolate OR "parasympathetic block*" OR "parasympathetic inhibitor*" OR parasympathicolytic* OR parasympatholytic* OR parasympatolytic* OR Pempidine OR penthienate OR "Pentolinium Tartrate" OR phenglutarimide OR Pipecuronium OR pipenzolate OR piperidolate OR piperphenamine OR pipethanate OR Pirenzepine OR piroheptine OR "poldine methylsulfate" OR pridinol OR "pridinol mesilate" OR "prifinium bromide" OR Procyclidine OR profenamine OR proglumide OR Propantheline OR propiverine OR "propylbenziloylcholine mustard" OR "Propylbenzilylcholine Mustard" OR pyrrinol OR Quinidine OR "Quinuclidinyl Benzilate" OR revatropate OR revefenacin OR rispenzepine OR SAMA OR SAMAs OR Scopolamine OR secoverine OR silahexocyclium OR siltenzepine OR sofpironium OR solifenacin OR "Solifenacin Succinate" OR stramonium OR sydnofen OR tarafenacin OR telenzepine OR tematropium OR temiverine OR thiazinamium OR "thiazinamium metilsulfate" OR thihexinol OR "tiemonium iodide" OR "tiemonium methylsulfate" OR tifenamil OR timepidium OR Tiotropium OR tofenacin OR tolterodine OR "Tolterodine Tartrate" OR tonopan OR Toxiferine OR tricyclamol OR "tridihexethyl chloride" OR Trihexyphenidyl OR Trimethaphan OR triperidene OR tripitramine OR tropacin OR Tropicamide OR tropine OR "tropine benzoate" OR "trospium chloride" OR troventol OR Tubocurarine OR umeclidinium OR valethamate OR vamicamide OR Vecuronium OR vedaclidine OR zamifenacin OR zolenzepine)

5 TITLE-ABS-KEY("adrenal cortex hormone*" OR "adrenal cortex steroid*" OR "adrenal cortical hormone*" OR "adrenal cortical steroid*" OR "adrenal steroid*" OR "adreno cortical steroid*" OR "adreno corticosteroid*" OR "adrenocortical hormone*" OR "adrenocortical steroid*" OR adrenocorticosteroid* OR adreson OR alclometasone OR aldosterone OR algestone OR "algestone acetonide" OR amcinonide OR amelometasone OR beclometasone OR budesonide OR butixocort OR chloroprednisone OR ciclesonide OR ciprocinonide OR clioquinol OR

clobetasol OR clobetasone OR clocortolone OR cloprednol OR "cortical steroid*" OR corticalsteroid* OR "cortico steroid*" OR corticoid* OR corticosteroid* OR corticosterone OR corticotherap* OR cortifair OR cortisol OR cortisone OR cortivazol OR cortril OR deflazacort OR dehydrocorticosterone OR dehydrocortisone OR deoxycorticosterone OR dermocorticosteroid* OR dexamethasone OR diflorasone OR diflucortolone OR difluprednate OR domoprednate OR drocinonide OR dutimelan OR epicortisol OR "etiprednol dicloacetate" OR fluclorolone OR fludrocortisone OR fludroxycortide OR flumetasone OR flumoxonide OR flunisolide OR fluocinolone OR fluocinonide OR fluocortin OR fluocortolone OR fluorometholone OR fluprednidene OR fluprednisolone OR fluticasone OR formocortal OR "formoterol fumarate" OR Glucocorticoid* OR glucocorticoidsteroid* OR glucocorticosteroid* OR glucocortoid* OR glycocorticoid* OR glycocorticosteroid* OR halcinonide OR halometasone OR halopredone OR hydrocortisone OR "hydroxy norcorticosterone" OR hydroxycorticoid* OR hydroxycorticosteroid* OR hydroxycorticosterone OR hydroxydeoxycorticosterone OR hydroxyhydrocortisone OR "icometasone enbutate" OR isoflupredone OR itrocinonide OR "locicortolone dicibate" OR "lorinden a" OR "lorinden t" OR loteprednol OR mazipredone OR medrysone OR meprednisone OR mineralcorticosteroid* OR mineralocorticosteroid* OR minerocorticoid* OR mometasone OR nicocortonide OR nivacortol OR nordeoxycorticosterone OR oropivalone OR oxohydrocortisone OR oxycorticosteroid* OR paramethasone OR prednisolone OR prednisone OR pregnenolone OR procinonide OR promestriene OR resocortol OR rimexolone OR rofleponide OR steroid* OR tetrahydrodeoxycorticosterone OR ticabesone OR timobesone OR tipredane OR tixocortol OR triamcinolone OR "ulobetasol propionate" OR uniderm OR zoticasone)

6 TITLE-ABS-KEY(apremilast OR arofylline OR atizoram OR benzafentrine OR catramilast OR cilomilast OR cipamfylline OR daxalipram OR denbufylline OR elbimilast OR filaminast OR ibudilast OR indimilast OR lavamilast OR nitraquazone OR oglemilast OR "PDE 4 inhibitor*" OR "PDE IV inhibitor*" OR "PDE type 4 inhibitor*" OR "PDE type IV inhibitor*" OR "pde-4 inhibitor*" OR "PDE4 inhibitor*" OR "phosphodiesterase 4 inhibitor*" OR "phosphodiesterase IV inhibitor*" OR "phosphodiesterase type 4 inhibitor*" OR "phosphodiesterase type IV inhibitor*" OR piclamilast OR pumafentrine OR revamilast OR roflumilast OR Rolipram OR tetomilast OR tibenelast OR tilivapram OR tipelukast OR tofimilast OR tolafentrine OR zardaverine)

7 1 and (2 or 3 or 4 or 5 or 6)

8 TITLE-ABS-KEY((meta W/1 analys*) OR (systematic* W/3 review*))

9 7 and 8

10 DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)

11 9 and not 10

12 PMID(0*) OR PMID(1*) OR PMID(2*) OR PMID(3*) OR PMID(4*) OR PMID(5*) OR PMID(6*) OR PMID(7*) OR PMID(8*) OR PMID(9*)

13 11 and not 12

Part 2

1 TITLE-ABS-KEY("chronic airflow disease*" OR "chronic airflow disorder*" OR "chronic airflow limitation*" OR "chronic airflow obstruction*" OR "chronic airway disease*" OR "chronic airway disorder*" OR "chronic airway limitation*" OR "chronic airway obstruction*" OR "chronic bronchitis" OR "chronic obstructive airflow disease*" OR "chronic obstructive airflow disorder*" OR "chronic obstructive airway disease*" OR "chronic obstructive airway disorder*" OR "chronic obstructive bronchitis" OR "chronic obstructive bronchopulmonary disease*" OR "chronic obstructive broncho-pulmonary disease*" OR "chronic obstructive bronchopulmonary disorder*" OR "chronic obstructive broncho-pulmonary disorder*" OR "chronic obstructive lung disease*" OR "chronic obstructive lung disorder*" OR "chronic obstructive pulmonary disease*" OR "chronic obstructive pulmonary disorder*" OR "chronic obstructive respiratory disease*" OR "chronic obstructive respiratory disorder*" OR coad OR copd OR emphysema OR "obstructive lung disease" OR "obstructive lung disorder*" OR "obstructive pulmonary disease*" OR "obstructive pulmonary disorder*" OR "obstructive pulmonary tract disease*" OR "obstructive pulmonary tract disorder*" OR "obstructive respiratory disease*" OR "obstructive respiratory disorder*" OR "obstructive respiratory tract disease*" OR "obstructive respiratory tract disorder*")

2 TITLE-ABS-KEY(Acetylcysteine OR Ambroxol OR aminophylline OR Bromhexine OR bron OR cafedrine OR Carbocysteine OR diprophylline OR etofylline OR eucalyptus OR expectorant* OR fudosteine OR guaiacol OR "guaiacol carbonate" OR guaietolin OR Guaifenesin OR guaifylline OR "iodinated glycerol" OR ipecac OR mucolytic* OR "Potassium Citrate" OR "primula flower" OR stepronin OR "stepronin lysine" OR sulfoguaiacol OR tipepidine OR ulogesic)

3 TITLE-ABS-KEY("1 methylmocimycin*" OR "11 deoxydaunorubicin*" OR "14 hydroxyclarithromycin*" OR "19 deformyl 4 deoxydesmycosin*" OR "19 deformyldesmycosin*" OR "2 acetylerythromycin*" OR "2 fluoroidarubicin*" OR "2 n ethylnetilmicin*" OR "2 pyrrolinodoxorubicin*" OR "21 aminoepothilone B" OR "3 3 cyanomorpholino 3 deaminodoxorubicin*" OR "3 deamino 2 fluoro 3 hydroxydoxorubicin 14 pimelate" OR "3 deamino 3 morpholinodoxorubicin*" OR "3 deamino 3 morpholinooxaunomycin*" OR "4 demethoxy 11 deoxydaunomycinone" OR "4 demethoxydaunomycinone" OR "4 demethoxydoxorubicin*" OR "4 deoxydesmycosin*" OR "4 iodoesorubicin*" OR "5 iminodaunorubicin*" OR "6 n ethylnetilmicin*" OR "6beta iodopenicillanic acid" OR "9 deacetyl 9 methylidarubicin*" OR "9 deoxydoxorubicin*" OR "9 dihydroerythronolide A" OR "a 102395" OR "a 10255" OR "a 10947" OR "a 130b" OR "a 192411" OR "a 63075" OR abkhazomycin* OR abyssomicin* OR acetomycin* OR acetylspiramycin* OR aclacinomycin* OR aclarubicin* OR actagardin* OR actaplanin* OR actinorhodine OR "aculeacin A" OR aculeximycin* OR adicillin* OR aditoprim OR adriamycinone OR agglomerin* OR aklavinone OR alafosfalin* OR Alamethicin* OR albocycline OR aldecalmycin* OR aldoxorubicin* OR alisamycin* OR allicin* OR almecillin* OR "alpha defensin*" OR ambruticin* OR Amdinocillin* OR amfomycin* OR Amikacin* OR aminoglycoside* OR aminopenicillin* OR "Aminosalicylic Acid" OR Amoxicillin* OR "Amphotericin B" OR Ampicillin* OR amrubicin* OR "angucycline derivative" OR anhydrochlortetracycline OR anhydroepitetracycline OR anhydrotetracycline OR anidulafungin* OR Anisomycin* OR annamycin* OR ansamitocin* OR "ansamycin derivative" OR anthracycline* OR anthracyclinone* OR antibacterial* OR "anti-bacterial*" OR antibiotic* OR "anti-biotic*" OR "antimicrobial cationic peptide*" OR Antimycin* OR antimycobacterial* OR "anti-mycobacterial*" OR Antitreponemal* OR "Anti-treponemal*" OR Antitubercular* OR "Anti-tubercular*" OR apalcillin* OR aplasmomycin* OR "aplysianin E" OR apramycin* OR aristeromycin* OR Arsphenamine OR aspoxicillin* OR astromicin* OR asukamycin* OR "atpenin B" OR auricularum OR Aurodox OR aurograb OR avibactam OR avilamycin* OR avoparcin* OR azidamfenicol OR azidocillin* OR Azithromycin* OR Azlocillin* OR Aztreonam OR "aztreonam lysine" OR azurocidin* OR bacampicillin* OR Bacitracin* OR bacmecillinam OR bactenecin* OR bacteriocid* OR Bacteriocin* OR bafilomycin* OR balhimycin* OR "baliz 2" OR Bambermycin* OR baquiloprim OR "barminomycin I" OR baycuten OR beauvericin* OR beroline OR berubicin* OR berythromycin* OR "beta defensin*" OR betafectin* OR "beta-Lactam*" OR "betaLactamase Inhibitor*" OR "beta-Lactamase Inhibitor*" OR betamipron OR bialaphos OR biapenem OR bicozamycin* OR "biphenomycin A" OR bluensomycin* OR bombinin* OR "Bongkrekic Acid" OR boromycin* OR borrelidin* OR "Brefeldin A" OR brilacidin* OR brobactam OR butalactin* OR butirosin* OR cadazolid OR Calcimycin* OR Candicidin* OR Capreomycin* OR carbacephem OR carbadox OR carbapenem OR "carbazomycin A" OR Carbenicillin* OR carbomycin* OR Carfecillin* OR carindacillin* OR carubicin* OR carumonam OR caspofungin* OR cathelicidin* OR cecropin* OR cefacetrile OR Cefaclor OR Cefadroxil OR cefalexin* OR cefaloglycin* OR cefaloram OR cefaloridine OR cefalotin* OR Cefamandole OR cefapirin* OR Cefatrizine OR cefazaflur OR cefazedone OR Cefazolin* OR cefbuperazone OR cefcanel OR cefcapene OR cefclidin* OR cefdaloxime OR cefdinir OR cefditoren OR cefepime OR cefetamet OR cefetecol OR cefilavancin* OR Cefixime OR cefluprenam OR cefmatilen OR Cefmenoxime OR Cefmetazole OR cefminox OR cefodizime OR Cefonicid OR Cefoperazone OR ceforanide OR cefoselis OR Cefotaxime OR Cefotetan OR Cefotiam OR cefovecin* OR Cefoxitin* OR cefozopran OR cefpimizole OR cefpiramide OR cefpirome OR cefpodoxime OR cefprozil OR cefquinome OR cefradine OR cefroxadine OR Cefsulodin* OR ceftaroline OR Ceftazidime OR cefteram OR ceftezole OR ceftibuten OR ceftiofur OR Ceftizoxime OR ceftobiprole OR ceftolozane OR Ceftriaxone OR Cefuroxime OR cefuzonam OR Cephacetrile OR Cephalexin* OR Cephaloglycin* OR Cephaloridine OR cephalosporin* OR Cephalothin* OR cephamycin* OR Cephapirin* OR Cephradine OR chalcomycin* OR Chloramphenicol* OR chloroorienticin* OR chloropolysporin* OR chlorothricin* OR chlorothricolide OR Chlortetracycline OR "chymotrypsin trypsin*" OR ciadox

OR "cilastatin plus imipenem" OR "cinerubin A" OR "cinerubin B" OR cinoquidox OR Ciprofloxacin* OR cirramycin* OR Citrinin* OR Clarithromycin* OR "clavulanate potassium" OR "Clavulanic Acid*" OR Clindamycin* OR clomocycline OR Cloxacillin* OR colicin* OR colistimethate OR Colistin* OR "concanamycin A" OR coumamidine OR coumamycin* OR "cp 63956" OR cryptosporin* OR Cyclacillin* OR cycloheximide OR Cycloserine OR cystargin* OR "cytarabine plus daunorubicin*" OR cytovaricin* OR dactimicin* OR Dactinomycin* OR dalbaheptide OR dalbavancin* OR dalfopristin* OR "damavaricin Fc pentyl ether" OR Daptomycin* OR daunomycinone OR daunorubicin* OR daunorubicinol OR "deacetoxycephalosporin C" OR deacetylcefotaxime OR "deacetylcephalosporin C" OR dealanylalahopcin* OR decaplanin* OR dechloroeremomycin* OR decilorubicin* OR defensin* OR Demeclocycline OR dermaseptin* OR dermcidin* OR dermostatin* OR desmycosin* OR detorubicin* OR Diarylquinoline* OR Dibekacin* OR Dicloxacillin* OR dihydrostreptomycin* OR Diketopiperazines OR dimethylchlortetracycline OR dioxidine OR dirithromycin* OR Distamycin* OR "ditrisarubicin B" OR doripenem OR doxorubicin* OR doxorubicinol OR Doxycycline OR drosocin* OR echinocandin* OR Echinomycin* OR Edeine OR efepristin* OR efrotomycin* OR emimycin* OR endusamycin* OR enniatin* OR Enoxacin* OR Enviomycin* OR eperezolid OR epetraborole OR epicillin* OR epidermin* OR epiderstatin* OR epiroprim OR epirubicin* OR epirubicinol OR epitetracycline OR epothilone* OR "epsilon rhodomycinone" OR eravacycline OR eremomycin* OR ertapenem OR Erythromycin* OR erythromycylamine OR erythronolide* OR esorubicin* OR Ethambutol OR Ethionamide OR ethylhydrocupreine OR etimicin* OR evernimicin* OR everninomicin* OR faeriefungin* OR fidaxomicin* OR Filipin* OR "fleroxacin deacetylcefotaxime ester" OR flomoxef OR flopristin* OR florfenicol OR Floxacillin* OR flucloxacillin* OR flumoxil OR Fluoroquinolone* OR flurithromycin* OR fomidacillin* OR fortimicin* OR Fosfomycin* OR fosmidomycin* OR Framycetin* OR fropenem OR fungichromin* OR furaquinocin* OR furazidin* OR "furazolium chloride" OR furbenicillin* OR fusafungine OR "fusidate sodium" OR "Fusidic Acid" OR fuzlocillin* OR galarubicin* OR gallidermin* OR gamithromycin* OR ganefromycin* OR "ge 2270a" OR gentamicin* OR gepotidacin* OR globomycin* OR gloximonam OR "glycylcycline derivative" OR "gonadorelin6 dextro lysine 2 pyrrolinodoxorubicin*" OR "goniodomin A" OR Gramicidin* OR granulysin* OR grisein* OR guamecycline OR habekacin* OR hamycin* OR hatomamicin* OR hedamycin* OR heliomycin* OR hepcidin* OR hetacillin* OR hexacycline OR hidamicin* OR "histatin 5" OR histatin* OR hygromycin* OR hymeglusin* OR hypothemycin* OR iclaprim OR idarubicin* OR idarubicinol OR ikarugamycin* OR "imidacloprid plus moxidectin*" OR Imipenem OR indolicidin* OR inostamycin* OR iseganan OR isepamicin* OR Isoniazid OR "isopenicillin N" OR "isoswinholide A" OR istamycin* OR "iturin A" OR ixabepilone OR Josamycin* OR "k 252a" OR kalafungin* OR Kanamycin* OR kanendomycin* OR kasugamycin* OR kelfiprim OR ketolide OR kidamycin* OR kinamycin* OR Kitasamycin* OR "l 156602" OR "l 733560" OR "l 786392" OR lactacystin* OR Lactams OR lactivicin* OR "lactocin S" OR lactococcin* OR lactoferricin* OR ladirubicin* OR laidlomycin* OR lancovutide OR lankamycin* OR lanopepden OR lanthiopeptin* OR lantibiotic OR Lasalocid OR latamoxef OR lavanducyanin* OR lefamulin* OR lenampicillin* OR lenapenem OR lenoremycin* OR Leprostatic* OR "leucinostatin A" OR "leucinostatin B" OR Leucomycin* OR leurubicin* OR Levofloxacin* OR lexithromycin* OR "lff 571" OR Lincomycin* OR lincosamide* OR Linezolid OR linopristin* OR lividomycin* OR "lonomycin A" OR loracarbef OR lotilibcin* OR Lucensomycin* OR lydicamycin* OR Lymecycline OR lysobactin* OR lysocellin* OR lysostaphin* OR macrolide OR magainin* OR malyngolide OR manumycin* OR maridomycin* OR "mdl 62208" OR "mdl 62211" OR mecillinam OR meclocycline OR megacin* OR megalomicin* OR Mepartricin* OR meropenem OR mersacidin* OR metacycline OR metampicillin* OR Methacycline OR Methicillin* OR "methylenomycin A" OR "methylenomycin B" OR methymycin* OR methynolide OR meticillin* OR Mezlocillin* OR "microcin b17" OR "microcin J25" OR micronomicin* OR midecamycin* OR mideplanin* OR "mikamycin B" OR Mikamycin* OR "milbemycin oxime" OR milbemycin* OR Minocycline OR Miocamycin* OR miokamycin* OR miporamicin* OR miraxid OR mocimycin* OR "moenomycin A" OR monensin* OR "monobactam derivative" OR Moxalactam OR moxidectin* OR "ms 8209" OR Mupirocin* OR mureidomycin* OR murepavadin* OR mycinamicin* OR Mycobacillin* OR mycolog OR mycoticin* OR myxothiazol OR "n benzyldoxorubicin 14 valerate" OR "n trifluoroacetyldoxorubicin*" OR Nafcillin* OR "Nalidixic Acid" OR narasin* OR Natamycin* OR neamine OR nebacetin* OR Nebramycin* OR

negamycin* OR nemadectin* OR nemorubicin* OR Neomycin* OR neosporin* OR Netilmicin* OR Netropsin* OR niddamycin* OR Nigericin* OR Nisin* OR nitrocefin* OR nitrosochloramphenicol OR "nocardicin A" OR "nocardicin E" OR "nocardicinic acid derivative*" OR Norfloxacin* OR nosiheptide OR nourseothricin* OR Novobiocin* OR "nvb 302" OR nybomycin* OR Nystatin* OR "oasomycin A" OR obelmycin* OR Ofloxacin* OR olaquindox OR oleandolide OR Oleandomycin* OR oligomycin* OR omadacycline OR omiganan OR optocillin* OR "orienticin A" OR orientiparcin* OR oritavancin* OR oropivalone OR Oxacillin* OR oxaunomycin* OR "Oxolinic Acid" OR Oxytetracycline OR paldimycin* OR panipenem OR pardaxin* OR Paromomycin* OR patulin* OR pediazole OR pediocin* OR Pefloxacin* OR penamecillin* OR penethamate OR "Penicillanic Acid" OR "Penicillic Acid" OR penicillin* OR "penicilloic acid" OR pentalenolactone OR pentisomicin* OR peptaibol OR pexiganan OR "pf 708093" OR phenelfamycin* OR pheneticillin* OR phleomycin* OR pikromycin* OR "Pipemidic Acid" OR Piperacillin* OR pirarubicin* OR pirazmonam OR pirlimycin* OR Pivampicillin* OR pivmecillinam OR platensimycin* OR plazomicin* OR plectasin* OR pleuromutilin* OR pluramycin* OR pneumocandin* OR "polyactin A" OR polyfungin* OR polymyxin* OR "polyoxin B" OR "polyoxin D" OR polysporin* OR polytrim OR posizolid OR "pr 39" OR Pristinamycin* OR Prodigiosin* OR prohepcidin* OR propicillin* OR protegrin* OR Prothionamide OR prothracarcin* OR "pseudomonic acid" OR Pyrazinamide OR pyrromycinone OR pyrroxamycin* OR quinacillin* OR quinomycin* OR quinupristin* OR radezolid OR radicicol OR ramoplanin* OR ranalexin* OR ranbezolid OR razupenem OR retacillin* OR retapamulin* OR "rhodomycin A" OR Ribostamycin* OR Rifabutin* OR Rifampin* OR Rifamycin* OR rimocidin* OR Ristocetin* OR ritipenem OR "ritipenem acoxil" OR rodorubicin* OR roflamycoin* OR rokitamycin* OR Rolitetracycline OR rosaramicin* OR Roxarsone OR Roxithromycin* OR ruboxyl OR Rutamycin* OR sabarubicin* OR sagopilone OR sanfetrinem OR sarecycline OR "simaomicin alpha" OR "simocyclinone D8" OR Sirolimus OR "sisomicin sulfate" OR Sisomicin* OR "skf 104662" OR sofradex OR Spectinomycin* OR "spinosyn A" OR Spiramycin* OR squalamine OR stigmatellin* OR streptoduocin* OR Streptogramin* OR streptolydigin* OR Streptomycin* OR streptothricin* OR streptotriad OR Streptovaricin* OR streptovirudin* OR "streptovitacin A" OR stubomycin* OR subtilin* OR Sulbactam OR Sulbenicillin* OR Sulfamerazine OR Sulfamethoxypyridazine OR sulfazecin* OR sulopenem OR sultamicillin* OR surfactin* OR surotomycin* OR "swinholide A" OR "swinholide B" OR tachyplesin* OR Talampicillin* OR tameticillin* OR tazobactam OR tebipenem OR tedizolid OR Teicoplanin* OR teixobactin* OR telavancin* OR temocillin* OR terdecamycin* OR tetracyclin* OR Tetracycline OR tetramycin* OR tetronasin* OR tetronomycin* OR tetroxoprim OR Thiamphenicol OR Thienamycin* OR Thioacetazone OR thiolactomycin* OR "thionin peptide" OR thiopeptin* OR thiophenoxycefalotin* OR Thiostrepton OR tiamulin* OR "tibezonium iodide" OR Ticarcillin* OR tigecycline OR tigemonam OR tildipirosin* OR tilmicosin* OR timentin* OR tirandamycin* OR tizoxanide OR tobicillin* OR Tobramycin* OR tolramycin* OR tomopenem OR toyocamycin* OR tresaderm OR tribactam OR trichomycin* OR "trichostatic acid" OR "trichostatin A" OR trimethoprim* OR "trinem derivative" OR "triostin A" OR triplopen OR trisep OR Troleandomycin* OR trospectomycin* OR tuftsin* OR tulathromycin* OR Tunicamycin* OR tutofusin* OR Tylosin* OR tylvalosin* OR Tyrocidine OR Tyrothricin* OR "u 78608" OR "uk 69753" OR unphenelfamycin* OR "urdamycin C" OR "urdamycin D" OR "urdamycin H" OR ureidopenicillin* OR urobiotic OR "vacidin A" OR validamycin* OR Valinomycin* OR valnemulin* OR valrubicin* OR Vancomycin* OR venturicidin* OR vernamycin* OR "violamycin B1" OR Viomycin* OR "virginiae butanolide A" OR "virginiae butanolide C" OR "virginiamycin M" OR "virginiamycin S" OR Virginiamycin* OR "viriplanin A" OR viscosin* OR volpristin* OR "ws 9659 b" OR "zibrofusidic acid" OR zineryt OR "zoptarelin doxorubicin*" OR zorbamycin* OR zorubicin*)

4 TITLE-ABS-KEY(Alprazolam OR arfendazam OR benzodiazepin OR benzodiazepine* OR Benzodiazepinone* OR bromazepam OR camazepam OR Chlordiazepoxide OR cinolazepam OR clobazam OR clonazepam OR clorazepate OR "Clorazepate Dipotassium" OR "clorazepate potassium" OR dealkylflurazepam OR delorazepam OR demoxepam OR devazepide OR diazepam OR doxefazepam OR Estazolam OR fludiazepam OR flunitrazepam OR flurazepam OR flutoprazepam OR fosazepam OR gidazepam OR girisopam OR halazepam OR loflazepate OR lorazepam OR lormetazepam OR lotrafiban OR meclonazepam OR Medazepam OR metaclazepam OR Midazolam OR nastorazepide OR nerisopam OR netazepide OR nimetazepam OR nitrazepam OR nitrosochlordiazepoxide OR norchlordiazepoxide OR

	norclobazam OR nordazepam OR norfludiazepam OR norflunitrazepam OR oxazepam OR phenazepam OR pinazepam OR prazepam OR quazepam OR "ro 7 0213" OR talampanel OR tampramine OR tarazepide OR temazepam OR tetrazepam OR tibezonium OR tifluadom OR tofisopam OR tomaymycin OR Triazolam OR tuclazepam OR uxepam)
5	TITLE-ABS-KEY(acetorphine OR acetylcodeine OR acetylmethadol OR Alfentanil OR Alphaprodine OR anileridine OR apadoline OR azidomorphine OR benzhydrocodone OR bezitramide OR bremazocine OR "Brompton mixture" OR Buprenorphine OR Butorphanol OR ciramadol OR cocodamol OR Codeine OR codydramol OR conorfone OR cyclazocine OR Dextromoramide OR Dextropropoxyphene OR dextrorphan OR dezocine OR diamorphine OR diconal OR dihydrocodeine OR dihydroetorphine OR Dihydromorphine OR dimethylthiambutene OR Diphenoxylate OR dipipanone OR enadoline OR eptazocine OR ethylketazocine OR Ethylketocyclazocine OR Ethylmorphine OR etonitazene OR Etorphine OR etoxeridine OR faxeladol OR Fentanyl OR furethidine OR gelonida OR Heroin OR Hydrocodone OR isalmadol OR isomethadone OR ketazocine OR ketobemidone OR ketogan OR kyotorphin OR lefetamine OR levacetylmethadol OR levomethadone OR Levorphanol OR Meperidine OR Meptazinol OR metazocine OR Methadone OR "Methadyl Acetate" OR methylsamidorphan OR Morphine OR "morphinomimetic agent*" OR "morphinomimetic drug*" OR morphinone OR Nalbuphine OR narcotic* OR nicocodine OR nicomorphine OR noracymethadol OR norbuprenorphine OR nordextropropoxyphene OR normorphine OR norpethidine OR norpropoxyphene OR "o nortramadol" OR oliceridine OR opiate OR Opiate* OR opioid* OR Opium OR oripavine OR Oxycodone OR Oxymorphone OR pentamorphone OR Pentazocine OR pethidine OR phenadoxone OR phenaridine OR Phenazocine OR phencyclidine OR Phenoperidine OR picenadol OR piminodine OR Pirinitramide OR piritramide OR profadol OR Promedol OR propiram OR sameridine OR samidorphan OR semorphone OR Sufentanil OR tapentadol OR thebaine OR tifluadom OR Tilidine OR tonazocine OR Tramadol OR trimeperidine)
6	TITLE-ABS-KEY("airflow clearance" OR "airway clearance" OR BLVR OR bronchoscop* OR ELVR OR "lung clearance" OR "lung denervation" OR LVRS OR pneumectom* OR pneumonectom* OR pneumoresection* OR "pulmonary clearance" OR "volume reducing" OR "volume reduction*")
7	1 and (2 or 3 or 4 or 5 or 6)
8	TITLE-ABS-KEY((meta W/1 analys*) OR (systematic* W/3 review*))
9	7 and 8
10	DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
11	9 and not 10
12	PMID(0*) OR PMID(1*) OR PMID(2*) OR PMID(3*) OR PMID(4*) OR PMID(5*) OR PMID(6*) OR PMID(7*) OR PMID(8*) OR PMID(9*)
13	11 and not 12

Part 3

1	TITLE-ABS-KEY("chronic airflow disease*" OR "chronic airflow disorder*" OR "chronic airflow limitation*" OR "chronic airflow obstruction*" OR "chronic airway disease*" OR "chronic airway disorder*" OR "chronic airway limitation*" OR "chronic airway obstruction*" OR "chronic bronchitis" OR "chronic obstructive airflow disease*" OR "chronic obstructive airflow disorder*" OR "chronic obstructive airway disease*" OR "chronic obstructive airway disorder*" OR "chronic obstructive bronchitis" OR "chronic obstructive bronchopulmonary disease*" OR "chronic obstructive broncho-pulmonary disease*" OR "chronic obstructive bronchopulmonary disorder*" OR "chronic obstructive broncho-pulmonary disorder*" OR "chronic obstructive lung disease*" OR "chronic obstructive lung disorder*" OR "chronic obstructive pulmonary disease*" OR "chronic obstructive pulmonary disorder*" OR "chronic obstructive respiratory disease*" OR "chronic obstructive respiratory disorder*" OR coad OR copd OR emphysema OR "obstructive lung disease" OR "obstructive lung disorder*" OR "obstructive pulmonary disease*" OR "obstructive pulmonary disorder*" OR "obstructive pulmonary tract disease*" OR "obstructive pulmonary tract disorder*" OR "obstructive respiratory disease*" OR "obstructive respiratory disorder*" OR "obstructive respiratory tract disease*" OR "obstructive respiratory tract disorder*")
2	TITLE-ABS-KEY((smoking* or tobacco* or cigar* or cigarette* or cigaret*) and (quit* or discontinu* or ceas* or cessation*))
3	TITLE-ABS-KEY(aerobics OR anaerobics OR "artificial respiration*" OR bicycling OR biking OR "Chest Wall Oscillation*" OR dance OR dancing OR "endurance training" OR exercis* OR "Extracorporeal Membrane Oxygen*" OR "fitness training" OR "inhalation therap*" OR isometrics OR oxygen OR "physical activit*" OR "physical exertion" OR "postural drain*" OR rehab* OR "resistance training" OR "respiration care*" OR "respiration therap*" OR "respiratory care*" OR "respiratory therap*" OR running OR "strength training" OR swimming OR "Tai Chi" OR "Tai Ji" OR walking OR weightlifting OR yoga)
4	TITLE-ABS-KEY(diet OR dietary OR diets OR nutrition* OR supplementation OR supplements)
5	TITLE-ABS-KEY(immuniz* OR innoculat* OR moniarix OR "pcv 13" OR pcv13 OR "pneu immune" OR "pneumo 23" OR pneumopur OR pneumovax OR "pnu immune" OR "pnu imune" OR "polysaccharide vaccine pneumococcal" OR prevenar OR prevnar OR "streptococcus pneumoniae vaccine" OR streptopur OR streptorix OR synflorix OR vaccin*)
6	((TITLE-ABS-KEY((((domestic or home or domiciliary) and (residence or residences or setting or settings or care or nurs* or help or service* or treatment* or therap* or "respiratory care" or "respiratory treatment*" or "respiratory therap*" or "respiratory service*" or "respiratory assist*" or ventilat*)) or "assisted living" or homecare)) and (TITLE-ABS-KEY(((((respiration* or respiratory or breathing) and (assist* or controlled or mechanical)) or (facial or face or nasal)) and mask*) or "artificial respiration*" or BiPAP or CPAP or "Fluidic Breathing Assister" or HMV or IPPB or IPPV or NIAV or NIV or NPPV or "Oxygen Regulator*" or PAP or PAV or "Portable Oxygen" or "Positive Airway Pressure*" or "positive end-expiratory pressure*" or "positive pressure*" or respirator or respirators or "Respiratory insufficiency" or Tracheostom* or ventilation or ventilator*)))
7	1 and (2 or 3 or 4 or 5 or 6)
8	TITLE-ABS-KEY((meta W/1 analys*) OR (systematic* W/3 review*))
9	7 and 8
10	DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
11	9 and not 10
12	PMID(0*) OR PMID(1*) OR PMID(2*) OR PMID(3*) OR PMID(4*) OR PMID(5*) OR PMID(6*) OR PMID(7*) OR PMID(8*) OR PMID(9*)
13	11 and not 12

Part 4

1	TITLE-ABS-KEY("chronic airflow disease*" OR "chronic airflow disorder*" OR "chronic airflow limitation*" OR "chronic airflow obstruction*" OR "chronic airway disease*" OR "chronic airway disorder*" OR "chronic airway limitation*" OR "chronic airway obstruction*" OR "chronic bronchitis" OR "chronic obstructive airflow disease*" OR "chronic obstructive airflow disorder*" OR "chronic obstructive airway disease*" OR "chronic obstructive airway disorder*" OR "chronic

	obstructive bronchitis" OR "chronic obstructive bronchopulmonary disease*" OR "chronic obstructive broncho-pulmonary disease*" OR "chronic obstructive bronchopulmonary disorder*" OR "chronic obstructive broncho-pulmonary disorder*" OR "chronic obstructive lung disease*" OR "chronic obstructive lung disorder*" OR "chronic obstructive pulmonary disease*" OR "chronic obstructive pulmonary disorder*" OR "chronic obstructive respiratory disease*" OR "chronic obstructive respiratory disorder*" OR coad OR copd OR emphysema OR "obstructive lung disease" OR "obstructive lung disorder*" OR "obstructive pulmonary disease*" OR "obstructive pulmonary disorder*" OR "obstructive pulmonary tract disease*" OR "obstructive pulmonary tract disorder*" OR "obstructive respiratory disease*" OR "obstructive respiratory disorder*" OR "obstructive respiratory tract disease*" OR "obstructive respiratory tract disorder*")
2	TITLE-ABS-KEY(CBT OR coach* OR "Cognitive behavioral therap*" OR "Cognitive therap*" OR "health promotion*" OR meditat* OR mentor* OR "mind body" OR mindfulness OR psychological OR psychosocial OR psychotherap*)
3	TITLE-ABS-KEY("action plan*" OR android OR app OR apps OR ehealth OR "e-health" OR internet OR ipad* OR iphone* OR mhealth OR "m-health" OR "mobile app*" OR "mobile health" OR "mobile technolog*" OR "portable computer*" OR "portable electronic app*" OR "portable software app*" OR "remote consultation*" OR "self care" OR "self help" OR "self management" OR "self treatment" OR "smart phone*" OR smartphone* OR "tablet computer*" OR teleconsultation* OR "tele-consultation*" OR telehealth OR "tele-health" OR telemedicine OR "tele-medicine" OR teletherap* OR "tele-therap*" OR web)
4	TITLE-ABS-KEY(acupuncture OR agent* OR "alternative medicine" OR "care package*" OR chemotherap* OR "complementary medicine" OR drug* OR "electric stimulation*" OR holistic OR "integrated care" OR "integrated health care" OR "integrated healthcare" OR intervention* OR manag* OR medication* OR "muscle stimulation*" OR operat* OR pharmacotherap* OR procedure* OR reconstruction* OR repair* OR resect* OR surg* OR therap* OR treat* OR wellness)
5	1 and (2 or 3 or 4)
6	TITLE-ABS-KEY((meta W/1 analys*) OR (systematic* W/3 review*))
7	5 and 6
8	DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
9	7 and not 8
10	PMID(0*) OR PMID(1*) OR PMID(2*) OR PMID(3*) OR PMID(4*) OR PMID(5*) OR PMID(6*) OR PMID(7*) OR PMID(8*) OR PMID(9*)
11	9 and not 10

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Treatment of stable chronic obstructive pulmonary disease: a protocol for a systematic review and evidence map

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Abstract

Introduction: Chronic obstructive pulmonary (COPD) disease is a progressive lung disease, usually caused by tobacco smoking, but other important risk factors include exposures to combustion products of biomass fuels and environmental pollution. The introduction of several new (combination) inhaler therapies, increasing uncertainty about the role of inhaled corticosteroids and a rapid proliferation of the literature on management of stable COPD in general, call for novel ways of evidence synthesis in this area. A systematic review and evidence map can provide the basis for shared decision-making tools and help establish a future research agenda.

Methods and analysis: This systematic review will follow an umbrella systematic review design (also called overview of reviews). We plan to conduct a comprehensive literature search of Ovid MEDLINE (including Epub Ahead of Print, In-Process and Other Non-Indexed Citations), Ovid EMBASE, Ovid Cochrane Database of Systematic Reviews, and Scopus from database inception to the present. We will include systematic reviews that assessed the effectiveness of any pharmacological or non-pharmacological intervention on one or more patient-important outcomes and/or lung function in patients with stable COPD. For every intervention/outcome pair one systematic review will be included. An a priori protocol will guide which systematic reviews will be chosen, how their credibility will be evaluated, and how the quality of the body of evidence will be rated. Data will be synthesized into an evidence map that will present a matrix that depicts each available treatment for stable COPD with a quantitative estimate on symptoms/outcomes from the patient perspective, along with an indication of the size and certainty in the evidence.

Ethics and dissemination: Approval by a research ethics committee is not required since the review will only include published data. The systematic review will be published in a peer-reviewed journal.

Systematic review registration: PROSPERO registration number CRD42018095079

Keywords

Chronic obstructive pulmonary disease, pharmacological interventions, non-pharmacological interventions, umbrella review, evidence map, knowledge translation, decision aid

Article Summary

Strengths and limitations of this study

- The planned evidence synthesis will summarise a very large body of literature on pharmacological and non-pharmacological interventions thus making research evidence more accessible for stakeholders
- The systematic review will be the first to use an evidence map to identify evidence gaps and to facilitate evidence communication in clinical encounters for COPD.
- For patients and clinicians, the map will facilitate the production of decision aids. For policymakers and researchers, the map helps in establishing a future research agenda.
- The systematic review uses an a priori protocol to identify the most up-to-date systematic reviews of the highest possible quality, and the level of evidence for many intervention/outcome pairs will therefore likely be high
- As we will only include one systematic review per intervention/outcome pair, it is possible that some studies will not have been captured in included systematic reviews

Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive lung disease characterized by chronic obstruction of airflow and permanent damage to the air sacs that leads to breathing problems. COPD is mainly a consequence of tobacco smoking, but other important risk factors include exposures to combustion products of biomass fuels and environmental pollution.[1] COPD is the fourth most common cause of death globally and is predicted to be the third by 2030.[2] In 2010, the number of COPD cases was estimated at 384 million, which corresponded to a global prevalence of 11.7% (95% confidence interval [CI] 8.4%–15.0%).[2] COPD was responsible for about 5% of global disability–adjusted life years (76.7 million) and 5% of total deaths (2.9 million) based on data from the 2010 Global Burden of Disease study.[3 4] In some low- and middle income countries COPD has become a growing, but often neglected, epidemic, with a recent study showing a prevalence of COPD of 13.7% (95% CI 12.1–15.5) in Chinese people aged 40 years or older.[5] Patients with COPD are frequent users of the health care system and often need to be admitted to hospital repeatedly, often within short intervals.[6]

Recently, there has been a rapid increase in inhaler therapies available for the management of COPD. In particular, several new inhalers including fixed-dose combinations (containing bronchodilator(s) with or without inhaled corticosteroids) have been introduced. Concurrently, the literature on pharmacological and non-pharmacological interventions for COPD has proliferated substantially. Multiple systematic reviews have been conducted to synthesise the evidence on inhalation treatments in COPD.[7-16]

The role of inhaled corticosteroids for the treatment of stable COPD is increasingly questioned, including in patients with severe disease, driven by the growing evidence of an increased risk of pneumonia associated with inhaled corticosteroids,[17 18] and the introduction of combined dual long acting bronchodilator inhalation therapy as a plausible treatment alternative.[19 20]

A search of the Cochrane Database of Systematic Reviews (Issue 5 of 12, May 2018) with the keyword “chronic obstructive pulmonary disease” yielded 132 unique records, indicating that keeping track not just

of original studies, but also evidence syntheses, has become a daunting task for decision makers in this area.

The implementation of evidence-based practice in the management of patients with COPD is challenging for medical practitioners due to the rapidly growing body of evidence. Additionally, non-adherence of patients with COPD to prescribed treatments is an ongoing challenge, with many patients being overburdened with the treatment work they need to do for their COPD care.[21-24] Patients' beliefs and concerns about the safety and benefits of their treatment and complex treatment regimens all impact on adherence. Non-pharmacological interventions such as pulmonary rehabilitation are persistently underutilised despite scientific evidence of their effectiveness.[25]

Faced with these challenges, novel tools of evidence synthesis and evidence communication in CODP for the patient-clinician encounter are needed that will allow collaborative deliberation of treatment options between patients and clinicians to make health care decisions together, taking into account the best scientific evidence available, as well as the patient's values and preferences.[26-29] Further, given the rapidly growing body of evidence on treatments for stable COPD, it is timely to identify current knowledge gaps to inform future research needs.

Consequently, the aim of our systematic review is 1) to synthesise the evidence on pharmacological and non-pharmacological treatments in patients with stable COPD, 2) produce an evidence map that identifies evidence gaps in order to inform future research, and that provides information that can be incorporated into a decision/communication aid for use during clinical encounters between patients and clinicians.

Methods and analysis

This protocol adheres to the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols (PRISMA-P) (see "Additional file 1 PRISMA-P checklist.pdf").[30]

Patient and Public Involvement

No patients or the public were involved in this systematic review of the literature.

Review question

What are the impacts of pharmacological and non-pharmacological interventions in patients with stable COPD on patient-important outcomes (including dyspnea and other symptoms such as anxiety, functional/exercise capacity, frequency of acute exacerbations, health-related quality of life, hospitalizations, emergency department visits) and lung function parameters?

Eligibility criteria

Types of studies

We will include systematic reviews that assessed the effectiveness of any pharmacological or non-pharmacological intervention on one or more relevant outcomes (see below) in patients with stable COPD. For every intervention/outcome pair (e.g. effectiveness of pulmonary rehabilitation to improve dyspnea) one systematic review will be included. The rationale for including only one systematic review per intervention/outcome pair is to avoid duplication in included original studies. Alternatively, an umbrella review could be conducted at the level of the original studies included in different systematic reviews, which would require a new meta-analysis. The latter approach is significantly more resource-intensive and time consuming and would not necessarily result in a more accurate pooled estimate compared with the result from a single systematic review, provided that the chosen review is a recent comprehensive high quality systematic review.

The following a priori protocol will guide which systematic reviews will be chosen, how their credibility will be evaluated, and how the quality of the body of evidence will be rated.

Systematic reviews will be excluded if:

- their pooled estimates were (partially) derived from studies that had not been published in the peer-reviewed literature (e.g. abstracts, studies only published on pharmaceutical company websites)
- they only contained indirect or mixed indirect and direct comparisons (network meta-analysis)

- they were umbrella reviews (reviews of reviews)
- they included patient populations other than patients with COPD and did not report outcomes separately for patients with COPD

We will derive a single pooled estimate per outcome per intervention. If multiple systematic reviews provided multiple estimates for the same intervention and outcome, we will choose a systematic review based on the following a priori defined scoring system:

a. Availability of one or more meta-analyses, as opposed to narrative data synthesis only (number of available meta-analyses positively correlated with scores)
b. Year of publication, date of literature search (higher scores for more recent systematic reviews)
c. Size based on a) Number of studies included, b) Number of participants included (higher scores for greater number of studies and participants)
d. Type of studies: randomized controlled trials (RCTs) generally provide stronger evidence than observational studies (highest score for RCTs, followed by prospective cohort studies, retrospective cohort studies, and case-control studies)
e. Synthesis of data from drug classes rather than specific drugs (higher scores if pooled estimates are available for drug classes compared to specific drugs only)

If we encounter the scenario in which despite the above mentioned criteria we still have to choose between two or more systematic reviews, we will make this choice based on these additional criteria:

a. Consensus among two practicing pulmonologists
b. Credibility of the systematic reviews as judged using the “A Measurement Tool to Assess Systematic Reviews” (AMSTAR2) criteria.[31]

Types of participants

Studies that evaluated patients aged 40 years and older with stable COPD defined as “persistent respiratory symptoms and airflow limitations that are due to airway and/or alveolar abnormalities usually

caused by significant exposure to noxious particles or gases" [32] will be included. Studies conducted in patients with an acute exacerbation of COPD will be excluded.

Types of interventions

We will include any pharmacological or non-pharmacological intervention. Interventions that we are expecting are the following: inhaled and other medications, smoking cessation, vaccinations, exercise and pulmonary rehabilitation, airway clearance techniques, nutrition and dietary interventions, COPD action plans, psychological interventions, home oxygen therapy, home mechanical ventilation, interventional bronchoscopy, and surgery. Complex interventions with multiple components such as exercise, smoking cessation advice, psychological support and home visits will be excluded. We will also exclude interventions only relevant during an acute exacerbation of COPD.

Comparators will include placebo or usual/standard care as well as active interventions.. We will exclude indirect comparisons between interventions or mixed direct and indirect comparisons (network meta-analyses).

Types of outcomes

The following outcomes will be included:

a. Dyspnea and other symptoms (e.g. cough, sputum production, and fatigue)
b. Exercise capacity and functional capacity
c. COPD exacerbations
d. Health-related quality of life
e. Hospitalizations, emergency department visits
f. Mortality
g. Lung function parameters
h. Adverse events

There will be no restrictions based on measurement methods.

Information sources and search strategy

This systematic review will follow an umbrella systematic review design (also called overview of reviews). We plan to conduct a comprehensive literature search of six databases, including Ovid MEDLINE Epub Ahead of Print, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE, Ovid EMBASE, Ovid Cochrane Database of Systematic Reviews, and Scopus from database inception to the present. We have developed a preliminary database search strategy and found that these databases can adequately identify the relevant literature. Reference mining of relevant publications will be conducted. The search strategy will be designed and conducted by an experienced librarian with input from the study's principle investigator. Controlled vocabulary supplemented with keywords will be used to search for systematic reviews and meta-analyses of pharmacological and non-pharmacological treatments for stable COPD. Search strategies are shown in Additional file 2.

All citations identified through the process will be imported to a reference management system (EndNote® Version X7 and X8; Thomson Reuters, Philadelphia, PA). We will use a web-based systematic review software, DistillerSR (Evidence Partners Incorporated, Ottawa, Canada), to facilitate the study selection process.

Data extraction

For every intervention/outcome pair one systematic review will be chosen following the priori protocol outlined above. At the beginning of data abstraction, we will develop a standardized data extraction form to extract study characteristics (author, study design, inclusion and exclusion criteria, patient characteristics, interventions, comparisons, outcomes, and related items for assessing study quality and applicability). The standardized form will be pilot-tested by all study team members. We will iteratively continue testing the form until no additional items or unresolved questions exist. All study details will be extracted by two independent reviewers. A third reviewer will review data extraction, and resolve conflicts.

Strategy for data synthesis

Data will be synthesized into an evidence map. An evidence map is defined as a systematic search of a broad field to identify gaps in knowledge and/or future research needs that presents results in a user-friendly format, often a visual figure or graph, or a searchable database.[33] The planned map will present a matrix that depicts each available treatment for stable COPD with a quantitative estimate on symptoms/outcomes from the patient perspective, along with an indication of the size and certainty in the evidence.

We will also provide a narrative synthesis of the findings from the included systematic reviews, structured around the type of intervention, target population characteristics (e.g. severity of COPD), type of outcome and intervention content.

Analysis of subgroups or subsets

Pre-determined characteristics for subgroup analysis are:

- Severity of COPD, e.g. based on GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria,[34] FEV1 (forced expiratory volume in one second) in % predicted
- COPD phenotypes, e.g. patients with frequent exacerbations, eosinophilic inflammation, emphysema-hyperinflation[35]
- Duration of intervention
- Different study types (e.g. randomized controlled trials versus observational studies)

Credibility (methodological quality) assessment

We will use AMSTAR2[31] to assess the credibility of the included systematic reviews. The AMSTAR2 tool addresses the following 16 items:

- Use of the components of PICO (population, intervention, comparator, outcome) for research questions and inclusion criteria
- Protocol for the systematic review, justification of any significant protocol deviations
- Study selection
- Literature search strategy

- Study selection by two independent reviewers
- Data extraction by two independent reviewers
- Excluded studies
- Description of included studies
- Risk of bias assessment in individual studies
- Sources of funding
- Methods for meta-analysis
- Impact of risk of bias on the meta-analysis or other evidence synthesis
- Accounting for risk of bias in the interpretation/discussion of results
- Explanation for heterogeneity in the results
- Publication bias
- Conflicts of interest

Ethics and dissemination

This systematic review is registered with PROSPERO (registration number: CRD42018095079; http://www.crd.york.ac.uk/PROSPERO). Important protocol amendments will be documented in PROSPERO. Approval by a research ethics committee is not required since the review will only include published and publicly accessible data. The systematic review will be published in a peer-reviewed journal and will provide various stakeholders with an evidence map.

Discussion

The aim of this systematic review is to systematically identify, summarize and assess a large body of evidence on pharmacological and non-pharmacological interventions in stable COPD. The information will be used to produce an evidence map to identify knowledge gaps and to inform a decision/communication aid for the clinical encounter between patients and clinicians.

Strengths and limitations of this systematic review

We have not identified any systematic reviews that have provided an evidence map for the treatment of stable COPD, and this systematic review will therefore be the first to use an evidence map to identify evidence gaps and to facilitate evidence communication in clinical encounters for COPD. The systematic review uses an a priori protocol to identify the most up-to-date systematic reviews of the highest possible quality, and the level of evidence for many intervention/outcome pairs will therefore likely be high.
As we will only include one systematic review per intervention/outcome pair, it is possible that some studies will not have been captured in included systematic reviews.

Practical Implications

Evidence mapping is a relative novel method of evidence synthesis, which aims to identify gaps in knowledge and/or future research needs based on a comprehensive literature search and present results in an easy to understand format in a figure or graph.[33] Evidence presented in such a user-friendly way may facilitate knowledge dissemination and implementation among relevant stakeholder groups including policy makers.[36 37] In this proposed study, we are targeting two aims that address the needs of different stakeholders.

The first type of stakeholders is patients and clinicians. In the context of a clinical encounter, they require shared decision-making tools (decision aids) because the available treatments are numerous and the impact on the different symptoms varies by intervention. Traditional systematic reviews usually summarize evidence grouped around specific interventions. In clinical practice, however, discussions between patients and clinicians often focus on a problem that demands a solution (e.g. shortness of breath or limited functional capacity in patients with COPD). This requires that evidence is communicated from an outcome rather than an intervention perspective (e.g. which interventions can improve shortness of breath or functional capacity in patients with stable COPD?). We plan to present the results of our systematic review structured by outcomes to facilitate knowledge translation into a decision/communication aid (the COPD CHOICE decision aid project). This will hopefully contribute to patient-centred and transparent evidence communication in clinical encounters.

The second type of stakeholders is policymakers funding research and researchers. The presentation of results in the form of evidence map can quickly provide them with a snapshot of which symptoms (daily dilemmas that patients face) or which interventions are only supported by low quality evidence (or no evidence). Such areas are prime targets for future research.

The proposed approach (overview of reviews and evidence mapping) is ideal in the context of the very large volume of literature available on pharmacological and non-pharmacological interventions in stable COPD, and the need to synthesize and present summaries that cater to different stakeholders.

List of abbreviations

95% CI: 95% confidence interval; AMSTAR2: A Measurement Tool to Assess Systematic Reviews 2; COPD: Chronic obstructive pulmonary disease (COPD); FEV1: forced expiratory volume in one second; GOLD: Global Initiative for Chronic Obstructive Lung Disease; PICO: population, intervention, comparator, outcome; PRISMA-P: Preferred Reporting Items for Systematic Review and Meta-analysis Protocols; RCT: randomized controlled trial

Authors' contributions

Claudia C. Dobler drafted the manuscript. M. Hassan Murad made substantial contributions to the conception and design. Working with Claudia C. Dobler, Larry J. Prokop designed the search strategy for the systematic review. Claudia C. Dobler, Magdoleen H. Farah, Allison S. Morrow, Mouaz Alsawas, Raed Benkhadra, Bashar Hasan, Larry J. Prokop, Zhen Wang, and M. Hassan Murad revised the manuscript critically for important intellectual content and approved the final manuscript.

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Competing interests statement

No conflict of interest to declare.

Word count

Abstract 297, Main text 2,494

References

1. Postma DS, Bush A, van den Berge M. Risk factors and early origins of chronic obstructive pulmonary disease. *Lancet (London, England)* 2015;385(9971):899-909. doi: 10.1016/s0140-6736(14)60446-3 [published Online First: 2014/08/16]
2. Adeloye D, Chua S, Lee C, et al. Global and regional estimates of COPD prevalence: Systematic review and meta-analysis. *Journal of global health* 2015;5(2):020415. doi: 10.7189/jogh.05-020415 [published Online First: 2016/01/13]
3. Murray CJ,os T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet (London, England)* 2012;380(9859):2197-223. doi: 10.1016/s0140-6736(12)61689-4 [published Online First: 2012/12/19]
4. Lano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet (London, England)* 2012;380(9859):2095-128. doi: 10.1016/s0140-6736(12)61728-0 [published Online First: 2012/12/19]
5. Wang C, Xu J, Yang L, et al. Prevalence and risk factors of chronic obstructive pulmonary disease in China (the China Pulmonary Health [CPH] study): a national cross-sectional study. *Lancet (London, England)* 2018;391(10131):1706-17. doi: 10.1016/s0140-6736(18)30841-9 [published Online First: 2018/04/14]
6. Hakim MA, Garden FL, Jennings MD, et al. Performance of the LACE index to predict 30-day hospital readmissions in patients with chronic obstructive pulmonary disease. *Clinical epidemiology* 2018;10:51-59. doi: 10.2147/clep.s149574 [published Online First: 2018/01/19]
7. Horita N, Goto A, Shibata Y, et al. Long-acting muscarinic antagonist (LAMA) plus long-acting beta-agonist (LABA) versus LABA plus inhaled corticosteroid (ICS) for stable chronic obstructive pulmonary disease (COPD). *Cochrane Database Syst Rev* 2017;2:CD012066. doi: https://dx.doi.org/10.1002/14651858.CD012066.pub2

8. Calzetta L, Ora J, Cavalli F, et al. Impact of LABA/LAMA combination on exercise endurance and lung hyperinflation in COPD: A pair-wise and network meta-analysis. *Respir Med* 2017;129:189-98. doi: https://dx.doi.org/10.1016/j.rmed.2017.06.020
9. Farne HA, Cates CJ. Long-acting beta2-agonist in addition to tiotropium versus either tiotropium or long-acting beta2-agonist alone for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2015(10):CD008989. doi: https://dx.doi.org/10.1002/14651858.CD008989.pub3
10. Rodrigo GJ, Price D, Anzueto A, et al. LABA/LAMA combinations versus LAMA monotherapy or LABA/ICS in COPD: a systematic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2017;12:907-22. doi: https://dx.doi.org/10.2147/COPD.S130482
11. Karner C, Cates CJ. Combination inhaled steroid and long-acting beta(2)-agonist in addition to tiotropium versus tiotropium or combination alone for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2011(3):CD008532. doi: https://dx.doi.org/10.1002/14651858.CD008532.pub2
12. Kwak M-S, Kim E, Jang EJ, et al. The efficacy and safety of triple inhaled treatment in patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis using Bayesian methods. *Int J Chron Obstruct Pulmon Dis* 2015;10:2365-76. doi: https://dx.doi.org/10.2147/COPD.S93191
13. Nannini LJ, Lasserson TJ, Poole P. Combined corticosteroid and long-acting beta(2)-agonist in one inhaler versus long-acting beta(2)-agonists for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2012(9):CD006829. doi: https://dx.doi.org/10.1002/14651858.CD006829.pub2
14. Nannini LJ, Poole P, Milan SJ, et al. Combined corticosteroid and long-acting beta(2)-agonist in one inhaler versus inhaled corticosteroids alone for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2013(8):CD006826. doi: https://dx.doi.org/10.1002/14651858.CD006826.pub2
15. Rojas-Reyes MX, Garcia Morales OM, Dennis RJ, et al. Combination inhaled steroid and long-acting beta2-agonist in addition to tiotropium versus tiotropium or combination alone for chronic

obstructive pulmonary disease. *Cochrane Database Syst Rev* 2016(6):CD008532. doi: https://dx.doi.org/10.1002/14651858.CD008532.pub3

16. Welsh EJ, Cates CJ, Poole P. Combination inhaled steroid and long-acting beta2-agonist versus tiotropium for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2013(5)
17. Singh S, Amin AV, Loke YK. Long-term use of inhaled corticosteroids and the risk of pneumonia in chronic obstructive pulmonary disease: a meta-analysis. *Arch Intern Med* 2009;169(3):219-29. doi: https://dx.doi.org/10.1001/archinternmed.2008.550
18. Kew KM, Seniukovich A. Inhaled steroids and risk of pneumonia for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2014(3):CD010115. doi: https://dx.doi.org/10.1002/14651858.CD010115.pub2
19. Wedzicha JA, Banerji D, Chapman KR, et al. Indacaterol-Glycopyrronium versus Salmeterol-Fluticasone for COPD. *The New England journal of medicine* 2016;374(23):2222-34. doi: 10.1056/NEJMoa1516385 [published Online First: 2016/05/18]
20. Magnussen H, Disse B, Rodriguez-Roisin R, et al. Withdrawal of inhaled glucocorticoids and exacerbations of COPD. *The New England journal of medicine* 2014;371(14):1285-94. doi: 10.1056/NEJMoa1407154 [published Online First: 2014/09/10]
21. Bourbeau J, Bartlett SJ. Patient adherence in COPD. *Thorax* 2008;63(9):831-8. doi: 10.1136/thx.2007.086041 [published Online First: 2008/08/30]
22. Agh T, Inotai A, Meszaros A. Factors associated with medication adherence in patients with chronic obstructive pulmonary disease. *Respiration; international review of thoracic diseases* 2011;82(4):328-34. doi: 10.1159/000324453 [published Online First: 2011/04/02]
23. Harb N, Foster JM, Dobler CC. Patient-perceived treatment burden of chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2017;12:1641-52. doi: 10.2147/copd.s130353 [published Online First: 2017/06/16]
24. Dobler CC, Harb N, Maguire CA, et al. Treatment burden should be included in clinical practice guidelines. *BMJ (Clinical research ed)* 2018;363:k4065. doi: 10.1136/bmj.k4065 [published Online First: 2018/10/14]

25. Safka KA, McIvor RA. Non-pharmacological management of chronic obstructive pulmonary disease. *The Ulster medical journal* 2015;84(1):13-21. [published Online First: 2015/05/13]
26. Stiggelbout AM, Van der Weijden T, De Wit MP, et al. Shared decision making: really putting patients at the centre of healthcare. *BMJ (Clinical research ed)* 2012;344:e256. doi: 10.1136/bmj.e256 [published Online First: 2012/01/31]
27. Elwyn G, Frosch D, Thomson R, et al. Shared decision making: a model for clinical practice. *Journal of general internal medicine* 2012;27(10):1361-7. doi: 10.1007/s11606-012-2077-6 [published Online First: 2012/05/24]
28. Dobler CC, Sanchez M, Gionfriddo MR, et al. Impact of decision aids used during clinical encounters on clinician outcomes and consultation length: a systematic review. *BMJ quality & safety* 2018 doi: 10.1136/bmjqs-2018-008022 [published Online First: 2018/10/12]
29. Dobler CC, Midthun DE, Montori VM. Quality of Shared Decision Making in Lung Cancer Screening: The Right Process, With the Right Partners, at the Right Time and Place. *Mayo Clinic proceedings* 2017;92(11):1612-16. doi: 10.1016/j.mayocp.2017.08.010 [published Online First: 2017/11/06]
30. Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ (Clinical research ed)* 2015;350:g7647. doi: 10.1136/bmj.g7647 [published Online First: 2015/01/04]
31. Shea BJ, Reeves BC, Wells G, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. *BMJ (Clinical research ed)* 2017;358:j4008. doi: 10.1136/bmj.j4008 [published Online First: 2017/09/25]
32. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (2019 report) [Available from: https://goldcopd.org/gold-reports/ accessed January 28, 2019.
33. Miake-Lye IM, Hempel S, Shanman R, et al. What is an evidence map? A systematic review of published evidence maps and their definitions, methods, and products. *Systematic reviews* 2016;5:28. doi: 10.1186/s13643-016-0204-x [published Online First: 2016/02/13]

34. Global Strategy for Prevention, Diagnosis and Management of COPD, 2018 reprt. Available at: http://goldcopd.org/wp-content/uploads/2017/11/GOLD-2018-v6.0-FINAL-revised-20-Nov_WMS.pdf Accessed May 15, 2018.
35. Miravitlles M, Calle M, Soler-Cataluna JJ. Clinical phenotypes of COPD: identification, definition and implications for guidelines. *Archivos de bronconeumologia* 2012;48(3):86-98. doi: 10.1016/j.arbres.2011.10.007 [published Online First: 2011/12/27]
36. Bangerter LR, Griffin JM, Langer S, et al. The Effect of Psychosocial Interventions on Outcomes for Caregivers of Hematopoietic Cell Transplant Patients. *Current hematologic malignancy reports* 2018 doi: 10.1007/s11899-018-0445-y [published Online First: 2018/05/01]
37. Farah WH, Alsawas M, Mainou M, et al. Non-pharmacological treatment of depression: a systematic review and evidence map. *Evidence-based medicine* 2016;21(6):214-21. doi: 10.1136/ebmed-2016-110522 [published Online First: 2016/11/12]

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	p1 (title), p5
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	not applicable
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	abstract, p11
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	p1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	p11
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	p1
Support:			
Sources	5a	Indicate sources of financial or other support for the review	p13
Sponsor	5b	Provide name for the review funder and/or sponsor	p13
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	p13
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	p4-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	p7-8
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	p6-7
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	p9
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Additional file 2 (detailed search strategy)
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	p9-10

	Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis) p6-7
	Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators p9
Data items		12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications p9-11
Outcomes and prioritization		13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale p8
Risk of bias in individual studies		14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis p7, 10-11
Data synthesis		15a	Describe criteria under which study data will be quantitatively synthesised p10
		15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ) not applicable
		15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) p10
		15d	If quantitative synthesis is not appropriate, describe the type of summary planned p10
Meta-bias(es)		16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies) p10-11
Confidence in cumulative evidence		17	Describe how the strength of the body of evidence will be assessed (such as GRADE) p10

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

Literature search strategy for

Treatment of stable chronic obstructive pulmonary disease: a protocol for a systematic review and evidence map

Claudia C. Dobler,[1] Magdoleen H Farah,[1] Allison S. Morrow,[1] Mouaz Alsawas,[1] Raed Benkhadra[1] Bashar Hasan,[1] Larry J Prokop,[2] Zhen Wang,[1] M. Hassan Murad[1]

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2) Library Public Services, Mayo Clinic, Rochester, Minnesota, USA.

Ovid

Part 1

Database(s): Embase 1988 to 2018 Week 16, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 11, 2018, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search Strategy:

#	Searches	Results
1	exp Pulmonary Disease, Chronic Obstructive/dh, dt, px, rh, su, th [Diet Therapy, Drug Therapy, Psychology, Rehabilitation, Surgery, Therapy]	18829
2	exp chronic obstructive lung disease/dm, dt, rh, su, th [Disease Management, Drug Therapy, Rehabilitation, Surgery, Therapy]	27067
3	1 or 2	45896
4	("chronic airflow disease*" or "chronic airflow disorder*" or "chronic airflow limitation*" or "chronic airflow obstruction*" or "chronic airway disease*" or "chronic airway disorder*" or "chronic airway limitation*" or "chronic airway obstruction*" or "chronic bronchitis" or "chronic obstructive airflow disease*" or "chronic obstructive airflow disorder*" or "chronic obstructive airway disease*" or "chronic obstructive airway disorder*" or "chronic obstructive bronchitis" or "chronic obstructive bronchopulmonary disease*" or "chronic obstructive broncho-pulmonary disease*" or "chronic obstructive bronchopulmonary disorder*" or "chronic obstructive broncho-pulmonary disorder*" or "chronic obstructive lung disease*" or "chronic obstructive lung disorder*" or "chronic obstructive pulmonary disease*" or "chronic obstructive pulmonary disorder*" or "chronic obstructive respiratory disease*" or "chronic obstructive respiratory disorder*" or coad or copd or emphysema or "obstructive lung disease" or "obstructive lung disorder*" or "obstructive pulmonary disease*" or "obstructive pulmonary disorder*" or "obstructive pulmonary tract disease*" or "obstructive pulmonary tract disorder*" or "obstructive respiratory disease*" or "obstructive respiratory disorder*" or "obstructive respiratory tract disease*" or "obstructive respiratory tract disorder*").ti,ab,hw,kw.	248757

5	exp Bronchodilator Agents/	383398
6	(abediterol or acefylline or "acefylline clofibrol" or "acefylline piperazine" or "aclidinium bromide" or "adrenalin hydrogen tartrate" or Adrenomedullin or Albuterol or ambuphylline or Aminophylline or antibronchospastic or arformoterol or Atropine or bambuterol or bamifylline or baralgin or batefenterol or bitolterol or "bitolterol mesilate" or "bronchial dilating" or "bronchial-dilating" or bronchodilatant* or "broncho-dilatant*" or bronchodilatating or "broncho-dilatating" or bronchodilatator* or "broncho-dilatator*" or bronchodilating or "broncho-dilating" or bronchodilator* or "broncho-dilator*" or broncholytic* or broncholytica or bronchospasmolytic or broxaterol or Budesonide or carbuterol or carmoterol or "choline theophyllinate" or Clenbuterol or clorprenaline or Colforsin or Cromakalim or danirixin or "darotropium bromide" or dilator* or diprophylline or ditec or doxofylline or Dyphylline or elubrixin or enprofylline or ephedrine or "ephedrine sulfate" or Epinephrine or eprozinol or espatropate or etafedrine or etamiphyllin or "etamiphyllin camsilate" or etanterol or etofylline or Fenoterol or fenspiride or Fluticasone or "flutropium bromide" or formoterol or "Formoterol Fumarate" or furafylline or glycopyrronium or "gsk 159802" or "gsk 597901" or guaifylline or "gw 678007" or Hexoprenaline or Hyoscyamine or ibuterol or "ilmetropium iodide" or imoxiterol or indacaterol or inhaler* or Ipratropium or "ipratropium bromide" or isbufylline or isoetarine or "isoetarine mesylate" or Isoetharine or isoprenaline or Isoproterenol or Khellin or laprafylline or levalbuterol or mabuterol or marax or Metaproterenol or methoxyphenamine or milveterol or "n methylmequitazine" or naminterol or neobiphyllin or nestifylline or "Nitric Oxide" or olodaterol or orciprenaline or "oxitropium bromide" or "oxyphenonium bromide" or pibaxizine or pirbuterol or "pirbuterol acetate" or pneumodilator or Procaterol or protokylol or proxyphylline or Pseudoephedrine or racephedrine or Racepinephrine or reproterol or rimiterol or "ru 45703" or salbutamol or "salbutamol sulfate" or salmefamol or salmeterol or "Salmeterol Xinafoate" or sibenadet or "S-Nitrosoglutathione" or "S-Nitrosothiols" or soterenol or tazifylline or Terbutaline or Theobromine or Theophylline or "theophylline sodium glycinate" or thiazinamium or "thiazinamium metilsulfate" or Tiotropium or Tretoquinol or "tretoquinol derivative" or trimetaquinol or tulobuterol or "uk 432097" or Umeclidinium or vephylline or verofylline or vilanterol or "vilanterol trifenatate" or zindotrine).ti,ab,hw,kw.	860675
7	exp Adrenergic beta-2 Receptor Agonists/	82439
8	("adrenergic beta 2 agonist*" or "adrenergic beta 2 receptor agonist*" or "adrenergic beta2 agonist*" or "adrenergic beta-2 agonist*" or "adrenergic beta-2 receptor agonist*" or "adrenergic beta2-agonist*" or Albuterol or "beta 2 adrenergic agent*" or "beta 2 adrenergic agonist*" or "beta 2 adrenergic receptor agonist*" or "beta 2 adrenergic receptor stimulant*" or "beta 2 adrenergic receptor stimulat*" or "beta 2 adrenergic receptor stimulator*" or "beta 2 adrenergic stimulant*" or "beta 2 adrenergic stimulat*" or "beta 2 adrenergic stimulator*" or "beta 2 adrenoceptor agonist*" or "beta 2 adrenoceptor stimulant*" or "beta 2 adrenoceptor stimulat**" or "beta 2 adrenoceptor stimulator*" or "beta 2 agonist*" or "beta agonist*" or "beta receptor agonist*" or "beta receptor stimulant*" or "beta stimulant" or "beta2 adrenergic receptor stimulat*" or Fenoterol or formoterol or Hexoprenaline or indacaterol or Isoetharine or LABA or LABAs or Metaproterenol or Procaterol or Ritodrine or SABA or SABAs or salmeterol or "Salmeterol Xinafoate" or Terbutaline).ti,ab,hw,kw.	83917
9	exp Cholinergic Antagonists/	215195
10	("acetylcholine antagonist*" or "acetylcholine receptor block*" or "acetylcholine receptor inhibitor*" or "AChR inhibitor" or aclidinium or "aclidinium bromide" or acotiamide or adiphenine or afacifenacin or Alcuronium or "alpha conotoxin MII" or alvameline or alverine or "alverine citrate" or anisodamine or "anti cholinergics" or anticholinergic or anticholinergic* or "anti-cholinergic*" or antimuscarinic* or aprofene or aspaminol or Atracurium or Atropine or atropinic* or azaprophen or belladonna or bellergal or Benactyzine or benzetimide or benzilonium or "benzilylcholine mustard" or benzoquinonium or Benztropine or Biperiden or bornaprine or Butylscopolammonium or buzepide or catestatin or "central anticholinergic" or Chlorisondamine or chlorphenoxamine or cholinolytic* or cimetropium or clidinium or Curare or Cyclopentolate or cycrimine or darifenacin or darotropium or deptropine or desfesoterodine or Dexetimide or dexmecamylamine or "dibutoline sulfate" or Dicyclomine or	400683

	dicycloverine or diethazine or dimevamide or "diphemanil methylsulfate" or drofenine or elantrine or Emepronium or espatropate or Ethidium or "ethylcholine mustard aziridinium" or eucatropine or fenoverine or fenpipramide or fenpiverinium or fesoterodine or fluperlapine or flutropium or furtramine or "Gallamine Triethiodide" or ganglefene or Glycopyrrolate or glycopyrronium or "gsk 202405" or "h cholinoreactive cell*" or hemicholinium or hexahydrodifenidol or hexahydroprocyclidine or hexahydrosiladifenidol or Hexamethonium or hexbutinol or "hexbutinol methiodide" or "hexocyclium metilsulfate" or himbacine or homatropine or "homatropine methyl" or "homatropine terephthalate" or Hyoscyamine or imidafenacin or Ipratropium or isomylamine or "isopropamide iodide" or LAMA or LAMAs or levetimide or lophotoxin or mazaticol or Mecamylamine or mefurtramine or mepenzolate or meptazinol or "meta cholinoreactive cell*" or methantheline or methoctramine or methylatropine or methyllycaconitine or methylscopolamine or metixene or muscarinic* or muscarinolytic* or "nicotine tartrate" or nicotinic* or nuvenzepine or "octatropine methylbromide" or Orphenadrine or otenzepad or oxitropium or oxybutynin or oxyphencyclimine or Oxyphenonium or Pancuronium or "para fluorohexahydrosiladifenidol" or "para fluorohexbutinol" or parapenzolate or "parasympathetic block*" or "parasympathetic inhibitor*" or parasympathicolytic* or parasympatholytic* or parasympatolytic* or Pempidine or penthienate or "Pentolinium Tartrate" or phenglutarimide or Pipecuronium or pipenzolate or piperidolate or piperphenamine or pipethanate or Pirenzepine or piroheptine or "poldine methylsulfate" or pridinol or "pridinol mesilate" or "prifinium bromide" or Procyclidine or profenamine or proglumide or Propantheline or propiverine or "propylbenziloylcholine mustard" or "Propylbenzilylcholine Mustard" or pyrrinol or Quinidine or "Quinuclidinyl Benzilate" or revatropate or revefenacin or rispenzepine or SAMA or SAMAs or Scopolamine or secoverine or silahexocyclium or siltenzepine or sofpironium or solifenacin or "Solifenacin Succinate" or stramonium or sydnofen or tarafenacin or telenzepine or tematropium or temiverine or thiazinamium or "thiazinamium metilsulfate" or thihexinol or "tiemonium iodide" or "tiemonium methylsulfate" or tifenamil or timepidium or Tiotropium or tofenacin or tolterodine or "Tolterodine Tartrate" or tonopan or Toxiferine or tricyclamol or "tridihexethyl chloride" or Trihexyphenidyl or Trimethaphan or triperidene or tripitramine or tropacin or Tropicamide or tropine or "tropine benzoate" or "trospium chloride" or troventol or Tubocurarine or umeclidinium or valethamate or vamicamide or Vecuronium or vedaclidine or zamifenacin or zolenzepine).ti,ab,hw,kw.	
11	exp Phosphodiesterase 4 Inhibitors/	10642
12	(apremilast or arofylline or atizoram or benzafentrine or catramilast or cilomilast or cipamfylline or daxalipram or denbufylline or elbimilast or filaminast or ibudilast or indimilast or lavamilast or nitraquazone or oglemilast or "PDE 4 inhibitor*" or "PDE IV inhibitor*" or "PDE type 4 inhibitor*" or "PDE type IV inhibitor*" or "pde-4 inhibitor*" or "PDE4 inhibitor*" or "phosphodiesterase 4 inhibitor*" or "phosphodiesterase IV inhibitor*" or "phosphodiesterase type 4 inhibitor*" or "phosphodiesterase type IV inhibitor*" or piclamilast or pumafentrine or revamilast or roflumilast or Rolipram or tetomilast or tibenelast or tilivapram or tipelukast or tofimilast or tolafentrine or zardaverine).ti,ab,hw,kw.	12671
13	or/5-12	1192205
14	4 and 13	38943
15	3 or 14	67111
16	exp meta analysis/	229890
17	exp "systematic review"/	165306
18	((meta adj analys*) or (systematic* adj3 review*)).ti,ab,hw,kw,pt.	589817
19	16 or 17 or 18	589821
20	15 and 19	2911
21	limit 20 to (editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media	161

	or webcasts) [Limit not valid in Embase,CDSR,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	
22	20 not 21	2750
23	from 15 keep 41670-41728	59
24	22 or 23	2809
25	remove duplicates from 24	2077

Part 2

Database(s): Embase 1988 to 2018 Week 16, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 11, 2018, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search Strategy:

#	Searches	Results
1	("chronic airflow disease*" or "chronic airflow disorder*" or "chronic airflow limitation*" or "chronic airflow obstruction*" or "chronic airway disease*" or "chronic airway disorder*" or "chronic airway limitation*" or "chronic airway obstruction*" or "chronic bronchitis" or "chronic obstructive airflow disease*" or "chronic obstructive airflow disorder*" or "chronic obstructive airway disease*" or "chronic obstructive airway disorder*" or "chronic obstructive bronchitis" or "chronic obstructive bronchopulmonary disease*" or "chronic obstructive broncho-pulmonary disease*" or "chronic obstructive bronchopulmonary disorder*" or "chronic obstructive broncho-pulmonary disorder*" or "chronic obstructive lung disease*" or "chronic obstructive lung disorder*" or "chronic obstructive pulmonary disease*" or "chronic obstructive pulmonary disorder*" or "chronic obstructive respiratory disease*" or "chronic obstructive respiratory disorder*" or coad or copd or emphysema or "obstructive lung disease" or "obstructive lung disorder*" or "obstructive pulmonary disease*" or "obstructive pulmonary disorder*" or "obstructive pulmonary tract disease*" or "obstructive pulmonary tract disorder*" or "obstructive respiratory disease*" or "obstructive respiratory disorder*" or "obstructive respiratory tract disease*" or "obstructive respiratory tract disorder*").ti,ab,hw,kw.	248757
2	exp Antibiotic Prophylaxis/	39823
3	exp Anti-Bacterial Agents/	3061033
4	exp antibiotic agent/	986815
5	("1 methylmocimycin*" or "11 deoxydaunorubicin*" or "14 hydroxyclarithromycin*" or "19 deformyl 4 deoxydesmycosin*" or "19 deformyldesmycosin*" or "2 acetylerythromycin*" or "2 fluoroidarubicin*" or "2 n ethylnetilmicin*" or "2 pyrrolinodoxorubicin*" or "21 aminoepothilone B" or "3 3 cyanomorpholino 3 deaminodoxorubicin*" or "3 deamino 2 fluoro 3 hydroxydoxorubicin 14 pimelate" or "3 deamino 3 morpholinodoxorubicin*" or "3 deamino 3 morpholinooxaunomycin*" or "4 demethoxy 11 deoxydaunomycinone" or "4 demethoxydaunomycinone" or "4 demethoxydoxorubicin*" or "4 deoxydesmycosin*" or "4 iodoesorubicin*" or "5 iminodaunorubicin*" or "6 n ethylnetilmicin*" or "6beta iodopenicillanic acid" or "9 deacetyl 9 methylidarubicin*" or "9 deoxydoxorubicin*" or "9 dihydroerythronolide A" or "a 102395" or "a 10255" or "a 10947" or "a 130b" or "a 192411" or "a 63075" or abkhazomycin* or abyssomicin* or acetomycin* or acetylspiramycin* or aclacinomycin* or aclarubicin* or actagardin* or actaplanin* or actinorhodine or "aculeacin A" or aculeximycin* or adicillin* or aditoprim or adriamycinone or agglomerin* or aklavinone or alafosfalin* or Alamethicin* or albocycline or aldecalmycin* or aldoxorubicin* or alisamycin* or allicin* or almecillin* or "alpha defensin*" or ambruticin* or Amdinocillin* or amfomycin* or Amikacin* or aminoglycoside* or aminopenicillin* or "Aminosalicylic Acid" or Amoxicillin* or "Amphotericin B" or Ampicillin* or amrubicin* or "angucycline derivative" or anhydrochlortetracycline or anhydroepitetracycline or anhydrotetracycline or anidulafungin* or Anisomycin* or annamycin* or ansamitocin* or "ansamycin derivative" or anthracycline* or anthracyclinone* or antibacterial* or "anti-bacterial*" or antibiotic* or "anti-biotic*" or "antimicrobial cationic peptide*" or Antimycin* or antimycobacterial* or "anti-mycobacterial*" or Antitreponemal* or "Anti-treponemal*" or Antitubercular* or "Anti-tubercular*" or apalcillin* or aplasmomycin* or "aplysianin E" or apramycin* or aristeromycin* or Arsphenamine or aspoxicillin* or astromicin* or asukamycin* or "atpenin B" or auricularum or Aurodox or aurograb or avibactam or avilamycin* or avoparcin* or azidamfenicol or azidocillin* or Azithromycin* or Azlocillin* or Aztreonam or "aztreonam lysine" or azurocidin* or bacampicillin* or Bacitracin* or bacmecillinam or bactenecin* or bacteriocid* or Bacteriocin* or bafilomycin* or balhimycin* or "baliz 2" or Bambermycin* or baquiloprim or "barminomycin I" or baycuten or beauvericin*	2430080

or beroline or berubicin* or berythromycin* or "beta defensin*" or betafectin* or "beta-Lactam*" or "betaLactamase Inhibitor*" or "beta-Lactamase Inhibitor*" or betamipron or bialaphos or biapenem or bicozamycin* or "biphenomycin A" or bluensomycin* or bombinin* or "Bongkrekic Acid" or boromycin* or borrelidin* or "Brefeldin A" or brilacidin* or brobactam or butalactin* or butirosin* or cadazolid or Calcimycin* or Candicidin* or Capreomycin* or carbacephem or carbadox or carbapenem or "carbazomycin A" or Carbenicillin* or carbomycin* or Carfecillin* or carindacillin* or carubicin* or carumonam or caspofungin* or cathelicidin* or cecropin* or cefacetrile or Cefaclor or Cefadroxil or cefalexin* or cefaloglycin* or cefaloram or cefaloridine or cefalotin* or Cefamandole or cefapirin* or Cefatrizine or cefazaflur or cefazedone or Cefazolin* or cefbuperazone or cefcanel or cefcapene or cefclidin* or cefdaloxime or cefdinir or cefditoren or cefepime or cefetamet or cefetecol or cefilavancin* or Cefixime or cefluprenam or cefmatilen or Cefmenoxime or Cefmetazole or cefminox or cefodizime or Cefonicid or Cefoperazone or ceforanide or cefoselis or Cefotaxime or Cefotetan or Cefotiam or cefovecin* or Cefoxitin* or cefozopran or cefpimizole or cefpiramide or cefpirome or cefpodoxime or cefprozil or cefquinome or cefradine or cefroxadine or Cefsulodin* or ceftaroline or Ceftazidime or cefteram or ceftezole or ceftibuten or ceftiofur or Ceftizoxime or ceftobiprole or ceftolozane or Ceftriaxone or Cefuroxime or cefuzonam or Cephacetrile or Cephalexin* or Cephaloglycin* or Cephaloridine or cephalosporin* or Cephalothin* or cephamycin* or Cephapirin* or Cephradine or chalcomycin* or Chloramphenicol* or chloroorienticin* or chloropolysporin* or chlorothricin* or chlorothricolide or Chlortetracycline or "chymotrypsin trypsin*" or ciadox or "cilastatin plus imipenem" or "cinerubin A" or "cinerubin B" or cinoquidox or Ciprofloxacin* or cirramycin* or Citrinin* or Clarithromycin* or "clavulanate potassium" or "Clavulanic Acid*" or Clindamycin* or clomocycline or Cloxacillin* or colicin* or colistimethate or Colistin* or "concanamycin A" or coumamidine or coumamycin* or "cp 63956" or cryptosporin* or Cyclacillin* or cycloheximide or Cycloserine or cystargin* or "cytarabine plus daunorubicin*" or cytovaricin* or dactimicin* or Dactinomycin* or dalbaheptide or dalbavancin* or dalfopristin* or "damavaricin Fc pentyl ether" or Daptomycin* or daunomycinone or daunorubicin* or daunorubicinol or "deacetoxycephalosporin C" or deacetylcefotaxime or "deacetylcephalosporin C" or dealanylalahopcin* or decaplanin* or dechloroeremomycin* or decilorubicin* or defensin* or Demeclocycline or dermaseptin* or dermcidin* or dermostatin* or desmycosin* or detorubicin* or Diarylquinoline* or Dibekacin* or Dicloxacillin* or dihydrostreptomycin* or Diketopiperazines or dimethylchlortetracycline or dioxidine or dirithromycin* or Distamycin* or "ditrisarubicin B" or doripenem or doxorubicin* or doxorubicinol or Doxycycline or drosocin* or echinocandin* or Echinomycin* or Edeine or efepristin* or efrotomycin* or emimycin* or endusamycin* or enniatin* or Enoxacin* or Enviomycin* or eperezolid or epetraborole or epicillin* or epidermin* or epiderstatin* or epiroprim or epirubicin* or epirubicinol or epitetracycline or epothilone* or "epsilon rhodomycinone" or eravacycline or eremomycin* or ertapenem or Erythromycin* or erythromycylamine or erythronolide* or esorubicin* or Ethambutol or Ethionamide or ethylhydrocupreine or etimicin* or evernimicin* or everninomicin* or faeriefungin* or fidaxomicin* or Filipin* or "fleroxacin deacetylcefotaxime ester" or flomoxef or flopristin* or florfenicol or Floxacillin* or flucloxacillin* or flumoxil or Fluoroquinolone* or flurithromycin* or fomidacillin* or fortimicin* or Fosfomycin* or fosmidomycin* or Framycetin* or fropenem or fungichromin* or furaquinocin* or furazidin* or "furazolium chloride" or furbenicillin* or fusafungine or "fusidate sodium" or "Fusidic Acid" or fuzlocillin* or galarubicin* or gallidermin* or gamithromycin* or ganefromycin* or "ge 2270a" or gentamicin* or gepotidacin* or globomycin* or gloximonam or "glycylcycline derivative" or "gonadorelin6 dextro lysine 2 pyrrolinodoxorubicin*" or "goniodomin A" or Gramicidin* or granulysin* or grisein* or guamecycline or habekacin* or hamycin* or hatomamicin* or hedamycin* or heliomycin* or hepcidin* or hetacillin* or hexacycline or hidamicin* or "histatin 5" or histatin* or hygromycin* or hymeglusin* or hypothemycin* or iclaprim or idarubicin* or idarubicinol or ikarugamycin* or "imidacloprid plus moxidectin*" or Imipenem or indolicidin* or inostamycin* or iseganan or isepamicin* or Isoniazid or "isopenicillin N" or "isoswinholide A" or istamycin* or "iturin A" or ixabepilone or Josamycin* or "k 252a" or kalafungin* or Kanamycin* or kanendomycin* or kasugamycin* or kelfiprim or ketolide or kidamycin* or kinamycin* or Kitasamycin* or "l 156602" or "l 733560" or "l 786392" or lactacystin* or

Lactams or lactivicin* or "lactocin S" or lactococcin* or lactoferricin* or ladirubicin* or laidlomycin* or lancovutide or lankamycin* or lanopepden or lanthiopeptin* or lantibiotic or Lasalocid or latamoxef or lavanducyanin* or lefamulin* or lenampicillin* or lenapenem or lenoremycin* or Leprostatic* or "leucinostatin A" or "leucinostatin B" or Leucomycin* or leurubicin* or Levofloxacin* or lexithromycin* or "lff 571" or Lincomycin* or lincosamide* or Linezolid or linopristin* or lividomycin* or "lonomycin A" or loracarbef or lotilibcin* or Lucensomycin* or lydicamycin* or Lymecycline or lysobactin* or lysocellin* or lysostaphin* or macrolide or magainin* or malyngolide or manumycin* or maridomycin* or "mdl 62208" or "mdl 62211" or mecillinam or meclocycline or megacin* or megalomicin* or Mepartricin* or meropenem or mersacidin* or metacycline or metampicillin* or Methacycline or Methicillin* or "methylenomycin A" or "methylenomycin B" or methymycin* or methynolide or meticillin* or Mezlocillin* or "microcin b17" or "microcin J25" or micronomicin* or midecamycin* or mideplanin* or "mikamycin B" or Mikamycin* or "milbemycin oxime" or milbemycin* or Minocycline or Miocamycin* or miokamycin* or miporamicin* or miraxid or mocimycin* or "moenomycin A" or monensin* or "monobactam derivative" or Moxalactam or moxidectin* or "ms 8209" or Mupirocin* or mureidomycin* or murepavadin* or mycinamicin* or Mycobacillin* or mycolog or mycoticin* or myxothiazol or "n benzyldoxorubicin 14 valerate" or "n trifluoroacetyldoxorubicin*" or Nafcillin* or "Nalidixic Acid" or narasin* or Natamycin* or neamine or nebacetin* or Nebramycin* or negamycin* or nemadectin* or nemorubicin* or Neomycin* or neosporin* or Netilmicin* or Netropsin* or niddamycin* or Nigericin* or Nisin* or nitrocefin* or nitrosochloramphenicol or "nocardicin A" or "nocardicin E" or "nocardicinic acid derivative*" or Norfloxacin* or nosiheptide or nourseothricin* or Novobiocin* or "nvb 302" or nybomycin* or Nystatin* or "oasomycin A" or obelmycin* or Ofloxacin* or olaquindox or oleandolide or Oleandomycin* or oligomycin* or omadacycline or omiganan or optocillin* or "orienticin A" or orientiparcin* or oritavancin* or oropivalone or Oxacillin* or oxaunomycin* or "Oxolinic Acid" or Oxytetracycline or paldimycin* or panipenem or pardaxin* or Paromomycin* or patulin* or pediazole or pediocin* or Pefloxacin* or penamecillin* or penethamate or "Penicillanic Acid" or "Penicillic Acid" or penicillin* or "penicilloic acid" or pentalenolactone or pentisomicin* or peptaibol or pexiganan or "pf 708093" or phenelfamycin* or pheneticillin* or phleomycin* or pikromycin* or "Pipemidic Acid" or Piperacillin* or pirarubicin* or pirazmonam or pirlimycin* or Pivampicillin* or pivmecillinam or platensimycin* or plazomicin* or plectasin* or pleuromutilin* or pluramycin* or pneumocandin* or "polyactin A" or polyfungin* or polymyxin* or "polyoxin B" or "polyoxin D" or polysporin* or polytrim or posizolid or "pr 39" or Pristinamycin* or Prodigiosin* or prohepcidin* or propicillin* or protegrin* or Prothionamide or prothracarcin* or "pseudomonic acid" or Pyrazinamide or pyrromycinone or pyrroxamycin* or quinacillin* or quinomycin* or quinupristin* or radezolid or radicicol or ramoplanin* or ranalexin* or ranbezolid or razupenem or retacillin* or retapamulin* or "rhodomycin A" or Ribostamycin* or Rifabutin* or Rifampin* or Rifamycin* or rimocidin* or Ristocetin* or ritipenem or "ritipenem acoxil" or rodorubicin* or roflamycoin* or rokitamycin* or Rolitetracycline or rosaramicin* or Roxarsone or Roxithromycin* or ruboxyl or Rutamycin* or sabarubicin* or sagopilone or sanfetrinem or sarecycline or "simaomicin alpha" or "simocyclinone D8" or Sirolimus or "sisomicin sulfate" or Sisomicin* or "skf 104662" or sofradex or Spectinomycin* or "spinosyn A" or Spiramycin* or squalamine or stigmatellin* or streptoduocin* or Streptogramin* or streptolydigin* or Streptomycin* or streptothricin* or streptotriad or Streptovaricin* or streptovirudin* or "streptovitacin A" or stubomycin* or subtilin* or Sulbactam or Sulbenicillin* or Sulfamerazine or Sulfamethoxypyridazine or sulfazecin* or sulopenem or sultamicillin* or surfactin* or surotomycin* or "swinholide A" or "swinholide B" or tachyplesin* or Talampicillin* or tameticillin* or tazobactam or tebipenem or tedizolid or Teicoplanin* or teixobactin* or telavancin* or temocillin* or terdecamycin* or tetracyclin* or Tetracycline or tetramycin* or tetronasin* or tetronomycin* or tetroxoprim or Thiamphenicol or Thienamycin* or Thioacetazone or thiolactomycin* or "thionin peptide" or thiopeptin* or thiophenoxycefalotin* or Thiostrepton or tiamulin* or "tibezonium iodide" or Ticarcillin* or tigecycline or tigemonam or tildipirosin* or tilmicosin* or timentin* or tirandamycin* or tizoxanide or tobicillin* or Tobramycin* or tolramycin* or tomopenem or toyocamycin* or tresaderm or tribactam or trichomycin* or "trichostatic acid" or "trichostatin A" or trimethoprim* or "trinem derivative" or

	"triostin A" or triplopen or trisep or Troleandomycin* or trospectomycin* or tuftsin* or tulathromycin* or Tunicamycin* or tutofusin* or Tylosin* or tylvalosin* or Tyrocidine or Tyrothricin* or "u 78608" or "uk 69753" or unphenelfamycin* or "urdamycin C" or "urdamycin D" or "urdamycin H" or ureidopenicillin* or urobiotic or "vacidin A" or validamycin* or Valinomycin* or valnemulin* or valrubicin* or Vancomycin* or venturicidin* or vernamycin* or "violamycin B1" or Viomycin* or "virginiae butanolide A" or "virginiae butanolide C" or "virginiamycin M" or "virginiamycin S" or Virginiamycin* or "viriplanin A" or viscosin* or volpristin* or "ws 9659 b" or "zibrofusidic acid" or zineryt or "zoptarelin doxorubicin*" or zorbamycin* or zorubicin*).mp.	
6	or/2-5	3703559
7	1 and 6	28719
8	exp meta analysis/	229890
9	exp "systematic review"/	165306
10	((meta adj analys*) or (systematic* adj3 review*)).ti,ab,hw,kw,pt.	589817
11	8 or 9 or 10	589821
12	7 and 11	879
13	limit 12 to (editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,CDSR,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	64
14	12 not 13	815
15	from 7 keep 23035-23104	70
16	14 or 15	885
17	remove duplicates from 16	767

Part 3

Database(s): Embase 1988 to 2018 Week 16, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 11, 2018, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search Strategy:

#	Searches	Results
1	("chronic airflow disease*" or "chronic airflow disorder*" or "chronic airflow limitation*" or "chronic airflow obstruction*" or "chronic airway disease*" or "chronic airway disorder*" or "chronic airway limitation*" or "chronic airway obstruction*" or "chronic bronchitis" or "chronic obstructive airflow disease*" or "chronic obstructive airflow disorder*" or "chronic obstructive airway disease*" or "chronic obstructive airway disorder*" or "chronic obstructive bronchitis" or "chronic obstructive bronchopulmonary disease*" or "chronic obstructive broncho-pulmonary disease*" or "chronic obstructive bronchopulmonary disorder*" or "chronic obstructive broncho-pulmonary disorder*" or "chronic obstructive lung disease*" or "chronic obstructive lung disorder*" or "chronic obstructive pulmonary disease*" or "chronic obstructive pulmonary disorder*" or "chronic obstructive respiratory disease*" or "chronic obstructive respiratory disorder*" or coad or copd or emphysema or "obstructive lung disease" or "obstructive lung disorder*" or "obstructive pulmonary disease*" or "obstructive pulmonary disorder*" or "obstructive pulmonary tract disease*" or "obstructive pulmonary tract disorder*" or "obstructive respiratory disease*" or "obstructive respiratory disorder*" or "obstructive respiratory tract disease*" or "obstructive respiratory tract disorder*").ti,ab,hw,kw.	248757
2	exp Benzodiazepines/	223779
3	(Alprazolam or arfendazam or benzodiazepin or benzodiazepine* or Benzodiazepinone* or bromazepam or camazepam or Chlordiazepoxide or cinolazepam or clobazam or clonazepam or clorazepate or "Clorazepate Dipotassium" or "clorazepate potassium" or dealkylflurazepam or delorazepam or demoxepam or devazepide or diazepam or doxefazepam or Estazolam or fludiazepam or flunitrazepam or flurazepam or flutoprazepam or fosazepam or gidazepam or girisopam or halazepam or loflazepate or lorazepam or lormetazepam or lotrafiban or meclonazepam or Medazepam or metaclazepam or Midazolam or nastorazepide or nerisopam or netazepide or nimetazepam or nitrazepam or nitrosochlordiazepoxide or norchlordiazepoxide or norclobazam or nordazepam or norfludiazepam or norflunitrazepam or oxazepam or phenazepam or pinazepam or prazepam or quazepam or "ro 7 0213" or talampanel or tampramine or tarazepide or temazepam or tetrazepam or tibezonium or tifluadom or tofisopam or tomaymycin or Triazolam or tuclazepam or uxepam).ti,ab,hw,kw.	271678
4	exp Home Care Services/	101515
5	(((domestic or home or domiciliary) adj3 (residence or residences or setting or settings or care or nurs* or help or service* or treatment* or therap* or "respiratory care" or "respiratory treatment*" or "respiratory therap*" or "respiratory service*" or "respiratory assist*" or ventilat*)) or "assisted living" or homecare).ti,ab,hw,kw.	209664
6	"nursing home*".ti,ab,hw,kw.	90908
7	(4 or 5) not 6	151038
8	exp Respiration, Artificial/	225415
9	(((((respiration* or respiratory or breathing) adj3 (assist* or controlled or mechanical)) or (facial or face or nasal)) adj3 mask*) or "artificial respiration*" or BiPAP or CPAP or "Fluidic Breathing Assister" or HMV or IPPB or IPPV or NIAV or NIV or NPPV or "Oxygen Regulator*" or PAP or PAV or "Portable Oxygen" or "Positive Airway Pressure*" or "positive end-expiratory pressure*" or "positive pressure*" or respirator or respirators or "Respiratory insufficiency" or Tracheostom* or ventilation or ventilator*).ti,ab,hw,kw.	529399
10	8 or 9	549586
11	7 and 10	6909

12	2 or 3 or 11	280786
13	1 and 12	3036
14	exp meta analysis/	229890
15	exp "systematic review"/	165306
16	((meta adj analys*) or (systematic* adj3 review*)).ti,ab,hw,kw,pt.	589817
17	14 or 15 or 16	589821
18	13 and 17	119
19	limit 18 to (editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,CDSR,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	3
20	18 not 19	116
21	from 13 keep 2384	1
22	20 or 21	117
23	remove duplicates from 22	97

Part 4

Database(s): Embase 1988 to 2018 Week 16, EBM Reviews - Cochrane Database of Systematic Reviews 2005 to April 11, 2018, Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1946 to Present
Search Strategy:

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1	("chronic airflow disease*" or "chronic airflow disorder*" or "chronic airflow limitation*" or "chronic airflow obstruction*" or "chronic airway disease*" or "chronic airway disorder*" or "chronic airway limitation*" or "chronic airway obstruction*" or "chronic bronchitis" or "chronic obstructive airflow disease*" or "chronic obstructive airflow disorder*" or "chronic obstructive airway disease*" or "chronic obstructive airway disorder*" or "chronic obstructive bronchitis" or "chronic obstructive bronchopulmonary disease*" or "chronic obstructive broncho-pulmonary disease*" or "chronic obstructive bronchopulmonary disorder*" or "chronic obstructive broncho-pulmonary disorder*" or "chronic obstructive lung disease*" or "chronic obstructive lung disorder*" or "chronic obstructive pulmonary disease*" or "chronic obstructive pulmonary disorder*" or "chronic obstructive respiratory disease*" or "chronic obstructive respiratory disorder*" or coad or copd or emphysema or "obstructive lung disease" or "obstructive lung disorder*" or "obstructive pulmonary disease*" or "obstructive pulmonary disorder*" or "obstructive pulmonary tract disease*" or "obstructive pulmonary tract disorder*" or "obstructive respiratory disease*" or "obstructive respiratory disorder*" or "obstructive respiratory tract disease*" or "obstructive respiratory tract disorder*").ti,ab,hw,kw.	248757
2	exp Adrenal Cortex Hormones/	1085572
3	exp corticosteroid/	710384
4	exp corticosteroid therapy/	41274
5	("adrenal cortex hormone*" or "adrenal cortex steroid*" or "adrenal cortical hormone*" or "adrenal cortical steroid*" or "adrenal steroid*" or "adreno cortical steroid*" or "adreno corticosteroid*" or "adrenocortical hormone*" or "adrenocortical steroid*" or adrenocorticosteroid* or adreson or alclometasone or aldosterone or algestone or "algestone acetonide" or amcinonide or amelometasone or beclometasone or budesonide or butixocort or chloroprednisone or ciclesonide or ciprocinonide or clioquinol or clobetasol or clobetasone or clocortolone or cloprednol or "cortical steroid*" or corticalsteroid* or "cortico steroid*" or corticoid* or corticosteroid* or corticosterone or corticotherap* or cortifair or cortisol or cortisone or cortivazol or cortril or deflazacort or dehydrocorticosterone or dehydrocortisone or deoxycorticosterone or dermocorticosteroid* or dexamethasone or diflorasone or diflucortolone or difluprednate or domoprednate or drocinonide or dutimelan or epicortisol or "etiprednol dicloacetate" or fluclorolone or fludrocortisone or fludroxycortide or flumetasone or flumoxonide or flunisolide or fluocinolone or fluocinonide or fluocortin or fluocortolone or fluorometholone or fluprednidene or fluprednisolone or fluticasone or formocortal or "formoterol fumarate" or Glucocorticoid* or glucocorticoidsteroid* or glucocorticosteroid* or glucocortoid* or glycocorticoid* or glycocorticosteroid* or halcinonide or halometasone or halopredone or hydrocortisone or "hydroxy norcorticosterone" or hydroxycorticoid* or hydroxycorticosteroid* or hydroxycorticosterone or hydroxydeoxycorticosterone or hydroxyhydrocortisone or "icometasone enbutate" or isoflupredone or itrocinonide or "locicortolone dicibate" or "lorinden a" or "lorinden t" or loteprednol or mazipredone or medrysone or meprednisone or mineralcorticosteroid* or mineralocorticosteroid* or minerocorticoid* or mometasone or nicocortonide or nivacortol or nordeoxycorticosterone or oropivalone or oxohydrocortisone or oxycorticosteroid* or paramethasone or prednisolone or prednisone or pregnenolone or procinonide or promestriene or resocortol or rimexolone or rofleponide or steroid* or tetrahydrodeoxycorticosterone or ticabesone or timobesone or tipredane or tixocortol or	1707747

	triamcinolone or "ulobetasol propionate" or uniderm or zoticasone).ti,ab,hw,kw.	
6	exp Expectorants/	30553
7	(Acetylcysteine or Ambroxol or aminophylline or Bromhexine or bron or cafedrine or Carbocysteine or diprophylline or etofylline or eucalyptus or expectorant* or fudosteine or guaiacol or "guaiacol carbonate" or guaietolin or Guaifenesin or guaifylline or "iodinated glycerol" or ipecac or mucolytic* or "Potassium Citrate" or "primula flower" or stepronin or "stepronin lysine" or sulfoguaiacol or tipepidine or ulogesic).ti,ab,hw,kw.	91107
8	exp narcotic analgesic agent/	243598
9	exp Analgesics, Opioid/	347494
10	(acetorphine or acetylcodeine or acetylmethadol or Alfentanil or Alphaprodine or anileridine or apadoline or azidomorphine or benzhydrocodone or bezitramide or bremazocine or "Brompton mixture" or Buprenorphine or Butorphanol or ciramadol or cocodamol or Codeine or codydramol or conorfone or cyclazocine or Dextromoramide or Dextropropoxyphene or dextrorphan or dezocine or diamorphine or diconal or dihydrocodeine or dihydroetorphine or Dihydromorphine or dimethylthiambutene or Diphenoxylate or dipipanone or enadoline or eptazocine or ethylketazocine or Ethylketocyclazocine or Ethylmorphine or etonitazene or Etorphine or etoxeridine or faxeladol or Fentanyl or furethidine or gelonida or Heroin or Hydrocodone or isalmadol or isomethadone or ketazocine or ketobemidone or ketogan or kyotorphin or lefetamine or levacetylmethadol or levomethadone or Levorphanol or Meperidine or Meptazinol or metazocine or Methadone or "Methadyl Acetate" or methylsamidorphan or Morphine or "morphinomimetic agent*" or "morphinomimetic drug*" or morphinone or Nalbuphine or narcotic* or nicocodine or nicomorphine or noracymethadol or norbuprenorphine or nordextropropoxyphene or normorphine or norpethidine or norpropoxyphene or "o nortramadol" or oliceridine or opiate or Opiate* or opioid* or Opium or oripavine or Oxycodone or Oxymorphone or pentamorphone or Pentazocine or pethidine or phenadoxone or phenaridine or Phenazocine or phencyclidine or Phenoperidine or picenadol or piminodine or Pirinitramide or piritramide or profadol or Promedol or propiram or sameridine or samidorphan or semorphone or Sufentanil or tapentadol or thebaine or tifluadom or Tilidine or tonazocine or Tramadol or trimeperidine).ti,ab,hw,kw.	525567
11	exp Bronchoscopy/	68088
12	exp lung/su	8000
13	exp Pneumonectomy/	49308
14	("airflow clearance" or "airway clearance" or BLVR or bronchoscop* or ELVR or "lung clearance" or "lung denervation" or LVRS or pneumectom* or pneumonectom* or pneumoresection* or "pulmonary clearance" or "volume reducing" or "volume reduction*").ti,ab,hw,kw.	143837
15	exp Smoking Cessation/	76463
16	((smoking* or tobacco* or cigar* or cigarette* or cigaret*) and (quit* or discontinu* or ceas* or cessation*)).ti,ab,hw,kw.	110813
17	exp Respiratory Therapy/	107010
18	exp exercise/	423706
19	exp Exercise Therapy/	102223
20	exp Breathing Exercises/	8723
21	exp Exercise Movement Techniques/	66908
22	(aerobics or anaerobics or "artificial respiration*" or bicycling or biking or "Chest Wall Oscillation*" or dance or dancing or "endurance training" or exercis* or "Extracorporeal Membrane Oxygen*" or "fitness training" or "inhalation therap*" or isometrics or oxygen or "physical activit*" or "physical exertion" or "postural drain*" or rehab* or "resistance training" or "respiration care*" or "respiration therap*" or "respiratory care*" or "respiratory therap*" or running or "strength training" or swimming or "Tai Chi" or "Tai Ji" or walking or weightlifting	2620447

	or yoga).ti,ab,hw,kw.	
23	exp Nutrition Therapy/	384447
24	(diet or dietary or diets or nutrition* or supplementation or supplements).ti,ab,hw,kw.	1856949
25	exp Influenza Vaccines/	50514
26	exp Pneumococcal Vaccines/	22742
27	exp vaccination/	204458
28	(moniarix or "pcv 13" or pcv13 or "pneu immune" or "pneumo 23" or pneumopur or pneumovax or "pnu immune" or "pnu imune" or "polysaccharide vaccine pneumococcal" or prevenar or prevnar or "streptococcus pneumoniae vaccine" or streptopur or streptorix or synflorix or vaccin*).ti,ab,hw,kw.	702951
29	exp Psychotherapy/	367662
30	exp Cognitive Therapy/	66331
31	exp Cognitive Behavior Therapy/	28661
32	exp Mindfulness/	6317
33	exp Mind-Body Therapies/	90152
34	exp Mentoring/	1557
35	exp Health Promotion/	153501
36	(CBT or coach* or "Cognitive behavioral therap*" or "Cognitive therap*" or "health promotion*" or meditat* or mentor* or "mind body" or mindfulness or psychological or psychosocial or psychotherap*).ti,ab,hw,kw.	1535477
37	exp Self Care/	113331
38	exp Telemedicine/	53304
39	exp Therapy, Computer-Assisted/	67118
40	exp Mobile Applications/	8595
41	("action plan*" or android or app or apps or ehealth or "e-health" or internet or ipad* or iphone* or mhealth or "m-health" or "mobile app*" or "mobile health" or "mobile technolog*" or "portable computer*" or "portable electronic app*" or "portable software app*" or "remote consultation*" or "self care" or "self help" or "self management" or "self treatment" or "smart phone*" or smartphone* or "tablet computer*" or teleconsultation* or "tele-consultation*" or telehealth or "tele-health" or telemedicine or "tele-medicine" or teletherap* or "tele-therap*" or web).ti,ab,hw,kw.	603033
42	exp "Delivery of Health Care, Integrated"/	20570
43	exp Acupuncture/	38261
44	exp Complementary Therapies/	250389
45	exp Electric Stimulation Therapy/	260840
46	(acupuncture or agent* or "alternative medicine" or "care package*" or chemotherap* or "complementary medicine" or drug* or "electric stimulation*" or holistic or "integrated care" or "integrated health care" or "integrated healthcare" or intervention* or manag* or medication* or "muscle stimulation*" or operat* or pharmacotherap* or procedure* or reconstruction* or repair* or resect* or surg* or therap* or treat* or wellness).ti,ab,hw,kw.	26377389
47	or/2-46	30049403
48	1 and 47	182842
49	exp meta analysis/	229890
50	exp "systematic review"/	165306
51	((meta adj analys*) or (systematic* adj3 review*)).ti,ab,hw,kw,pt.	589817
52	49 or 50 or 51	589821
53	48 and 52	5613

54	limit 53 to (editorial or erratum or letter or note or addresses or autobiography or bibliography or biography or blogs or comment or dictionary or directory or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or overall or patient education handout or periodical index or portraits or published erratum or video-audio media or webcasts) [Limit not valid in Embase,CDSR,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained]	261
55	53 not 54	5352
56	from 48 keep 121215-121366	152
57	55 or 56	5504
58	remove duplicates from 57	3991

Scopus

Part 1

1 TITLE-ABS-KEY("chronic airflow disease*" OR "chronic airflow disorder*" OR "chronic airflow limitation*" OR "chronic airflow obstruction*" OR "chronic airway disease*" OR "chronic airway disorder*" OR "chronic airway limitation*" OR "chronic airway obstruction*" OR "chronic bronchitis" OR "chronic obstructive airflow disease*" OR "chronic obstructive airflow disorder*" OR "chronic obstructive airway disease*" OR "chronic obstructive airway disorder*" OR "chronic obstructive bronchitis" OR "chronic obstructive bronchopulmonary disease*" OR "chronic obstructive broncho-pulmonary disease*" OR "chronic obstructive bronchopulmonary disorder*" OR "chronic obstructive broncho-pulmonary disorder*" OR "chronic obstructive lung disease*" OR "chronic obstructive lung disorder*" OR "chronic obstructive pulmonary disease*" OR "chronic obstructive pulmonary disorder*" OR "chronic obstructive respiratory disease*" OR "chronic obstructive respiratory disorder*" OR coad OR copd OR emphysema OR "obstructive lung disease" OR "obstructive lung disorder*" OR "obstructive pulmonary disease*" OR "obstructive pulmonary disorder*" OR "obstructive pulmonary tract disease*" OR "obstructive pulmonary tract disorder*" OR "obstructive respiratory disease*" OR "obstructive respiratory disorder*" OR "obstructive respiratory tract disease*" OR "obstructive respiratory tract disorder*")

2 TITLE-ABS-KEY(abediterol OR acefylline OR "acefylline clofibrol" OR "acefylline piperazine" OR "aclidinium bromide" OR "adrenalin hydrogen tartrate" OR Adrenomedullin OR Albuterol OR ambuphylline OR Aminophylline OR antibronchospastic OR arformoterol OR Atropine OR bambuterol OR bamifylline OR baralgin OR batefenterol OR bitolterol OR "bitolterol mesilate" OR "bronchial dilating" OR "bronchial-dilating" OR bronchodilatant* OR "broncho-dilatant*" OR bronchodilatating OR "broncho-dilatating" OR bronchodilatator* OR "broncho-dilatator*" OR bronchodilating OR "broncho-dilating" OR bronchodilator* OR "broncho-dilator*" OR broncholytic* OR broncholytica OR bronchospasmolytic OR broxaterol OR Budesonide OR carbuterol OR carmoterol OR "choline theophyllinate" OR Clenbuterol OR clorprenaline OR Colforsin OR Cromakalim OR danirixin OR "darotropium bromide" OR dilator* OR diprophylline OR ditec OR doxofylline OR Dyphylline OR elubrixin OR enprofylline OR ephedrine OR "ephedrine sulfate" OR Epinephrine OR eprozinol OR espatropate OR etafedrine OR etamiphyllin OR "etamiphyllin camsilate" OR etanterol OR etofylline OR Fenoterol OR fenspiride OR Fluticasone OR "flutropium bromide" OR formoterol OR "Formoterol Fumarate" OR furafylline OR glycopyrronium OR "gsk 159802" OR "gsk 597901" OR guaifylline OR "gw 678007" OR Hexoprenaline OR Hyoscyamine OR ibuterol OR "ilmetropium iodide" OR imoxiterol OR indacaterol OR inhaler* OR Ipratropium OR "ipratropium bromide" OR isbufylline OR isoetarine OR "isoetarine mesylate" OR Isoetharine OR isoprenaline OR Isoproterenol OR Khellin OR laprafylline OR levalbuterol OR mabuterol OR marax OR Metaproterenol OR methoxyphenamine OR milveterol OR "n methylmequitazine" OR naminterol OR neobiphyllin OR nestifylline OR "Nitric Oxide" OR olodaterol OR orciprenaline OR "oxitropium bromide" OR "oxyphenonium bromide" OR pibaxizine OR pirbuterol OR "pirbuterol acetate" OR pneumodilator OR Procaterol OR protokylol OR proxyphylline OR Pseudoephedrine OR racephedrine OR Racepinephrine OR reproterol OR rimiterol OR "ru 45703" OR salbutamol OR "salbutamol sulfate" OR salmefamol OR salmeterol OR "Salmeterol Xinafoate" OR sibenadet OR "S-Nitrosoglutathione" OR "S-Nitrosothiols" OR soterenol OR tazifylline OR Terbutaline OR Theobromine OR Theophylline OR "theophylline sodium glycinate" OR thiazinamium OR "thiazinamium metilsulfate" OR Tiotropium OR Tretoquinol OR "tretoquinol derivative" OR trimetaquinol OR tulobuterol OR "uk 432097" OR Umeclidinium OR vephylline OR verofylline OR vilanterol OR "vilanterol trifenatate" OR zindotrine)

3 TITLE-ABS-KEY("adrenergic beta 2 agonist*" OR "adrenergic beta 2 receptor agonist*" OR "adrenergic beta2 agonist*" OR "adrenergic beta-2 agonist*" OR "adrenergic beta-2 receptor agonist*" OR "adrenergic beta2-agonist*" OR Albuterol OR "beta 2 adrenergic agent*" OR "beta 2 adrenergic agonist*" OR "beta 2 adrenergic receptor agonist*" OR "beta 2 adrenergic receptor stimulant*" OR "beta 2 adrenergic receptor stimulat*" OR "beta 2 adrenergic receptor stimulator*" OR "beta 2 adrenergic stimulant*" OR "beta 2 adrenergic stimulat*" OR "beta 2 adrenergic

stimulator*" OR "beta 2 adrenoceptor agonist*" OR "beta 2 adrenoceptor stimulant*" OR "beta 2 adrenoceptor stimulat**" OR "beta 2 adrenoceptor stimulator*" OR "beta 2 agonist*" OR "beta agonist*" OR "beta receptor agonist*" OR "beta receptor stimulant*" OR "beta stimulant" OR "beta2 adrenergic receptor stimulat*" OR Fenoterol OR formoterol OR Hexoprenaline OR indacaterol OR Isoetharine OR LABA OR LABAs OR Metaproterenol OR Procaterol OR Ritodrine OR SABA OR SABAs OR salmeterol OR "Salmeterol Xinafoate" OR Terbutaline)

4 TITLE-ABS-KEY("acetylcholine antagonist*" OR "acetylcholine receptor block*" OR "acetylcholine receptor inhibitor*" OR "AChR inhibitor" OR aclidinium OR "aclidinium bromide" OR acotiamide OR adiphenine OR afacifenacin OR Alcuronium OR "alpha conotoxin MII" OR alvameline OR alverine OR "alverine citrate" OR anisodamine OR "anti cholinergics" OR anticholinergic OR anticholinergic* OR "anti-cholinergic*" OR antimuscarinic* OR aprofene OR aspaminol OR Atracurium OR Atropine OR atropinic* OR azaprophen OR belladonna OR bellergal OR Benactyzine OR benzetimide OR benzilonium OR "benzilylcholine mustard" OR benzoquinonium OR Benztropine OR Biperiden OR bornaprine OR Butylscopolammonium OR buzepide OR catestatin OR "central anticholinergic" OR Chlorisondamine OR chlorphenoxamine OR cholinolytic* OR cimetropium OR clidinium OR Curare OR Cyclopentolate OR cycrimine OR darifenacin OR darotropium OR deptropine OR desfesoterodine OR Dexetimide OR dexmecamylamine OR "dibutoline sulfate" OR Dicyclomine OR dicycloverine OR diethazine OR dimevamide OR "diphemanil methylsulfate" OR drofenine OR elantrine OR Emepronium OR espatropate OR Ethidium OR "ethylcholine mustard aziridinium" OR eucatropine OR fenoverine OR fenpipramide OR fenpiverinium OR fesoterodine OR fluperlapine OR flutropium OR furtramine OR "Gallamine Triethiodide" OR ganglefene OR Glycopyrrolate OR glycopyrronium OR "gsk 202405" OR "h cholinoreactive cell*" OR hemicholinium OR hexahydrodifenidol OR hexahydroprocyclidine OR hexahydrosiladifenidol OR Hexamethonium OR hexbutinol OR "hexbutinol methiodide" OR "hexocyclium metilsulfate" OR himbacine OR homatropine OR "homatropine methyl" OR "homatropine terephthalate" OR Hyoscyamine OR imidafenacin OR Ipratropium OR isomylamine OR "isopropamide iodide" OR LAMA OR LAMAs OR levetimide OR lophotoxin OR mazaticol OR Mecamylamine OR mefurtramine OR mepenzolate OR meptazinol OR "meta cholinoreactive cell*" OR methantheline OR methoctramine OR methylatropine OR methyllycaconitine OR methylscopolamine OR metixene OR muscarinic* OR muscarinolytic* OR "nicotine tartrate" OR nicotinic* OR nuvenzepine OR "octatropine methylbromide" OR Orphenadrine OR otenzepad OR oxitropium OR oxybutynin OR oxyphencyclimine OR Oxyphenonium OR Pancuronium OR "para fluorohexahydrosiladifenidol" OR "para fluorohexbutinol" OR parapenzolate OR "parasympathetic block*" OR "parasympathetic inhibitor*" OR parasympathicolytic* OR parasympatholytic* OR parasympatolytic* OR Pempidine OR penthienate OR "Pentolinium Tartrate" OR phenglutarimide OR Pipecuronium OR pipenzolate OR piperidolate OR piperphenamine OR pipethanate OR Pirenzepine OR piroheptine OR "poldine methylsulfate" OR pridinol OR "pridinol mesilate" OR "prifinium bromide" OR Procyclidine OR profenamine OR proglumide OR Propantheline OR propiverine OR "propylbenziloylcholine mustard" OR "Propylbenzilylcholine Mustard" OR pyrrinol OR Quinidine OR "Quinuclidinyl Benzilate" OR revatropate OR revefenacin OR rispenzepine OR SAMA OR SAMAs OR Scopolamine OR secoverine OR silahexocyclium OR siltenzepine OR sofpironium OR solifenacin OR "Solifenacin Succinate" OR stramonium OR sydnofen OR tarafenacin OR telenzepine OR tematropium OR temiverine OR thiazinamium OR "thiazinamium metilsulfate" OR thihexinol OR "tiemonium iodide" OR "tiemonium methylsulfate" OR tifenamil OR timepidium OR Tiotropium OR tofenacin OR tolterodine OR "Tolterodine Tartrate" OR tonopan OR Toxiferine OR tricyclamol OR "tridihexethyl chloride" OR Trihexyphenidyl OR Trimethaphan OR triperidene OR tripitramine OR tropacin OR Tropicamide OR tropine OR "tropine benzoate" OR "trospium chloride" OR troventol OR Tubocurarine OR umeclidinium OR valethamate OR vamicamide OR Vecuronium OR vedaclidine OR zamifenacin OR zolenzepine)

5 TITLE-ABS-KEY("adrenal cortex hormone*" OR "adrenal cortex steroid*" OR "adrenal cortical hormone*" OR "adrenal cortical steroid*" OR "adrenal steroid*" OR "adreno cortical steroid*" OR "adreno corticosteroid*" OR "adrenocortical hormone*" OR "adrenocortical steroid*" OR adrenocorticosteroid* OR adreson OR alclometasone OR aldosterone OR algestone OR "algestone acetonide" OR amcinonide OR amelometasone OR beclometasone OR budesonide OR butixocort OR chloroprednisone OR ciclesonide OR ciprocinonide OR clioquinol OR

clobetasol OR clobetasone OR clocortolone OR cloprednol OR "cortical steroid*" OR corticalsteroid* OR "cortico steroid*" OR corticoid* OR corticosteroid* OR corticosterone OR corticotherap* OR cortifair OR cortisol OR cortisone OR cortivazol OR cortril OR deflazacort OR dehydrocorticosterone OR dehydrocortisone OR deoxycorticosterone OR dermocorticosteroid* OR dexamethasone OR diflorasone OR diflucortolone OR difluprednate OR domoprednate OR drocinonide OR dutimelan OR epicortisol OR "etiprednol dicloacetate" OR fluclorolone OR fludrocortisone OR fludroxycortide OR flumetasone OR flumoxonide OR flunisolide OR fluocinolone OR fluocinonide OR fluocortin OR fluocortolone OR fluorometholone OR fluprednidene OR fluprednisolone OR fluticasone OR formocortal OR "formoterol fumarate" OR Glucocorticoid* OR glucocorticoidsteroid* OR glucocorticosteroid* OR glucocortoid* OR glycocorticoid* OR glycocorticosteroid* OR halcinonide OR halometasone OR halopredone OR hydrocortisone OR "hydroxy norcorticosterone" OR hydroxycorticoid* OR hydroxycorticosteroid* OR hydroxycorticosterone OR hydroxydeoxycorticosterone OR hydroxyhydrocortisone OR "icometasone enbutate" OR isoflupredone OR itrocinonide OR "locicortolone dicibate" OR "lorinden a" OR "lorinden t" OR loteprednol OR mazipredone OR medrysone OR meprednisone OR mineralcorticosteroid* OR mineralocorticosteroid* OR minerocorticoid* OR mometasone OR nicocortonide OR nivacortol OR nordeoxycorticosterone OR oropivalone OR oxohydrocortisone OR oxycorticosteroid* OR paramethasone OR prednisolone OR prednisone OR pregnenolone OR procinonide OR promestriene OR resocortol OR rimexolone OR rofleponide OR steroid* OR tetrahydrodeoxycorticosterone OR ticabesone OR timobesone OR tipredane OR tixocortol OR triamcinolone OR "ulobetasol propionate" OR uniderm OR zoticasone)

6 TITLE-ABS-KEY(apremilast OR arofylline OR atizoram OR benzafentrine OR catramilast OR cilomilast OR cipamfylline OR daxalipram OR denbufylline OR elbimilast OR filaminast OR ibudilast OR indimilast OR lavamilast OR nitraquazone OR oglemilast OR "PDE 4 inhibitor*" OR "PDE IV inhibitor*" OR "PDE type 4 inhibitor*" OR "PDE type IV inhibitor*" OR "pde-4 inhibitor*" OR "PDE4 inhibitor*" OR "phosphodiesterase 4 inhibitor*" OR "phosphodiesterase IV inhibitor*" OR "phosphodiesterase type 4 inhibitor*" OR "phosphodiesterase type IV inhibitor*" OR piclamilast OR pumafentrine OR revamilast OR roflumilast OR Rolipram OR tetomilast OR tibenelast OR tilivapram OR tipelukast OR tofimilast OR tolafentrine OR zardaverine)

7 1 and (2 or 3 or 4 or 5 or 6)

8 TITLE-ABS-KEY((meta W/1 analys*) OR (systematic* W/3 review*))

9 7 and 8

10 DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)

11 9 and not 10

12 PMID(0*) OR PMID(1*) OR PMID(2*) OR PMID(3*) OR PMID(4*) OR PMID(5*) OR PMID(6*) OR PMID(7*) OR PMID(8*) OR PMID(9*)

13 11 and not 12

Part 2

1 TITLE-ABS-KEY("chronic airflow disease*" OR "chronic airflow disorder*" OR "chronic airflow limitation*" OR "chronic airflow obstruction*" OR "chronic airway disease*" OR "chronic airway disorder*" OR "chronic airway limitation*" OR "chronic airway obstruction*" OR "chronic bronchitis" OR "chronic obstructive airflow disease*" OR "chronic obstructive airflow disorder*" OR "chronic obstructive airway disease*" OR "chronic obstructive airway disorder*" OR "chronic obstructive bronchitis" OR "chronic obstructive bronchopulmonary disease*" OR "chronic obstructive broncho-pulmonary disease*" OR "chronic obstructive bronchopulmonary disorder*" OR "chronic obstructive broncho-pulmonary disorder*" OR "chronic obstructive lung disease*" OR "chronic obstructive lung disorder*" OR "chronic obstructive pulmonary disease*" OR "chronic obstructive pulmonary disorder*" OR "chronic obstructive respiratory disease*" OR "chronic obstructive respiratory disorder*" OR coad OR copd OR emphysema OR "obstructive lung disease" OR "obstructive lung disorder*" OR "obstructive pulmonary disease*" OR "obstructive pulmonary disorder*" OR "obstructive pulmonary tract disease*" OR "obstructive pulmonary tract disorder*" OR "obstructive respiratory disease*" OR "obstructive respiratory disorder*" OR "obstructive respiratory tract disease*" OR "obstructive respiratory tract disorder*")

2	TITLE-ABS-KEY(Acetylcysteine OR Ambroxol OR aminophylline OR Bromhexine OR bron OR cafedrine OR Carbocysteine OR diprophylline OR etofylline OR eucalyptus OR expectorant* OR fudosteine OR guaiacol OR "guaiacol carbonate" OR guaietolin OR Guaifenesin OR guaifylline OR "iodinated glycerol" OR ipecac OR mucolytic* OR "Potassium Citrate" OR "primula flower" OR stepronin OR "stepronin lysine" OR sulfoguaiacol OR tipepidine OR ulogesic)
3	TITLE-ABS-KEY("1 methylmocimycin*" OR "11 deoxydaunorubicin*" OR "14 hydroxyclarithromycin*" OR "19 deformyl 4 deoxydesmycosin*" OR "19 deformyldesmycosin*" OR "2 acetylerythromycin*" OR "2 fluoroidarubicin*" OR "2 n ethylnetilmicin*" OR "2 pyrrolinodoxorubicin*" OR "21 aminoepothilone B" OR "3 3 cyanomorpholino 3 deaminodoxorubicin*" OR "3 deamino 2 fluoro 3 hydroxydoxorubicin 14 pimelate" OR "3 deamino 3 morpholinodoxorubicin*" OR "3 deamino 3 morpholinooxaunomycin*" OR "4 demethoxy 11 deoxydaunomycinone" OR "4 demethoxydaunomycinone" OR "4 demethoxydoxorubicin*" OR "4 deoxydesmycosin*" OR "4 iodoesorubicin*" OR "5 iminodaunorubicin*" OR "6 n ethylnetilmicin*" OR "6beta iodopenicillanic acid" OR "9 deacetyl 9 methylidarubicin*" OR "9 deoxydoxorubicin*" OR "9 dihydroerythronolide A" OR "a 102395" OR "a 10255" OR "a 10947" OR "a 130b" OR "a 192411" OR "a 63075" OR abkhazomycin* OR abyssomicin* OR acetomycin* OR acetylspiramycin* OR aclacinomycin* OR aclarubicin* OR actagardin* OR actaplanin* OR actinorhodine OR "aculeacin A" OR aculeximycin* OR adicillin* OR aditoprim OR adriamycinone OR agglomerin* OR aklavinone OR alafosfalin* OR Alamethicin* OR albocycline OR aldecalmycin* OR aldoxorubicin* OR alisamycin* OR allicin* OR almecillin* OR "alpha defensin*" OR ambruticin* OR Amdinocillin* OR amfomycin* OR Amikacin* OR aminoglycoside* OR aminopenicillin* OR "Aminosalicylic Acid" OR Amoxicillin* OR "Amphotericin B" OR Ampicillin* OR amrubicin* OR "angucycline derivative" OR anhydrochlortetracycline OR anhydroepitetracycline OR anhydrotetracycline OR anidulafungin* OR Anisomycin* OR annamycin* OR ansamitocin* OR "ansamycin derivative" OR anthracycline* OR anthracyclinone* OR antibacterial* OR "anti-bacterial*" OR antibiotic* OR "anti-biotic*" OR "antimicrobial cationic peptide*" OR Antimycin* OR antimycobacterial* OR "anti-mycobacterial*" OR Antitreponemal* OR "Anti-treponemal*" OR Antitubercular* OR "Anti-tubercular*" OR apalcillin* OR aplasmomycin* OR "aplysianin E" OR apramycin* OR aristeromycin* OR Arsphenamine OR aspoxicillin* OR astromicin* OR asukamycin* OR "atpenin B" OR auricularum OR Aurodox OR aurograb OR avibactam OR avilamycin* OR avoparcin* OR azidamfenicol OR azidocillin* OR Azithromycin* OR Azlocillin* OR Aztreonam OR "aztreonam lysine" OR azurocidin* OR bacampicillin* OR Bacitracin* OR bacmecillinam OR bactenecin* OR bacteriocid* OR Bacteriocin* OR bafilomycin* OR balhimycin* OR "baliz 2" OR Bambermycin* OR baquiloprim OR "barminomycin I" OR baycuten OR beauvericin* OR beroline OR berubicin* OR berythromycin* OR "beta defensin*" OR betafectin* OR "beta-Lactam*" OR "betaLactamase Inhibitor*" OR "beta-Lactamase Inhibitor*" OR betamipron OR bialaphos OR biapenem OR bicozamycin* OR "biphenomycin A" OR bluensomycin* OR bombinin* OR "Bongkrekic Acid" OR boromycin* OR borrelidin* OR "Brefeldin A" OR brilacidin* OR brobactam OR butalactin* OR butirosin* OR cadazolid OR Calcimycin* OR Candicidin* OR Capreomycin* OR carbacephem OR carbadox OR carbapenem OR "carbazomycin A" OR Carbenicillin* OR carbomycin* OR Carfecillin* OR carindacillin* OR carubicin* OR carumonam OR caspofungin* OR cathelicidin* OR cecropin* OR cefacetrile OR Cefaclor OR Cefadroxil OR cefalexin* OR cefaloglycin* OR cefaloram OR cefaloridine OR cefalotin* OR Cefamandole OR cefapirin* OR Cefatrizine OR cefazaflur OR cefazedone OR Cefazolin* OR cefbuperazone OR cefcanel OR cefcapene OR cefclidin* OR cefdaloxime OR cefdinir OR cefditoren OR cefepime OR cefetamet OR cefetecol OR cefilavancin* OR Cefixime OR cefluprenam OR cefmatilen OR Cefmenoxime OR Cefmetazole OR cefminox OR cefodizime OR Cefonicid OR Cefoperazone OR ceforanide OR cefoselis OR Cefotaxime OR Cefotetan OR Cefotiam OR cefovecin* OR Cefoxitin* OR cefozopran OR cefpimizole OR cefpiramide OR cefpirome OR cefpodoxime OR cefprozil OR cefquinome OR cefradine OR cefroxadine OR Cefsulodin* OR ceftaroline OR Ceftazidime OR cefteram OR ceftezole OR ceftibuten OR ceftiofur OR Ceftizoxime OR ceftobiprole OR ceftolozane OR Ceftriaxone OR Cefuroxime OR cefuzonam OR Cephacetrile OR Cephalexin* OR Cephaloglycin* OR Cephaloridine OR cephalosporin* OR Cephalothin* OR cephamycin* OR Cephapirin* OR Cephradine OR chalcomycin* OR Chloramphenicol* OR chloroorienticin* OR chloropolysporin* OR chlorothricin* OR chlorothricolide OR Chlortetracycline OR "chymotrypsin trypsin*" OR ciadox

OR "cilastatin plus imipenem" OR "cinerubin A" OR "cinerubin B" OR cinoquidox OR Ciprofloxacin* OR cirramycin* OR Citrinin* OR Clarithromycin* OR "clavulanate potassium" OR "Clavulanic Acid*" OR Clindamycin* OR clomocycline OR Cloxacillin* OR colicin* OR colistimethate OR Colistin* OR "concanamycin A" OR coumamidine OR coumamycin* OR "cp 63956" OR cryptosporin* OR Cyclacillin* OR cycloheximide OR Cycloserine OR cystargin* OR "cytarabine plus daunorubicin*" OR cytovaricin* OR dactimicin* OR Dactinomycin* OR dalbaheptide OR dalbavancin* OR dalfopristin* OR "damavaricin Fc pentyl ether" OR Daptomycin* OR daunomycinone OR daunorubicin* OR daunorubicinol OR "deacetoxycephalosporin C" OR deacetylcefotaxime OR "deacetylcephalosporin C" OR dealanylalahopcin* OR decaplanin* OR dechloroeremomycin* OR decilorubicin* OR defensin* OR Demeclocycline OR dermaseptin* OR dermcidin* OR dermostatin* OR desmycosin* OR detorubicin* OR Diarylquinoline* OR Dibekacin* OR Dicloxacillin* OR dihydrostreptomycin* OR Diketopiperazines OR dimethylchlortetracycline OR dioxidine OR dirithromycin* OR Distamycin* OR "ditrisarubicin B" OR doripenem OR doxorubicin* OR doxorubicinol OR Doxycycline OR drosocin* OR echinocandin* OR Echinomycin* OR Edeine OR efepristin* OR efrotomycin* OR emimycin* OR endusamycin* OR enniatin* OR Enoxacin* OR Enviomycin* OR eperezolid OR epetraborole OR epicillin* OR epidermin* OR epiderstatin* OR epiroprim OR epirubicin* OR epirubicinol OR epitetracycline OR epothilone* OR "epsilon rhodomycinone" OR eravacycline OR eremomycin* OR ertapenem OR Erythromycin* OR erythromycylamine OR erythronolide* OR esorubicin* OR Ethambutol OR Ethionamide OR ethylhydrocupreine OR etimicin* OR evernimicin* OR everninomicin* OR faeriefungin* OR fidaxomicin* OR Filipin* OR "fleroxacin deacetylcefotaxime ester" OR flomoxef OR flopristin* OR florfenicol OR Floxacillin* OR flucloxacillin* OR flumoxil OR Fluoroquinolone* OR flurithromycin* OR fomidacillin* OR fortimicin* OR Fosfomycin* OR fosmidomycin* OR Framycetin* OR fropenem OR fungichromin* OR furaquinocin* OR furazidin* OR "furazolium chloride" OR furbenicillin* OR fusafungine OR "fusidate sodium" OR "Fusidic Acid" OR fuzlocillin* OR galarubicin* OR gallidermin* OR gamithromycin* OR ganefromycin* OR "ge 2270a" OR gentamicin* OR gepotidacin* OR globomycin* OR gloximonam OR "glycylcycline derivative" OR "gonadorelin6 dextro lysine 2 pyrrolinodoxorubicin*" OR "goniodomin A" OR Gramicidin* OR granulysin* OR grisein* OR guamecycline OR habekacin* OR hamycin* OR hatomamicin* OR hedamycin* OR heliomycin* OR hepcidin* OR hetacillin* OR hexacycline OR hidamicin* OR "histatin 5" OR histatin* OR hygromycin* OR hymeglusin* OR hypothemycin* OR iclaprim OR idarubicin* OR idarubicinol OR ikarugamycin* OR "imidacloprid plus moxidectin*" OR Imipenem OR indolicidin* OR inostamycin* OR iseganan OR isepamicin* OR Isoniazid OR "isopenicillin N" OR "isoswinholide A" OR istamycin* OR "iturin A" OR ixabepilone OR Josamycin* OR "k 252a" OR kalafungin* OR Kanamycin* OR kanendomycin* OR kasugamycin* OR kelfiprim OR ketolide OR kidamycin* OR kinamycin* OR Kitasamycin* OR "l 156602" OR "l 733560" OR "l 786392" OR lactacystin* OR Lactams OR lactivicin* OR "lactocin S" OR lactococcin* OR lactoferricin* OR ladirubicin* OR laidlomycin* OR lancovutide OR lankamycin* OR lanopepden OR lanthiopeptin* OR lantibiotic OR Lasalocid OR latamoxef OR lavanducyanin* OR lefamulin* OR lenampicillin* OR lenapenem OR lenoremycin* OR Leprostatic* OR "leucinostatin A" OR "leucinostatin B" OR Leucomycin* OR leurubicin* OR Levofloxacin* OR lexithromycin* OR "lff 571" OR Lincomycin* OR lincosamide* OR Linezolid OR linopristin* OR lividomycin* OR "lonomycin A" OR loracarbef OR lotilibcin* OR Lucensomycin* OR lydicamycin* OR Lymecycline OR lysobactin* OR lysocellin* OR lysostaphin* OR macrolide OR magainin* OR malyngolide OR manumycin* OR maridomycin* OR "mdl 62208" OR "mdl 62211" OR mecillinam OR meclocycline OR megacin* OR megalomicin* OR Mepartricin* OR meropenem OR mersacidin* OR metacycline OR metampicillin* OR Methacycline OR Methicillin* OR "methylenomycin A" OR "methylenomycin B" OR methymycin* OR methynolide OR meticillin* OR Mezlocillin* OR "microcin b17" OR "microcin J25" OR micronomicin* OR midecamycin* OR mideplanin* OR "mikamycin B" OR Mikamycin* OR "milbemycin oxime" OR milbemycin* OR Minocycline OR Miocamycin* OR miokamycin* OR miporamicin* OR miraxid OR mocimycin* OR "moenomycin A" OR monensin* OR "monobactam derivative" OR Moxalactam OR moxidectin* OR "ms 8209" OR Mupirocin* OR mureidomycin* OR murepavadin* OR mycinamicin* OR Mycobacillin* OR mycolog OR mycoticin* OR myxothiazol OR "n benzyldoxorubicin 14 valerate" OR "n trifluoroacetyldoxorubicin*" OR Nafcillin* OR "Nalidixic Acid" OR narasin* OR Natamycin* OR neamine OR nebacetin* OR Nebramycin* OR

negamycin* OR nemadectin* OR nemorubicin* OR Neomycin* OR neosporin* OR Netilmicin* OR Netropsin* OR niddamycin* OR Nigericin* OR Nisin* OR nitrocefin* OR nitrosochloramphenicol OR "nocardicin A" OR "nocardicin E" OR "nocardicinic acid derivative*" OR Norfloxacin* OR nosiheptide OR nourseothricin* OR Novobiocin* OR "nvb 302" OR nybomycin* OR Nystatin* OR "oasomycin A" OR obelmycin* OR Ofloxacin* OR olaquindox OR oleandolide OR Oleandomycin* OR oligomycin* OR omadacycline OR omiganan OR optocillin* OR "orienticin A" OR orientiparcin* OR oritavancin* OR oropivalone OR Oxacillin* OR oxaunomycin* OR "Oxolinic Acid" OR Oxytetracycline OR paldimycin* OR panipenem OR pardaxin* OR Paromomycin* OR patulin* OR pediazole OR pediocin* OR Pefloxacin* OR penamecillin* OR penethamate OR "Penicillanic Acid" OR "Penicillic Acid" OR penicillin* OR "penicilloic acid" OR pentalenolactone OR pentisomicin* OR peptaibol OR pexiganan OR "pf 708093" OR phenelfamycin* OR pheneticillin* OR phleomycin* OR pikromycin* OR "Pipemidic Acid" OR Piperacillin* OR pirarubicin* OR pirazmonam OR pirlimycin* OR Pivampicillin* OR pivmecillinam OR platensimycin* OR plazomicin* OR plectasin* OR pleuromutilin* OR pluramycin* OR pneumocandin* OR "polyactin A" OR polyfungin* OR polymyxin* OR "polyoxin B" OR "polyoxin D" OR polysporin* OR polytrim OR posizolid OR "pr 39" OR Pristinamycin* OR Prodigiosin* OR prohepcidin* OR propicillin* OR protegrin* OR Prothionamide OR prothracarcin* OR "pseudomonic acid" OR Pyrazinamide OR pyrromycinone OR pyrroxamycin* OR quinacillin* OR quinomycin* OR quinupristin* OR radezolid OR radicicol OR ramoplanin* OR ranalexin* OR ranbezolid OR razupenem OR retacillin* OR retapamulin* OR "rhodomycin A" OR Ribostamycin* OR Rifabutin* OR Rifampin* OR Rifamycin* OR rimocidin* OR Ristocetin* OR ritipenem OR "ritipenem acoxil" OR rodorubicin* OR roflamycoin* OR rokitamycin* OR Rolitetracycline OR rosaramicin* OR Roxarsone OR Roxithromycin* OR ruboxyl OR Rutamycin* OR sabarubicin* OR sagopilone OR sanfetrinem OR sarecycline OR "simaomicin alpha" OR "simocyclinone D8" OR Sirolimus OR "sisomicin sulfate" OR Sisomicin* OR "skf 104662" OR sofradex OR Spectinomycin* OR "spinosyn A" OR Spiramycin* OR squalamine OR stigmatellin* OR streptoduocin* OR Streptogramin* OR streptolydigin* OR Streptomycin* OR streptothricin* OR streptotriad OR Streptovaricin* OR streptovirudin* OR "streptovitacin A" OR stubomycin* OR subtilin* OR Sulbactam OR Sulbenicillin* OR Sulfamerazine OR Sulfamethoxypyridazine OR sulfazecin* OR sulopenem OR sultamicillin* OR surfactin* OR surotomycin* OR "swinholide A" OR "swinholide B" OR tachyplesin* OR Talampicillin* OR tameticillin* OR tazobactam OR tebipenem OR tedizolid OR Teicoplanin* OR teixobactin* OR telavancin* OR temocillin* OR terdecamycin* OR tetracyclin* OR Tetracycline OR tetramycin* OR tetronasin* OR tetronomycin* OR tetroxoprim OR Thiamphenicol OR Thienamycin* OR Thioacetazone OR thiolactomycin* OR "thionin peptide" OR thiopeptin* OR thiophenoxycefalotin* OR Thiostrepton OR tiamulin* OR "tibezonium iodide" OR Ticarcillin* OR tigecycline OR tigemonam OR tildipirosin* OR tilmicosin* OR timentin* OR tirandamycin* OR tizoxanide OR tobicillin* OR Tobramycin* OR tolramycin* OR tomopenem OR toyocamycin* OR tresaderm OR tribactam OR trichomycin* OR "trichostatic acid" OR "trichostatin A" OR trimethoprim* OR "trinem derivative" OR "triostin A" OR triplopen OR trisep OR Troleandomycin* OR trospectomycin* OR tuftsin* OR tulathromycin* OR Tunicamycin* OR tutofusin* OR Tylosin* OR tylvalosin* OR Tyrocidine OR Tyrothricin* OR "u 78608" OR "uk 69753" OR unphenelfamycin* OR "urdamycin C" OR "urdamycin D" OR "urdamycin H" OR ureidopenicillin* OR urobiotic OR "vacidin A" OR validamycin* OR Valinomycin* OR valnemulin* OR valrubicin* OR Vancomycin* OR venturicidin* OR vernamycin* OR "violamycin B1" OR Viomycin* OR "virginiae butanolide A" OR "virginiae butanolide C" OR "virginiamycin M" OR "virginiamycin S" OR Virginiamycin* OR "viriplanin A" OR viscosin* OR volpristin* OR "ws 9659 b" OR "zibrofusidic acid" OR zineryt OR "zoptarelin doxorubicin*" OR zorbamycin* OR zorubicin*)

4 TITLE-ABS-KEY(Alprazolam OR arfendazam OR benzodiazepin OR benzodiazepine* OR Benzodiazepinone* OR bromazepam OR camazepam OR Chlordiazepoxide OR cinolazepam OR clobazam OR clonazepam OR clorazepate OR "Clorazepate Dipotassium" OR "clorazepate potassium" OR dealkylflurazepam OR delorazepam OR demoxepam OR devazepide OR diazepam OR doxefazepam OR Estazolam OR fludiazepam OR flunitrazepam OR flurazepam OR flutoprazepam OR fosazepam OR gidazepam OR girisopam OR halazepam OR loflazepate OR lorazepam OR lormetazepam OR lotrafiban OR meclonazepam OR Medazepam OR metaclazepam OR Midazolam OR nastorazepide OR nerisopam OR netazepide OR nimetazepam OR nitrazepam OR nitrosochlordiazepoxide OR norchlordiazepoxide OR

	norclobazam OR nordazepam OR norfludiazepam OR norflunitrazepam OR oxazepam OR phenazepam OR pinazepam OR prazepam OR quazepam OR "ro 7 0213" OR talampanel OR tampramine OR tarazepide OR temazepam OR tetrazepam OR tibezonium OR tifluadom OR tofisopam OR tomaymycin OR Triazolam OR tuclazepam OR uxepam)
5	TITLE-ABS-KEY(acetorphine OR acetylcodeine OR acetylmethadol OR Alfentanil OR Alphaprodine OR anileridine OR apadoline OR azidomorphine OR benzhydrocodone OR bezitramide OR bremazocine OR "Brompton mixture" OR Buprenorphine OR Butorphanol OR ciramadol OR cocodamol OR Codeine OR codydramol OR conorfone OR cyclazocine OR Dextromoramide OR Dextropropoxyphene OR dextrorphan OR dezocine OR diamorphine OR diconal OR dihydrocodeine OR dihydroetorphine OR Dihydromorphine OR dimethylthiambutene OR Diphenoxylate OR dipipanone OR enadoline OR eptazocine OR ethylketazocine OR Ethylketocyclazocine OR Ethylmorphine OR etonitazene OR Etorphine OR etoxeridine OR faxeladol OR Fentanyl OR furethidine OR gelonida OR Heroin OR Hydrocodone OR isalmadol OR isomethadone OR ketazocine OR ketobemidone OR ketogan OR kyotorphin OR lefetamine OR levacetylmethadol OR levomethadone OR Levorphanol OR Meperidine OR Meptazinol OR metazocine OR Methadone OR "Methadyl Acetate" OR methylsamidorphan OR Morphine OR "morphinomimetic agent*" OR "morphinomimetic drug*" OR morphinone OR Nalbuphine OR narcotic* OR nicocodine OR nicomorphine OR noracymethadol OR norbuprenorphine OR nordextropropoxyphene OR normorphine OR norpethidine OR norpropoxyphene OR "o nortramadol" OR oliceridine OR opiate OR Opiate* OR opioid* OR Opium OR oripavine OR Oxycodone OR Oxymorphone OR pentamorphone OR Pentazocine OR pethidine OR phenadoxone OR phenaridine OR Phenazocine OR phencyclidine OR Phenoperidine OR picenadol OR piminodine OR Pirinitramide OR piritramide OR profadol OR Promedol OR propiram OR sameridine OR samidorphan OR semorphone OR Sufentanil OR tapentadol OR thebaine OR tifluadom OR Tilidine OR tonazocine OR Tramadol OR trimeperidine)
6	TITLE-ABS-KEY("airflow clearance" OR "airway clearance" OR BLVR OR bronchoscop* OR ELVR OR "lung clearance" OR "lung denervation" OR LVRS OR pneumectom* OR pneumonectom* OR pneumoresection* OR "pulmonary clearance" OR "volume reducing" OR "volume reduction*")
7	1 and (2 or 3 or 4 or 5 or 6)
8	TITLE-ABS-KEY((meta W/1 analys*) OR (systematic* W/3 review*))
9	7 and 8
10	DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
11	9 and not 10
12	PMID(0*) OR PMID(1*) OR PMID(2*) OR PMID(3*) OR PMID(4*) OR PMID(5*) OR PMID(6*) OR PMID(7*) OR PMID(8*) OR PMID(9*)
13	11 and not 12

Part 3

1	TITLE-ABS-KEY("chronic airflow disease*" OR "chronic airflow disorder*" OR "chronic airflow limitation*" OR "chronic airflow obstruction*" OR "chronic airway disease*" OR "chronic airway disorder*" OR "chronic airway limitation*" OR "chronic airway obstruction*" OR "chronic bronchitis" OR "chronic obstructive airflow disease*" OR "chronic obstructive airflow disorder*" OR "chronic obstructive airway disease*" OR "chronic obstructive airway disorder*" OR "chronic obstructive bronchitis" OR "chronic obstructive bronchopulmonary disease*" OR "chronic obstructive broncho-pulmonary disease*" OR "chronic obstructive bronchopulmonary disorder*" OR "chronic obstructive broncho-pulmonary disorder*" OR "chronic obstructive lung disease*" OR "chronic obstructive lung disorder*" OR "chronic obstructive pulmonary disease*" OR "chronic obstructive pulmonary disorder*" OR "chronic obstructive respiratory disease*" OR "chronic obstructive respiratory disorder*" OR coad OR copd OR emphysema OR "obstructive lung disease" OR "obstructive lung disorder*" OR "obstructive pulmonary disease*" OR "obstructive pulmonary disorder*" OR "obstructive pulmonary tract disease*" OR "obstructive pulmonary tract disorder*" OR "obstructive respiratory disease*" OR "obstructive respiratory disorder*" OR "obstructive respiratory tract disease*" OR "obstructive respiratory tract disorder*")
2	TITLE-ABS-KEY((smoking* or tobacco* or cigar* or cigarette* or cigaret*) and (quit* or discontinu* or ceas* or cessation*))
3	TITLE-ABS-KEY(aerobics OR anaerobics OR "artificial respiration*" OR bicycling OR biking OR "Chest Wall Oscillation*" OR dance OR dancing OR "endurance training" OR exercis* OR "Extracorporeal Membrane Oxygen*" OR "fitness training" OR "inhalation therap*" OR isometrics OR oxygen OR "physical activit*" OR "physical exertion" OR "postural drain*" OR rehab* OR "resistance training" OR "respiration care*" OR "respiration therap*" OR "respiratory care*" OR "respiratory therap*" OR running OR "strength training" OR swimming OR "Tai Chi" OR "Tai Ji" OR walking OR weightlifting OR yoga)
4	TITLE-ABS-KEY(diet OR dietary OR diets OR nutrition* OR supplementation OR supplements)
5	TITLE-ABS-KEY(immuniz* OR innoculat* OR moniarix OR "pcv 13" OR pcv13 OR "pneu immune" OR "pneumo 23" OR pneumopur OR pneumovax OR "pnu immune" OR "pnu imune" OR "polysaccharide vaccine pneumococcal" OR prevenar OR prevnar OR "streptococcus pneumoniae vaccine" OR streptopur OR streptorix OR synflorix OR vaccin*)
6	((TITLE-ABS-KEY((((domestic or home or domiciliary) and (residence or residences or setting or settings or care or nurs* or help or service* or treatment* or therap* or "respiratory care" or "respiratory treatment*" or "respiratory therap*" or "respiratory service*" or "respiratory assist*" or ventilat*)) or "assisted living" or homecare)) and (TITLE-ABS-KEY(((((respiration* or respiratory or breathing) and (assist* or controlled or mechanical)) or (facial or face or nasal)) and mask*) or "artificial respiration*" or BiPAP or CPAP or "Fluidic Breathing Assister" or HMV or IPPB or IPPV or NIAV or NIV or NPPV or "Oxygen Regulator*" or PAP or PAV or "Portable Oxygen" or "Positive Airway Pressure*" or "positive end-expiratory pressure*" or "positive pressure*" or respirator or respirators or "Respiratory insufficiency" or Tracheostom* or ventilation or ventilator*)))
7	1 and (2 or 3 or 4 or 5 or 6)
8	TITLE-ABS-KEY((meta W/1 analys*) OR (systematic* W/3 review*))
9	7 and 8
10	DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
11	9 and not 10
12	PMID(0*) OR PMID(1*) OR PMID(2*) OR PMID(3*) OR PMID(4*) OR PMID(5*) OR PMID(6*) OR PMID(7*) OR PMID(8*) OR PMID(9*)
13	11 and not 12

Part 4

1	TITLE-ABS-KEY("chronic airflow disease*" OR "chronic airflow disorder*" OR "chronic airflow limitation*" OR "chronic airflow obstruction*" OR "chronic airway disease*" OR "chronic airway disorder*" OR "chronic airway limitation*" OR "chronic airway obstruction*" OR "chronic bronchitis" OR "chronic obstructive airflow disease*" OR "chronic obstructive airflow disorder*" OR "chronic obstructive airway disease*" OR "chronic obstructive airway disorder*" OR "chronic

	obstructive bronchitis" OR "chronic obstructive bronchopulmonary disease*" OR "chronic obstructive broncho-pulmonary disease*" OR "chronic obstructive bronchopulmonary disorder*" OR "chronic obstructive broncho-pulmonary disorder*" OR "chronic obstructive lung disease*" OR "chronic obstructive lung disorder*" OR "chronic obstructive pulmonary disease*" OR "chronic obstructive pulmonary disorder*" OR "chronic obstructive respiratory disease*" OR "chronic obstructive respiratory disorder*" OR coad OR copd OR emphysema OR "obstructive lung disease" OR "obstructive lung disorder*" OR "obstructive pulmonary disease*" OR "obstructive pulmonary disorder*" OR "obstructive pulmonary tract disease*" OR "obstructive pulmonary tract disorder*" OR "obstructive respiratory disease*" OR "obstructive respiratory disorder*" OR "obstructive respiratory tract disease*" OR "obstructive respiratory tract disorder*")
2	TITLE-ABS-KEY(CBT OR coach* OR "Cognitive behavioral therap*" OR "Cognitive therap*" OR "health promotion*" OR meditat* OR mentor* OR "mind body" OR mindfulness OR psychological OR psychosocial OR psychotherap*)
3	TITLE-ABS-KEY("action plan*" OR android OR app OR apps OR ehealth OR "e-health" OR internet OR ipad* OR iphone* OR mhealth OR "m-health" OR "mobile app*" OR "mobile health" OR "mobile technolog*" OR "portable computer*" OR "portable electronic app*" OR "portable software app*" OR "remote consultation*" OR "self care" OR "self help" OR "self management" OR "self treatment" OR "smart phone*" OR smartphone* OR "tablet computer*" OR teleconsultation* OR "tele-consultation*" OR telehealth OR "tele-health" OR telemedicine OR "tele-medicine" OR teletherap* OR "tele-therap*" OR web)
4	TITLE-ABS-KEY(acupuncture OR agent* OR "alternative medicine" OR "care package*" OR chemotherap* OR "complementary medicine" OR drug* OR "electric stimulation*" OR holistic OR "integrated care" OR "integrated health care" OR "integrated healthcare" OR intervention* OR manag* OR medication* OR "muscle stimulation*" OR operat* OR pharmacotherap* OR procedure* OR reconstruction* OR repair* OR resect* OR surg* OR therap* OR treat* OR wellness)
5	1 and (2 or 3 or 4)
6	TITLE-ABS-KEY((meta W/1 analys*) OR (systematic* W/3 review*))
7	5 and 6
8	DOCTYPE(le) OR DOCTYPE(ed) OR DOCTYPE(bk) OR DOCTYPE(er) OR DOCTYPE(no) OR DOCTYPE(sh)
9	7 and not 8
10	PMID(0*) OR PMID(1*) OR PMID(2*) OR PMID(3*) OR PMID(4*) OR PMID(5*) OR PMID(6*) OR PMID(7*) OR PMID(8*) OR PMID(9*)
11	9 and not 10