

NHS priorities in the management of chronic respiratory disease

NIHR Programme grant 2017-2021

PHRI seminar
25th May 2021

Trusted evidence.
Informed decisions.
Better health.



Cochrane Airways

- Cochrane - global independent network of researchers, HCPs, patients, carers and people interested in health
- Work with authors (typically HCPs/researchers) to publish Reviews
- 370+ Reviews
- Respiratory conditions including asthma, COPD, bronchiectasis, OSA, chronic cough, interstitial lung diseases, sarcoid
- We curate (prioritise) and disseminate
- We produce reviews in house via NIHR programme grant funding



Programme grant overview

- Our 4th consecutive PG, but different from previous PGs
- 15 reviews (including new reviews and updates)
- Focus on chronic obstructive pulmonary disease (COPD) (and a little on asthma)
- Titles prioritised with strong consumer involvement
- Working closely with clinical co-applicant and two steering groups (1 patient group and 1 multi-disciplinary group)



The patient group



- Meeting with the group twice a year (with tea and biscuits!)
- Nine patients were interested to be part of the group
- Discussion of review questions and PICOs
- Chance for patients to tell us about their experiences of living with COPD
- Chance for patients to exchange experiences among themselves
- One patient involved as an author on one review

Patient voice

“I have eHealth - thrice weekly monitoring of pulse, lung function etc - the nurse doesn't come round to visit anymore. I get occasional telephone calls, but they are brief and not nearly as helpful as seeing a nurse.”

“If someone is not well, the nurse can see – because it's animal instinct – whereas on the phone I might say I feel fine, but the nurse couldn't see that I was unwell”.

Became 2 reviews on telehealth



Patient voice

“You get to know when it’s coming –you have had your body for a long time”

Became a series of reviews on antibiotics

“Tai Chi can give you the confidence to do more exercise and learn how to breathe properly. This helps if you get out of breath so you know what to do to be able to take in deep breaths”.

Became a review on maintenance rehabilitation



Patient voice

“I cannot go out if the temperature is 6 degrees or below. If it is too cold, I simply stop breathing before I get to the gate at the end of the path”

One person avoids Garratt Lane in the rush hour – it is too difficult to breathe in the polluted air

We asked – is it worth knowing about the pollution, or would it only worry you? **“You have to go out!”**

“If we were to have guidance, we would need clear levels and actions rather than just a number (e.g. concentration)”

Became a review on air pollution



The steering group

- Multidisciplinary group
- Met twice a year
- Presentation of review questions and draft PICOs
- Discussion of PICOs for each topic
- Helpful advice on complex topics e.g. management of multi-morbidities in people with COPD, advice on air pollution, telehealth interventions
- We also had initial input from the NIHR complex review support unit about some of our review topics

Survey to triangulate with patient group

- People diagnosed with any chronic respiratory condition
- Disseminated on social media (including BLF and ELF)
- 9 questions to explore patients experiences and knowledge of their condition



Survey – questions 1

- What is your main lung condition?
- What do you know about your condition? How would you explain it to your friends?
- When you were diagnosed with this condition, how did you feel?
- What is it like living with this condition now? How does it affect you emotionally?

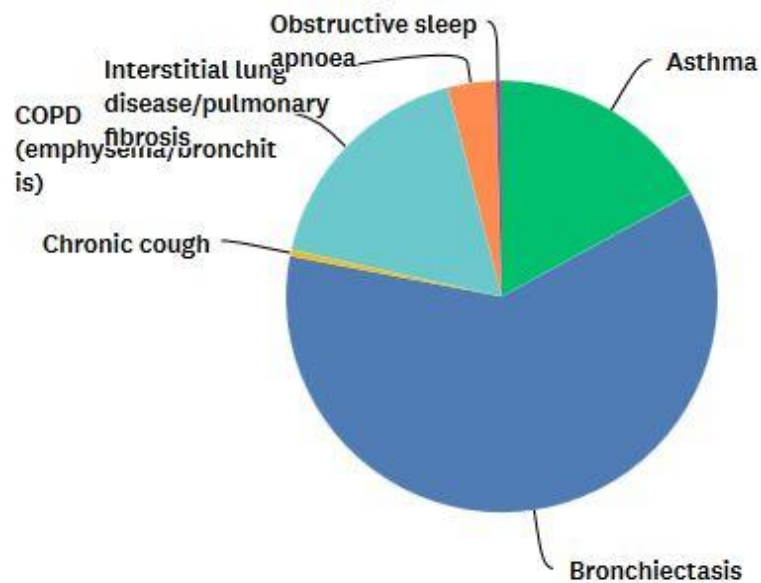


Survey – questions 2

- Thinking about living with your condition day-to-day, what's your experience of routine healthcare in: Your hospital clinic/Primary care
- Do you find your condition easy to manage on a day-to-day basis?
- If you take medication for your condition, do you have any difficulties with taking it as prescribed?
- Are there things that your lung condition prevents you from doing that you would like to be able to do? What are they and why does it stop you?
- When you last had an exacerbation (flare-up), what happened? What triggered the exacerbation? What was the impact on you? Where did you go for help? Were you happy with the care you received?

What is your main lung condition?

Answered: 223 Skipped: 6



Survey Results - COPD

- Explored using thematic analysis of 41 COPD responses
- Identified eight main themes (1) attitudes and knowledge, (2) psychological impact, (3) exacerbating factors, (4) relieving factors, (5) medication, (6) healthcare systems, (7) self-care and (8) support.
- The most recurring theme was the significant psychological impact the condition had
- Roaa Al-Bedaery presented at SAPC Madingley



Reviews published (8)

- Prophylactic antibiotics versus placebo in the management of COPD
- Head to head comparison of different prophylactic antibiotics in the management of COPD
- Interventions for promoting physical activity in people with COPD
- Prophylactic antibiotics for chronic obstructive pulmonary disease (COPD): a network meta-analysis
- Phosphodiesterase 4 inhibitors for COPD (update)
- Regular treatment with salmeterol and inhaled steroids for chronic asthma: serious adverse events (update)
- Regular treatment with formoterol and inhaled steroids for chronic asthma: serious adverse events (update)
- Regular treatment with formoterol and an inhaled corticosteroid versus regular treatment with salmeterol and an inhaled corticosteroid for chronic asthma: serious adverse events (update)

Reviews in press (7)

- Telehealthcare for remote monitoring and consultations for people with COPD
- Digital interventions for the management of COPD
- Tailored interventions and approaches to care for people living with chronic obstructive pulmonary disease and at least one other long-term condition: a mixed methods review
- Individual-level interventions to reduce personal exposure to outdoor air pollution and their effects on long-term respiratory conditions
- Interventions to improve adherence to pharmacological therapy for COPD
- Nocturnal non-invasive positive pressure ventilation for stable chronic obstructive pulmonary disease (update)
- Maintenance pulmonary rehabilitation for COPD

Reviews delayed (2)

- Biomarkers in the management of COPD exacerbations (BIO1-COP)
- Vitamin D supplementation for COPD (VITD-COP)

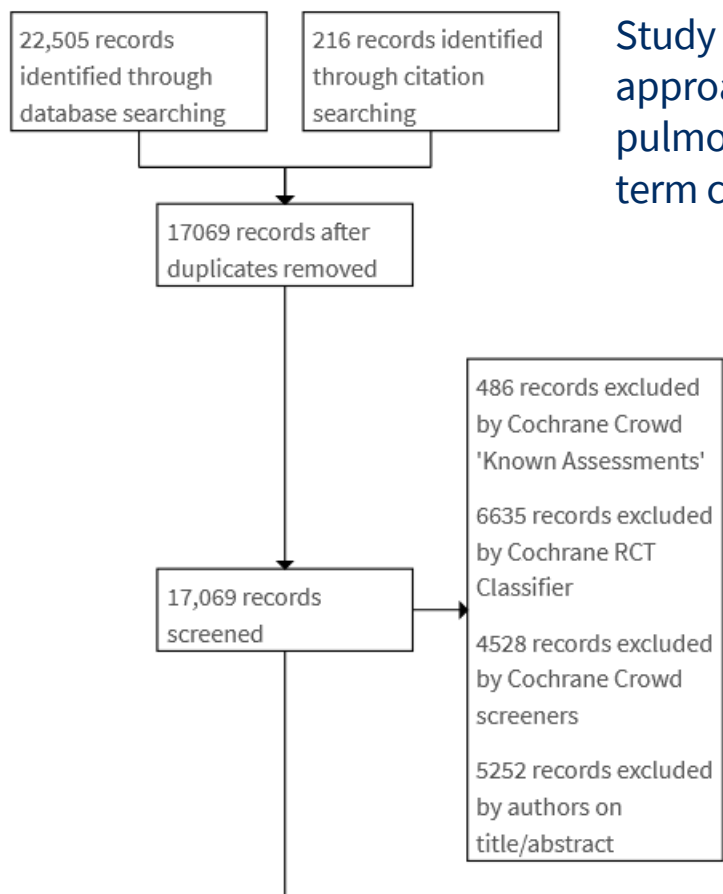


Reviews abandoned

- Long-acting inhaled therapy (beta-agonists, anticholinergics and steroids) for COPD: a network meta-analysis” (update)
- Prognostic factors at the end of life in COPD
- Pharmacotherapy in frequent exacerbators
- The safety of long acting beta-agonists in asthma (LABA) overview



Crowd sourcing & automation



Study identification for: Targeted interventions and approaches to care for people with chronic obstructive pulmonary disease (COPD) and at least one other long-term condition: a mixed methods review

Using all 3 components of the Cochrane Screen4Me workflow reduced screening burden by 68%

S4M

Selected review results



Aims:

1. To assess the effectiveness of any single intervention for COPD adapted or tailored their comorbidity(s) compared to any other intervention for people with comorbid COPD (quantitative data, RCTs)
2. To assess the effectiveness of an adapted or tailored single COPD intervention (simple or complex) that is aimed at changing the management of people with comorbid COPD (quantitative data, RCTs) compared to usual care
3. To identify emerging themes that describe the views and experiences of patients, carers and HCPs (qualitative data)
4. To use a mixed-methods approach to combine quantitative and qualitative data
5. To identify any gaps in the evidence as a recommendation for further research.

Tailored interventions and approaches for people with COPD and at least one long-term condition: mixed methods

- **Study design:** RCTs and qualitative studies
- **Population:** primary diagnosis of COPD of any severity (GOLD or ATS, spirometry), and living with at least one other long-term condition (e.g. asthma, CHD, T2DM, AF, HF, hypertension, lung cancer, osteoporosis)
- Included carers and health professionals when receiving/providing care to manage multi-morbidities
- **Interventions/comparator:** **a.** aimed at changing management of people with COPD and at least one other co-existing condition *or* **b.** any single intervention for COPD delivered to people with COPD adapted to or tailored to their comorbidities (e.g. pulmonary rehabilitation, exercise, ventilation, pharmacotherapy compared to control, usual care or active control)
- **Outcomes:** quality of life (e.g. SGRQ, CAT), exacerbations (number of people experiencing one or more, or exacerbation rate, or both depending on data available), functional status (6MWD), mortality

Tailored interventions and approaches to care for people with chronic obstructive pulmonary disease (COPD) and at least one other long-term condition: a mixed methods review



For adults with COPD and at least one other long term condition, rehabilitation or multi-component interventions may help to improve quality of life (moderate certainty evidence) and functional status (low certainty evidence). Effects of other approaches may have little impact on exacerbations (very low certainty evidence), hospital admissions (low certainty evidence), and deaths (low to very low certainty evidence).



There was not enough information about harms



Cochrane Review (to be published 2021); 8 studies with 1398 adults. There was not enough evidence around interventions aimed at COPD that are adapted for comorbidity. Evidence around opinions and experiences of people with COPD and comorbidity, therefore, a mixed methods approach could not be taken. The findings should be interpreted with caution.

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Pre-publication - confidential



Pre-publication - confidential

Aims:

- **To assess efficacy, safety and acceptability of individual-level interventions that aim to help people with or without chronic respiratory conditions to reduce their exposure to outdoor pollution**
- **To assess efficacy, safety and acceptability of individual-level interventions that aim to help people with chronic respiratory conditions to reduce personal impacts of outdoor air pollution and improve health outcomes**

- **Study design:** RCTs and non-randomised studies (i.e. comparative arm investigating effectiveness of interventions)
- **Population:** healthy children and adults, adults diagnosed with respiratory condition, and mixed populations of chronic respiratory conditions
- **Intervention/comparator:** any individual-level interventions aimed to reduce personal exposure to ambient air pollution (e.g. physical, behavioural, technological, pharmacological, or combination and of any duration) compared to control group
- **Outcomes:**
 - a. **measures of air pollution exposure** as reported in studies, including but not limited to mobile monitoring units and physiological measures (e.g. metabolic or heart rate variability)
 - b. **acute exacerbations of respiratory condition** (i.e. worsening of respiratory condition requiring change in medication/management or unscheduled visit to health care provider/hospitalisation);
 - c. **quality of life**
 - d. **SAEs** (i.e. death, life-threatening event, hospitalisation, prolonged existing hospitalisation, persistent or significant disability)

Individual-level interventions to reduce personal exposure to outdoor air pollution and their effects on long-term respiratory conditions



For healthy adults, wearing masks or choosing a lower-level pollution cycle route may have a small effect on measures that indicate exposure to air pollution (blood pressure, heart rate variability, exhaled nitrous oxide) (very low certainty evidence). There was little to no difference of air quality alerts on avoiding air pollution or improving breathing symptoms



There was not enough information about harms



Cochrane Review (to be published 2021); 11 studies with 15 to 1395 adults. There was not enough evidence from randomised or non-randomised trials to clearly demonstrate what the best advice is to give to people who what to reduce the impact of air pollution in their daily lives

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Pre-publication - confidential

Collaboration with Richard Atkinson, Pippa Powell from the ELF and WHO



Network meta-analysis of prophylactic antibiotics for COPD

- Original aim of review: to identify whether there are any antibiotics that are more effective/safer than others
- Issue: there are not many head-to-head studies that investigate this
- Approach: We already had antibiotics vs placebo data, so this data was used in the NMA to look at indirect antibiotics vs antibiotics comparisons
- Complex review support unit advised on the PICO and methodology
- The analysis was performed by Sofia Dias



- **Study design:** RCTs of minimum 12 weeks intervention duration
- **Population:** COPD diagnosis (guidelines: ERS, ATS, GOLD), stable or during exacerbations, provided that antibiotic administered long term, any COPD severity
- **Intervention/comparator:** any prophylactic oral antibiotic class for at least 12 weeks given continuously, intermittently, or pulsed (min 5 days every 8 weeks) compared to placebo or each other
- **Outcomes:** COPD exacerbation (time to first (HR), rates, and number of participants with one or more), quality of life (SGRQ), all-cause SAEs (number of participants with one or more)

Prophylactic antibiotics for adults with chronic obstructive pulmonary disease (COPD): a network meta-analysis



For adults with COPD, macrolides reduced exacerbations and quality of life compared to placebo. Quinolones and tetracyclines had little to no effect on exacerbations or quality of life. Given the trade-off between effectiveness, safety and risk of antibiotic resistance, prophylactic antibiotics may be best reserved for selected people, such as those experiencing frequent exacerbations



Macrolides reduced unwanted serious side effects; 49 fewer per 1000 people experienced side effects compared with placebo. There was little to no difference with quinolone or tetracycline plus macrolide compared with placebo.



Cochrane Review (published January 2021); Exacerbations: 9 studies with 2732 participants; quality of life: 7 studies with 2237 participants; serious adverse effects: 9 studies with 3180 participants. 10 studies concluded that prophylactic antibiotic administration was associated with development of antimicrobial resistance

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Janjua S et al. Prophylactic antibiotics for adults with chronic obstructive pulmonary disease: a network meta-analysis. CDSR 2021 (1)



NICE Journey

Prophylactic antibiotics vs placebo review underpinned
NICE guideline NG115 Chronic obstructive pulmonary
disease in over 16s: diagnosis and management [E]
Predicting and preventing exacerbations

- Very low to low quality evidence from up to 9 RCTs with up to 2,825 people found meaningful improvements in exercise capacity, and reductions in the number of people experiencing exacerbations and the rate of exacerbations pppp
- Very low quality evidence from up to 5 RCTs with up to 2,723 people could not differentiate all-cause mortality

NICE recommendation

- While prophylactic antibiotics reduce the risk of people having an exacerbation and the number of exacerbations per year in people with COPD and sputum production...
- ...prescribing these to large numbers of people with COPD could increase levels of antibiotic resistance.
- Problems with adherence may make this worse
- **Committee recommended azithromycin for** people who would benefit the most from prophylactic antibiotics i.e. whose exacerbations were not being managed well by other treatments. Plus strict criteria for reviewing



Dissemination

- Patient leaflet
- HTA Programme funding call informed by prophylactic and head-to-head antibiotics reviews
- Reviews cited in 6 clinical guidelines (BTS, GINA report, NICE, Kaiser Permanente, Saudi Initiative for Asthma)
- Air pollution review Evidently Cochrane Blog



Dissemination

- Podcast: inhaled steroids with and without regular formoterol for asthma: SAEs
- Interventions for promoting physical activity for COPD review included in Cochrane Special Collection about health ageing
- 2 x antibiotics reviews included in Cochrane Special Collection for World COPD Day in 2019
- Five reviews are now Cochrane Clinical Answers
- Submitted abstracts to the Cochrane Colloquium 2019 (Santiago, Chile) and 2020 (Toronto)



Summary

- Nearly all the reviews are nearly completed
- Some great dissemination and uptake so far
- Programme grant funding covers one full time systematic reviewer plus a small amount of project management time and expenses
- We have more control over reviews done in house, and they require a lot of additional voluntary authorship
- Protocol development of these complex topics took more time than anticipated...
- ...advice from NIHR complex review support unit and stakeholder groups refined PICO for more relevant reviews
- Added stress of the pandemic, but we got through it!



For more information

- Webpage campaign under construction
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- Twitter @CochraneAirways
- Browse cochranelibrary.com



Thank you

- Funded by NIHR
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- Cochrane Airways group
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