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Care pathways versus usual care for chronic obstructive pulmonary disease (COPD) (Protocol)

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[Intervention Protocol]

Care pathways versus usual care for chronic obstructive pulmonary disease (COPD)

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ABSTRACT

Objectives

This is a protocol for a Cochrane Review (intervention). The objectives are as follows:

To assess the effects of care pathways (CPs) compared to usual care/no CPs for people with chronic obstructive pulmonary disease (COPD).

BACKGROUND

Description of the condition

Chronic obstructive pulmonary disease (COPD) is a condition characterised by a limitation of respiratory function due to the progressive destruction of the airways (ratio of the forced expiratory volume in the first second to the forced vital capacity of the lungs (FEV1/FVC ratio) of ≤ 0.7 post-bronchodilatation) (GOLD 2023). It is caused by inhalation of noxious substances from tobacco or occupational exposure, creating an inflammatory response that stimulates mucus production and hyperinflation (Bruce 2000; Hogg 2017). The main symptoms of COPD are shortness of breath, cough, and abnormal sputum production, which are linked to a decline in lung function (Allinson 2016).

COPD has significant morbidity and mortality. It is the third leading cause of death (WHO 2022), with a prevalence of 10.3% among people aged 30 to 79 years (Adeloye 2022). COPD exacerbations, which are an acute worsening of symptoms, are the main cause of COPD death. Furthermore, COPD creates functional and psychological burdens such as reduced physical capacity, fatigue, a decline in quality of life, anxiety and depression (Kim 2000; Negewo 2015; Torres-Sánchez 2016). The increasing prevalence of COPD creates continuous economic and logistical pressure on healthcare systems, which are related to direct (e.g. hospitalisation, medications) and indirect (e.g. disability and loss of productivity) medical costs (Chapman 2006; Safiri 2022).

Early diagnosis and management of COPD are essential to slow the progression of the disease and improve the individual's overall health outcomes (Welte 2014). Bronchodilators are the key treatment for COPD. However, optimal disease management, such as systematic guidelines and cost-effective access to healthcare resources, are also critical to proper treatment planning for physicians and patients.

Description of the intervention

Care pathways (CPs), also known as critical or clinical pathways, are fundamental tools healthcare systems use to translate standardised, evidence-informed guidelines into care processes. They are multidisciplinary management plans that aim to outline and co-ordinate the sequence of timing, tasks, and interventions for a specific condition and population and focus on integrating the clinical care journey across different settings and providers (Rotter 2010; Kinsman 2010). Specialist respiratory services consist of healthcare services provided by medical professionals (e.g. pulmonologists, respiratory nurses, respiratory physiotherapists, specialists in allergology and sleep medicine) involved in diagnosing, treating, and managing lung-related conditions. CPs and specialist respiratory services work together to provide co-ordinated and efficient care.

CPs were introduced in the 1980s in the US health system and have been used globally ever since. By the 1990s, CPs had become a widely accepted tool for improving healthcare delivery and patient outcomes (Rotter 2011). In the early 2000s, the development of electronic health records (EHRs) and clinical decision support systems (CDSSs) led to the further evolution of CPs (Evans 2016; Wasylewicz 2019). EHRs allowed for the automated longitudinal collection and analysis of patient data, which generated personalised care plans based on the patient's medical history and current condition (Gunter 2005). CDSSs provide healthcare professionals with real-time clinical guidance and recommendations, further enhancing the effectiveness of CPs (Neame 2019; Sutton 2020). Today, they have become essential for improving healthcare quality and reducing costs (Bartlett 2022; Carlson 2009). They are used in various clinical settings, including hospitals, clinics, and long-term care facilities, and are often integrated into EHRs and other digital health technologies (Bartlett 2022).

CPs are a complex and standardised approach aiming to develop a multidisciplinary care plan for patients with a specific medical condition (Rotter 2011). Indeed, healthcare providers ensure that patients receive high-quality, evidence-based care tailored to their needs (Lavelle 2015). This may lead to better patient outcomes and improved efficiency and cost-effectiveness for healthcare organisations (Everink 2018). Furthermore, CPs enhance communication and collaboration between healthcare professionals by developing a co-ordinated approach to care. They also improve patient satisfaction by providing a clear care plan focusing on their needs and satisfaction (Evans-Lacko 2010). They set specific benchmarks and treatment goals for patients, which allow healthcare professionals to track progress and identify areas for improvement. As a result, they ensure that patients receive the best possible care and that the CP is constantly improving. Moreover, CPs may reduce in-hospital complications and lead to better documentation (Rotter 2010).

In the context of COPD, CPs could be implemented in multiple settings, including primary care practices, hospitals, and long-term facilities, and involve different healthcare providers. COPD CPs typically comprise a series of steps designed to standardise and optimise patient care while also considering the individual needs and preferences of each patient. These steps may include early identification and diagnosis of COPD, assessment of the severity of the disease, development of an individualised treatment plan, ongoing monitoring, and evaluation of the patient's progress. Furthermore, CPs assist in co-ordinating care across different healthcare settings and providers.

As a complex intervention, designing a CP is a long, rigorous, and challenging procedure involving the development of sequential, evidence-based components that aim to foster the standardisation of care (i.e. providing clear guidelines and thus reducing variability) and enhance its co-ordination and continuity (Lawal 2016; Schrijvers 2012). CPs may exhibit common sequences of steps and components, such as defining the objective, identifying the population, conducting a needs assessment, establishing a multidisciplinary team, incorporating evidence-based guidelines into the CP components, evidence synthesis, dissemination, evaluation, and quality improvement (Koolen 2018; Plishka 2019; Vanhaecht 2012). On the other hand, there are no standard criteria for developing CPs, and significant variability exists in their design (Latina 2020). Factors involved in CP development include the population, setting, involvement of stakeholders, local healthcare policies, and financial resources. For example, Yadav 2021 embraced a strategy called the "co-design" approach, which was based on involving various stakeholders to develop an integrated care model that took into account the specific needs and contexts of a local community in Nepal, while Combi 2017 elaborated methodological frameworks for the design and implementation of a COPD CP for the region of Veneto (Italy)

via the simulation of two models (business process model and notation, and decision model and notation). Furthermore, other frameworks have been used to design a CP for COPD (Koolen 2018), such as the seven-phase model developed by the European Pathway Association (EPA) in 2012 (Vanhaecht 2012). The EPA revised this model in 2019 and designed a framework focusing on the interaction between the care context, intervention mechanism, intervention fidelity, and outcomes (Seys 2019).

CP implementation may be challenging because of the complexity of healthcare systems and the unique needs of patients, with effective implementation requiring a collaborative and systemised approach involving all relevant stakeholders. Furthermore, ongoing monitoring is essential to ensure the pathway achieves its intended goals. Patient preferences are occasionally disregarded by CPs, which is a main concern. In some cases, they may be a one-size-fits-all model that disregards the variety of treatments available (Abrahams 2017; Allen 2008; Sariyar 2019).

Overall, CPs may improve the quality of care and outcomes for COPD patients by facilitating a co-ordinated, evidence-based approach to care delivery. However, some challenges surround their implementation, the addressing of which is essential to promote the level of care and achieve the best possible outcomes.

How the intervention might work

CPs are a potentially valuable tool for promoting the translation of evidence into practice. Standardising the clinical care process by incorporating evidence-based knowledge has been an effective strategy for reducing adverse treatment variance and decreasing the potential for medical errors (Kohn 2000). Through data collection, CPs hold sufficient information on how and why the intervention might work. Therefore, the database is likely to help process the information systematically to adapt the subsequent steps of the CP (Lodewijckx 2012). The main objective of CPs is to enhance the quality of care for broad crowds by adapting and adjusting the risk to improve patient safety and satisfaction and to advance access to specialist services (Schrijvers 2012).

CPs are complex interventions due to their various components. They require qualitative and quantitative evidence assessment, given their multidisciplinary approach, which leads to high-quality treatment plans (Campbell 2000). This aspect benefits countries and healthcare providers with limited access to high-quality scientific research and means.

Given that low socioeconomic status (SES) is a known risk factor for lower health-related quality of life in people with COPD, CPs can help improve access to health care, including medication and treatments, thereby improving COPD management (Cohen 1977). Affected individuals may have limited access to health care, which can impact their ability to manage their COPD symptoms effectively. Additionally, low SES is associated with a higher prevalence of smoking, which is a significant risk factor for COPD development and progression (Hitchman 2014; Terzikhan 2016).

Typical components of COPD CPs include standardised assessments for determining the severity of the condition. These include tools for assessing lung function, symptoms, and overall quality of life (Adhikari 2021; Lange 2016). Based on the patient's assessment, the CP may recommend specific interventions such as medication management, smoking cessation support, pulmonary rehabilitation, and follow-up visits (Li 2021; McCarthy 2015; van Eerd 2016). Additionally, some CPs may include patient education and support recommendations to help patients understand their condition and manage their symptoms (Zwerink 2014).

Access to respiratory services is multidimensional and has various entering points, as well as international differences depending on the medical infrastructure of the country. Primary care is the most common starting point for accessing respiratory services, and patients may be referred to respiratory physicians (Koolen 2018). However, if the patient is undiagnosed, cannot access primary care, or experiences exacerbations, the most likely choice may be to seek consultation through an emergency room at a hospital.

By following a CP, healthcare providers can ensure that all necessary information is available and that patients receive consistent, high-quality care. This may lead to improved outcomes, reduced healthcare costs, and better quality of life for patients.

Why it is important to do this review

COPD is a progressive respiratory disease affecting millions globally and a leading cause of morbidity and mortality. Its burden on public health is therefore expected to expand continuously due to an increasingly ageing society (WHO 2022). The condition requires complex, long-term treatment management, which CPs support through healthcare providers. Specialist respiratory services are essential for early and effective diagnosis and management (Hurst 2020).

While some literature exists on CPs for managing COPD, there remain gaps on this topic. Many studies have focused on the effectiveness of individual interventions, such as smoking cessation programmes, pulmonary rehabilitation, and medication management. However, there is limited research on how CP can improve the overall management of COPD (Meiwald 2022; Plishka 2019). Moreover, there is a need to check the impact of CPs on diverse populations, including those in rural or low-income countries, who may face unique challenges in accessing specialist respiratory services (Parekh 2020). It is also worth exploring the most effective components of CPs for managing COPD, including patient education, self-management strategies, and co-ordinated care between primary care providers and respiratory specialists.

Overall, a Cochrane review on this topic may provide valuable information on the effectiveness of CPs in managing COPD and help guide clinical practice.

OBJECTIVES

To assess the effects of care pathways (CPs) compared to usual care/no CPs for people with chronic obstructive pulmonary disease (COPD).

METHODS

Criteria for considering studies for this review

Types of studies

CPs cannot be implemented on an individual level. We therefore do not expect to find randomised clinical trials (RCTs) with individual randomisation, but that CPs will mainly be evaluated using cluster-RCTs and quasi-experimental designs. Thus, limiting the eligibility criteria to RCTs may not provide a comprehensive understanding

of the topic. In addition, including different study designs may support investigating the applicability of CPs and evaluating equity aspects. We will include cluster-RCTs, controlled-before-after studies (CBAs), and interrupted-time series studies (ITSs), as these are considered to be robust quasi-experimental designs (EPOC). We will include the last if three measures were conducted before and after the intervention.

Types of participants

We will include adults ≥ 18 years with a diagnosis of COPD according to international standards (GOLD 2023), regardless of the stage of the condition. We will exclude participants with the following comorbidities/characteristics: asthma, cystic fibrosis, and lung cancer. If a study reports different conditions for the same intervention of interest, we will extract individual data or contact the study authors for this information.

We will use the COPD classification according to the FEV1 stages (GOLD 2023):

- GOLD 1: mild: FEV1 ≥ 80% predicted;
- GOLD 2: moderate: 50% FEV1 ≤ 80% predicted;
- GOLD 3: severe: 30% FEV1 ≤ 50% predicted;
- GOLD 4: very severe: FEV1 ≤ 30% predicted.

Types of interventions

The review will consist of three parts in accordance with the targeted setting of the CP, as follows.

- **COPD care pathways for inpatient care:** these CPs focus on the services provided to patients with COPD exacerbations.
- **COPD care pathways for outpatient care:** these CPs focus on the services provided to patients who do not require immediate hospitalisation or intensive interventions.
- **Integrated care pathways:** these CPs cover inpatient and outpatient care and address the entire journey to ensure the continuity of care.

We will include trials comparing a CP with usual care (no CP) during specialist respiratory services such as hospitalisation, outpatient care, and pulmonary rehabilitation.

We will consider an intervention as a CP if it was designed through a carefully planned and executed methodology, consists of a number of components that outline the sequence of COPD management according to evidence-based guidelines, and highlights the entire patient journey in the process of care (starting from patient identification to follow-up). Since there are no standards for an ideal CP, we will not restrict our inclusion criteria to specific components, sequences of actions, or durations.

We will define usual care as a management strategy that was not standardised for COPD patients across a particular healthcare setting, and that was not designed according to specific interventions, activities, and timelines that defined the entire care service.

Types of outcome measures

We will evaluate the following outcomes, but will not limit our study search based on them.

Primary outcomes

We will group the primary outcomes according to the follow-up: short (less than three months), medium (three to six months), and long term (six or more months). Our primary time point will be the medium term, and we will pool the last follow-up within the same analysis.

- Health-related quality of life (HRQoL): We will analyse the scales with respect to the concept of interest:
  - general quality of life: EQ-5D (Rabin 2001) and Short Form Health Survey (SF) instruments (Brazier 2004; Ware 1992; Ware 1996);
  - disease-specific measure: We will include all validated scales such as the COPD Assessment Test (CAT) (Jones 2009), Chronic Respiratory Questionnaire (CRQ) (Wijkstra 1994), and St. George's Respiratory Questionnaire (SGRQ) (Jones 1992). These scales assess distinct measurement concepts.
- Hospital admission
- Mortality
  - In-hospital mortality
  - Overall mortality

Secondary outcomes

- COPD exacerbations: defined as an increase in dyspnoea and/or cough and sputum that worsens in fewer than 14 days (GOLD 2023).
- Patient satisfaction: this can be assessed using various methods, such as surveys, focus groups, etc. These methods can provide valuable feedback on the quality of care and help identify areas of improvement.
- Adverse events: all types of hospital and provider visits due to complications or adverse events of COPD medication.

Search methods for identification of studies

Electronic searches

We will search the following databases for primary studies from inception to the search date.

- Cochrane Central Register of Controlled Trials (CENTRAL; latest issue), in the Cochrane Library
- PubMed (1946 to date of search)
- Embase Ovid (1974 to date of search)
- Physiotherapy Evidence Database (PEDro) (1999 onwards)

We will combine terms for COPD with terms for CPs. We will add validated search filters for RCTs and non-RCTs (Lefebvre 2022; Waffenschmidt 2020). A preliminary search strategy is shown in Appendix 1.

We will also search ClinicalTrials.gov (www.clinicaltrials.gov) and the World Health Organization International Clinical Trials Registry Platform (www.who.int/clinical-trials-registry-platform).

There will be no restrictions on the language of publication.

Searching other resources

We will examine the reference lists of both primary studies and review articles to identify any additional references.

We will search for errata or retractions from included studies published in full text on PubMed (pubmed.ncbi.nlm.nih.gov) and report the date this was done in the review. We will search Epistemonikos to identify relevant systematic reviews. Where appropriate, we will contact experts in the field to ask for any ongoing trials or newly published papers.

Data collection and analysis

Selection of studies

Two review authors (MPB and OA) will independently screen the titles and abstracts of records identified by the search for potential relevance. We will retrieve the full-text reports/publications of those studies deemed potentially relevant, and the same two review authors will independently screen the full texts for inclusion in the review, and identify and record the reasons for exclusion of ineligible studies. Any disagreements will be resolved through discussion or by consulting a third review author (TM) if necessary.

We will list the excluded studies and their reasons for exclusion in the 'Characteristics of excluded studies' table. We will collate multiple reports of the same study so that each study, rather than each report, is the unit of interest in the review. We will also provide details of any ongoing studies. We will record the selection process in sufficient detail to complete a PRISMA flow diagram (Liberati 2009).

Data extraction and management

We will extract data using Covidence or an Excel spreadsheet following the guidance of Cochrane Effective Practice and Organisation of Care (EPOC) resources for review authors (Covidence; EPOC 2017a). We will pilot the form on at least one study in the review. We will extract the following study characteristics from the included studies.

- Methods: study design, total duration of study, number of study centres and location, study setting, withdrawals, and date of study.
- Participants: N, mean age, age range, gender, severity of the condition, diagnostic criteria, baseline lung function, smoking history, inclusion criteria, and exclusion criteria.
- Interventions: intervention, comparison.
- Outcomes: primary and secondary outcomes specified and collected, and time points reported.
- Notes: funding for trial, and notable conflicts of interest of trial authors.

One review author (MPB) will extract study characteristics from the included studies, and a second review author will check the accuracy of the data extraction (OA). We will note in the 'Characteristics of included studies' table if outcome data were not reported in a usable way. Any disagreements will be resolved through consensus or by involving a third review author (TM). One review author (MPB) will transfer data into the RevMan file (RevMan 2024). We will double-check that data have been entered correctly by comparing the data presented in the systematic review with the study reports. A second review author (SS) will spot-check the study characteristics for accuracy against the trial report.

Assessment of risk of bias in included studies

Two review authors (MPB and OA) will independently assess the risk of bias of subjective (HRQoL) and objective outcomes separately, and use the last follow-up time point according to the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2023).

We will use the Cochrane RoB 2 tool to assess the risk of bias of RCTs (Sterne 2019), employing the RoB 2 Excel tool (RoB 2). We will use the Robvis tool to generate 'traffic light' and weighted bar plots (robvis). We will judge risk of bias as low risk of bias, some concerns, or high risk of bias.

Our effect of interest is starting the intervention, and we will assess the following domains and report a justification for each judgement.

- Bias arising from the randomisation process
- Bias due to deviations from intended interventions
- Bias due to missing outcome data
- Bias in measurement of the outcome
- Bias in selection of the reported result

We will use the test version of RoB 2 to assess cluster-RCTs (RoB 2 CRT). We will judge risk of bias as low risk of bias, some concerns, or high risk of bias.

We will use ROBINS-I to assess non-randomised studies, as suggested in the *Cochrane Handbook for Systematic Reviews of Interventions* (Sterne 2022), considering the following domains (Sterne 2016).

- Bias due to confounding
- Bias in selection of participants into the study
- Bias in classification of interventions
- Bias due to deviations from intended interventions
- Bias due to missing data
- Bias in measurement of the outcome
- Bias in selection of the reported results

We will judge risk of bias as low, moderate, serious, or critical. Our baseline confounding factors are age, SES (e.g. income, education), hospitalisation, disease severity (as determined by GOLD 2023), and COPD exacerbation in the last six months. Our time-varying confounding factor is COPD severity. For CBAs and ITSs, we will use the domains suggested for each study type (Sterne 2022).

We will reach consensus through discussion or by consulting a third review author (TM) when necessary.

We will report the risk of bias assessment in the Results section of the review, and it will inform our assessment of the certainty of evidence. Our primary analysis will include all studies without considering the risk of bias.

Assessment of bias in conducting the systematic review

We will conduct the review according to this published protocol and report any deviations from it in the 'Differences between protocol and review' section of the systematic review.

Measures of treatment effect

The appropriate statistical analysis method is contingent upon the nature of the outcome. For dichotomous data, the preferred analysis is risk ratio (RR), while continuous data will be assessed by calculating mean difference (MD) if the same scale is used, or standardised mean difference (SMD) if different scales are used to measure the same concept. We will analyse ordinal data as dichotomous or continuous, depending on how they were reported (continuous if the scale is longer than five). We will use hazard ratio (HR) to analyse time-to-event data. We will present all findings with a 95% confidence interval (CI). A statistical and methodological expert team (OA and TM) will analyse the data using R (R Foundation for Statistical Computing).

We will express skewed data narratively with medians and interquartile ranges for each group. When both change-from-baseline and endpoint scores are available for continuous data, we will employ change-from-baseline unless there is a low correlation between individual measurements. We will prefer adjusted analyses (e.g. analysis of variance (ANOVA) or analysis of covariance (ANCOVA)) for meta-analyses if obtainable. We will only include relevant arms from studies that report multiple trial arms. In meta-analyses combining two comparisons, the active arms will be merged, or the control group will be halved to prevent double-counting.

Unit of analysis issues

- **Cluster-RCTs:** we will perform the analyses on the same unit as the allocation. If the appropriate information is missing (e.g. intracluster correlations), we will pool the results using the effective sample size approach (Rao 1992).
- **Repeated observations on participants:** if studies report outcomes at multiple time points, we will choose post-intervention data and then the longest period of follow-up. If relevant, we will divide the duration of follow-up into categories to explore possible differences in the effect estimate.
- **Studies with more than two arms:** as the intervention is provided on a group level (e.g. hospitals), we do not expect studies with more than two arms.
- **Dichotomous outcomes:** we will use participants, rather than events, as the unit of analysis (i.e. the number of people admitted to the hospital, rather than the number of admissions per person). However, if rate ratios are reported in a study, we will analyse them on this basis.

Dealing with missing data

We will contact investigators to verify key study characteristics and to obtain missing outcome data where possible (e.g. when a study is identified as abstract only). We will attempt to compute missing summary data from other reported statistics. If data are unobtainable, we will report the level of missingness and consider how it might impact the certainty of the evidence.

Assessment of heterogeneity

As a starting point, we will group studies according to setting (inpatient, outpatient, or integrated care), and map the components of the care pathways. We will prepare a process-oriented logical model to describe the complexity of the CPs and illustrate the possible underlying relationships. In addition, we will construct a matrix of potential effects deduced from theoretical literature on the effects of the CPs. Based on this, we will describe the underlying mechanism through which the intervention affects specific outcomes.

We will extract the characteristics of CPs to explore clinical (e.g. timeliness of care, clinical and laboratory assessments, pharmacological and non-pharmacological care, educational programmes, counselling, prevention, multidisciplinary collaboration) and methodological (e.g. length of follow-up, study design, development and implementation of CP, updates, consumer and stakeholder involvement, organisational factors, evaluation processes) heterogeneity.

We will analyse heterogeneity in depth to decide which studies are sufficiently homogenous to be pooled. This includes differences in populations, design of the CPs, and setting. In addition, we will consider methodological (study design, outcome measurement, follow-up time) and statistical heterogeneity. We will use the I^2 statistic and prediction intervals to measure statistical heterogeneity among the studies in each analysis. If we identify substantial heterogeneity, we will report it and explore possible causes by prespecified subgroup analysis. The assessment of heterogeneity will also be part of the GRADE assessment (inconsistency domain).

Assessment of reporting biases

If more than 10 trials can be pooled, we will create and examine a funnel plot to explore possible small-study and publication biases.

Data synthesis

Before calculating pooled results, we will explore heterogeneity. We will only conduct a meta-analysis if the studies for comparison are sufficiently clinically, methodologically, and statistically homogenous. We will not pool data from RCTs with data from CBAs and ITSs. Our primary analysis will include all eligible studies regardless of their risk of bias.

We will perform random-effects meta-analyses using the Paule-Mandel heterogeneity variance estimator and modified Hartung-Knapp CIs to determine the overall effectiveness. For meta-analyses of fewer than five studies, we will use Bayesian random-effects meta-analyses with weakly informative priors for Tau^2; for zero event studies Bayesian random-effects meta-analyses with weakly informative priors for the treatment effect or sensitivity analyses (Günhan 2019), we will use beta-binomial models (Felsch 2022). We will perform all analyses at the same level as the allocation unit to avoid unit of analysis errors.

For ITSs, we will use data from segmented regression, including time trends before and after the intervention, adjusting for autocorrelation and any periodic changes, or autoregressive integrated moving average (ARIMA) models. If papers with ITS design do not provide an analysis that adequately accounts for time trends, but the necessary data points are available, we will re-analyse the data using the linear model:

$$Y_{(t)} = B_0 + B_1{*}\text{Pre-intervention } T + B_2{*}\text{Post-intervention } (T - T_i) + B_3{*}\text{intervention } X_t + e_{(t)}.$$

Where $Y_{(t)}$ is the outcome in months. Pre-intervention is a continuous variable indicating time from the start of the study up to the last point in the pre-intervention phase and coded

constant thereafter. Post-intervention is coded 0 up to the first point post-intervention and coded sequentially from 1 thereafter. Intervention is coded 0 for pre-intervention time points and 1 for post-intervention time points. In this model, B_1 estimates the slope of the pre-intervention data; B_2 estimates the slope of the post-intervention data; and B_3 estimates the change in the level of outcome as the difference between the estimated first point post-intervention and the extrapolated first point post-intervention if the pre-intervention line was continued into the post-intervention phase. The difference in slopes is calculated by $B_2 - B_1$. The error term $e_{(t)}$ is assumed to be first-order autoregressive. Similar models will be used for binary and count data.

We will pool binary and count data across ITSs using one-stage meta-analyses models, more concrete generalised-linear-mixed-models (e.g. Poisson regression with random effect for study).

We will calculate 95% CIs for all effect measures.

We will perform meta-analyses in the current version of (package meta, bayesmeta, and netmeta).

If studies differ significantly in terms of clinical or methodological heterogeneity, we will opt for a structured narrative synthesis using visual displays and tabulations instead, as recommended in the *Cochrane Handbook for Systematic Reviews of Interventions* (McKenzie 2022). We will report studies without usable data narratively.

Subgroup analysis and investigation of heterogeneity

We will consider the following subgroups.

- Age
- Gender
- Disease severity
- Socioeconomic status (SES)
- Continent: North America, South America, Europe, Africa, Middle East, East and South East Asia, Oceania

We plan to conduct subgroup analyses for the following outcomes.

- HRQoL
- Mortality: short (less than three months), medium (three to six months), and long term (six or more months)

If available, we will prefer information from within-study subgroup analyses to avoid ecological bias. For this purpose, we will use or recalculate interaction terms within the study, which will be subsequently combined in the meta-analyses (Godolphin 2024). If it is impossible to use such within-study subgroup analyses, we will pool the subgroups separately and report the results descriptively.

Sensitivity analysis

We plan to conduct a sensitivity analysis by removing RCTs at high risk of bias, and non-RCTs at critical and serious risk of bias.

Summary of findings and assessment of the certainty of the evidence

Two review authors (MPB and OA) will independently assess the certainty of the evidence as high, moderate, low, or very low using the five GRADE considerations (risk of bias (based on the overall RoB 2 judgement), consistency of effect, imprecision, indirectness, and publication bias) (Guyatt 2008). We will use the methods and recommendations described in Section 8.5 and Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2022) and the EPOC worksheets (EPOC 2017b), employing GRADEpro GDT software (GRADEpro GDT).

We will summarise the findings in the summary of findings table(s) for each setting separately and include the most important outcomes (HRQoL; hospital admission; mortality; COPD exacerbations; patient satisfaction).

We will prioritise outcome measurements that were combined in the meta-analysis. Otherwise, we will assess the evidence of the entire outcome narratively. We will evaluate the certainty of the evidence using the GRADE approach for ROBINS-I by integrating findings from both randomised and non-randomised studies (Schünemann 2019). We will justify our reasons for down- or upgrading the certainty of evidence using comments and footnotes in the table. We will prioritise evidence from RCT for presentation in the summary of findings tables, unless the outcome was only reported by non-randomised studies.

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Editorial and peer-reviewer contributions

The following people conducted the editorial process for this article:

- Sign-off Editor (final editorial decision): Toby Lasserson, Cochrane Central Editorial Service;
- Managing Editor (selected peer reviewers, provided editorial guidance to authors, edited the article): Anupa Shah, Cochrane Central Editorial Service;
- Assistant Editor (conducted editorial policy checks, collated peer-reviewer comments, and supported the editorial team): Justin Mann, Cochrane Central Editorial Service;
- Copy Editor (copy editing and production): Lisa Winer, Cochrane Central Production Service;
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APPENDICES

Appendix 1. Preliminary MEDLINE (PubMed) search strategy

#1	"Pulmonary Disease, Chronic Obstructive"[Mesh] OR COPD[tiab] OR “Chronic Obstructive Pulmonary Disease*”[tiab] OR “Chronic Obstructive Lung Disease*”[tiab] OR “Chronic Obstructive Airway Disease*”[tiab] OR “Chronic Airflow Obstruction*”[tiab]

(Continued)

#2	Critical Pathways[Mesh] OR “care map” [tiab] OR “care plan” [tiab] OR “care algorithm“[tiab] OR “treatment algorithm“[tiab] OR "critical pathway"[tiab:~1] OR "clinical pathway"[tiab:~1] OR "care pathway"[tiab:~1]
#3	cohort[all] OR (control[all] AND study[all]) OR (control[tw] AND group*[tw]) OR epidemiologic studies[mh] OR program[tw] OR clinical trial[pt] OR comparative stud*[all] OR evaluation studies[all] OR statistics as topic[mh] OR survey*[tw] OR follow-up*[all] OR time factors[all] OR ci[tw]
#4	Interrupted Time Series Analysis[Mesh] OR interrupted time series[tiab] OR interrupted times series[tiab] OR"segmented regression"[tiab:~3] OR integrat* moving average[tiab] OR slope change[tiab] OR"piecewise regression"[tiab:~3] OR"piece-wise regression"[tiab:~3] OR ((time series[tiab] OR timesseries[tiab]) AND ("pre post"[tiab:~5] OR"before after"[tiab:~5] OR quasi-experiment*[tiab] OR quasiexperiment*[tiab] OR natural experiment*[tiab] OR ARIMA[tiab] OR autoregress*[tiab] OR auto-regress*[tiab] OR segmented[tiab] OR segments[tiab] OR piecewise[tiab] OR piece-wise[tiab] OR interrupt*[tiab] OR implement*[tiab] OR guideline*[tiab] OR prescription*[tiab] OR prescrib*[tiab] OR stewardship[tiab] OR rates[tiab] OR intervention[tiab]))
#5	randomized controlled trial[pt] OR random*[tiab]
#6	#1 AND #2 AND (#3 OR #4 OR #5)

CONTRIBUTIONS OF AUTHORS

Conception and co-ordination of the protocol: Pajand Birjandi M, Ammous O, Mathes T, Stanzel S, Wollsching Strobel M, Kampo R

Writing the protocol: Pajand Birjandi M, Ammous O, Mathes T

Search strategy: Mathes T, Bridges C

Clinical and statistical comments: Ammous O, Mathes T, Stanzel S, Wollsching Strobel M, Kampo R

DECLARATIONS OF INTEREST

Pajand Birjandi M: none known.

Ammous O: none known.

Kampo R: none known.

Stanzel S: received a personal travel grant from CSL Behring (from 25 May 2022 to 27 May 2022), an institutional grant (Cologne Research Group) from Löwenstein Medical, a grant from Chiesi USA, and now holds the position of chairman section of respiratory and intensive care medicine at the German Society of Pneumology.

Wollsching Strobel M: received two personal travel grants from CSL Behring (from 24 May 2022 to 28 May 2022) and Löwenstein Medical (9 June 2022 to 12 June 2022), payment for a lecture on 18 November 2022 from Novartis Pharma, and works as a doctor at Kliniken der Stadt Köln gGmbH.

Mathes T: none known.

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