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Prevalence and Influencing Factors of Cognitive Frailty in Older Adults with COPD: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 October 2025 and was last updated on 26 October 2025.

INTRODUCTION

Review question / Objective P (Population): What is the pooled prevalence of cognitive frailty in community-dwelling or hospitalized older adults (e.g., aged ≥60 years) with a confirmed diagnosis of COPD?

I/E (Indicator/Exposure): What are the demographic, clinical, lifestyle, and social factors (e.g., age, disease severity, comorbidities, nutritional status, physical activity, social support) associated with cognitive frailty in this population?

C (Comparator): How do the prevalence and associated factors compare within the COPD population (e.g., across different levels of disease severity) or against non-COPD controls if reported in included studies?

O (Outcomes): The primary outcomes are: 1) the prevalence rate of cognitive frailty, and 2) the identified factors significantly associated with cognitive frailty, reported as odds ratios, risk ratios, regression coefficients, or other appropriate measures of association.

Condition being studied This systematic review and meta-analysis focuses on **Cognitive Frailty** within the specific population of older adults diagnosed with **Chronic Obstructive Pulmonary Disease (COPD)**.

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable, and treatable persistent respiratory disease characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lungs to noxious particles or gases. Key symptoms include persistent breathlessness, chronic cough, sputum production, and exacerbations. It is a major cause of chronic morbidity and mortality worldwide, placing a significant burden on healthcare systems and severely impacting patients' quality of life.

Cognitive Frailty is a clinical syndrome characterized by the simultaneous presence of both physical frailty and mild cognitive impairment (MCI), where the cognitive impairment is not attributable to neurodegenerative diseases like Alzheimer's disease or other forms of dementia. Physical frailty is a state of increased vulnerability to stressors due to age-related declines in physiological reserves across multiple systems, often identified by phenotypes such as weakness, slowness, low physical activity, exhaustion, and unintentional weight loss.

The co-occurrence of these two conditions—COPD and Cognitive Frailty—in older adults is a critical geriatric concern. The systemic inflammation, hypoxemia, and physical deconditioning associated with COPD are hypothesized to accelerate both physical decline and cognitive impairment, creating a vicious cycle that worsens overall health outcomes. Studying cognitive frailty in this vulnerable population is essential for understanding its burden and for developing targeted interventions to break this cycle, improve functional independence, and enhance the quality of life.

METHODS

Participant or population Older adults (e.g., typically defined as aged 60 years or older) with a physician-diagnosed or clinically confirmed diagnosis of Chronic Obstructive Pulmonary Disease (COPD), based on established international criteria such as those from the Global Initiative for Chronic Obstructive Lung Disease (GOLD).

Intervention This item is not applicable to the proposed systematic review and meta-analysis.

Comparator This item is not applicable to the proposed systematic review and meta-analysis.

Study designs to be included **Observational studies, including cross-sectional, cohort, and case-control designs, that report the prevalence and/or associated factors of cognitive frailty in older adults with COPD.**

Eligibility criteria Studies that use validated operational criteria for both physical frailty (e.g., Fried phenotype, FRAIL scale) and cognitive impairment (e.g., MoCA, MMSE with established cut-offs) to define cognitive frailty.

Studies published in either English or Chinese.

Full-text articles available.

Exclusion Criteria:

Studies where the study population has a confirmed diagnosis of dementia (e.g., Alzheimer's disease, vascular dementia).

Conference abstracts, editorials, reviews, case reports, and non-peer-reviewed publications.

Studies with a sample size of fewer than 50 participants to ensure methodological robustness.

Information sources Electronic Databases:

English Databases: PubMed/MEDLINE, Embase, Web of Science Core Collection, Cochrane Central Register of Controlled Trials (CENTRAL), and PsycINFO.

Chinese Databases: China National Knowledge Infrastructure (CNKI), Wanfang Data, and VIP Chinese Science and Technology Periodical Database (CQVIP).

Grey Literature:

We will search for dissertations and theses via ProQuest Dissertations & Theses Global and the CNKI Outstanding Doctoral and Master's Theses Dissertations Database.

Clinical trial registries, including ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP), will be searched for ongoing or completed but unpublished studies.

Supplementary Searching:

The reference lists of all included studies and relevant systematic reviews will be manually screened to identify any additional eligible publications.

If necessary, corresponding authors of included studies will be contacted to inquire about unpublished or additional data.

Main outcome(s) Prevalence of Cognitive Frailty:

Description: The proportion of older adults with COPD who are identified as having cognitive frailty.

Effect Measure: The primary measure will be the pooled prevalence rate with a 95% confidence interval (CI). Data will be extracted as raw numbers (numerator and denominator) from each study.

Factors Associated with Cognitive Frailty:

Description: Demographic, clinical, psychosocial, and lifestyle factors that demonstrate a statistically significant association with cognitive frailty in the COPD population.

Effect Measures: The association will be quantified using effect measures reported in the included studies, such as:

Odds Ratio (OR) or Adjusted Odds Ratio (aOR)

Risk Ratio (RR)

Hazard Ratio (HR)

Regression Coefficients (β) along with their 95% CIs.

Quality assessment / Risk of bias analysis For cross-sectional studies, the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Analytical Cross-Sectional Studies will be used. It assesses key domains including sample representativeness, exposure and outcome measurement, confounding management, and statistical analysis.

For cohort studies, the JBI Critical Appraisal Checklist for Cohort Studies will be employed. It evaluates selection bias, exposure measurement, confounding identification and handling, outcome assessment, and adequacy of follow-up.

For case-control studies, the JBI Critical Appraisal Checklist for Case-Control Studies will be applied, focusing on the appropriateness of case and control definitions, comparability of groups, exposure measurement, and standard ascertainment of exposure for both groups.

Strategy of data synthesis Narrative Synthesis: A structured summary will be provided for all included studies, tabulating their characteristics, reported prevalence, identified factors, and risk of bias assessment.

Meta-Analysis (if feasible):

Prevalence: The pooled prevalence of cognitive frailty with a 95% confidence interval (CI) will be calculated using a random-effects model to account for anticipated heterogeneity. Prevalence estimates will be transformed using the Freeman-Tukey double arcsine transformation before pooling to stabilize variances.

Associated Factors: For factors reported in at least three studies, pooled effect estimates (e.g., Odds Ratios) with 95% CIs will be calculated using a random-effects model (e.g., the generic inverse variance method). If adjusted estimates are available, they will be prioritized.

Assessment of Heterogeneity: Statistical heterogeneity will be assessed using the I^2 statistic and Cochran's Q test. An I^2 value > 50% will be considered to represent substantial heterogeneity.

Subgroup and Sensitivity Analysis:

Subgroup analyses will explore sources of heterogeneity based on study design, geographical region, diagnostic criteria for frailty/cognition, and COPD severity.

Sensitivity analyses will be performed by excluding studies with a high risk of bias to test the robustness of the results.

Subgroup analysis Study Characteristics:

Study Design: Cross-sectional studies vs. cohort (baseline) studies.

Geographical Region: e.g., East Asia, Europe, North America, to explore geographical/cultural variations.

Methodological Factors:

Operational Definition of Frailty: Studies using the Fried Phenotype vs. other frailty scales (e.g., FRAIL scale, Clinical Frailty Scale).

Cognitive Assessment Tool: Studies using the Montreal Cognitive Assessment (MoCA) vs. Mini-Mental State Examination (MMSE) vs. other validated instruments.

Clinical and Population Factors:

COPD Severity: Based on GOLD grades (1-2 vs. 3-4) or GOLD groups (A-B vs. C-D).

Clinical Setting: Community-dwelling populations vs. outpatient clinics vs. hospitalized patients.

Age Group: Mean or median age below 75 years vs. 75 years and above.

Sensitivity analysis Risk of Bias: The primary analysis will be repeated after sequentially excluding studies judged to have a high overall risk of bias. This will evaluate whether the conclusions

are unduly influenced by methodologically weaker studies.

Statistical Model: The pooled estimates will be recalculated using a fixed-effect model and compared with the primary random-effects model results to check for significant discrepancies.

Analysis Method for Prevalence: For the prevalence meta-analysis, the results based on the Freeman-Tukey double arcsine transformation will be compared with those derived from alternative methods, such as the logit transformation, to ensure the findings are not dependent on the choice of statistical transformation.

Sample Size: The analysis will be repeated after excluding studies with a small sample size (e.g., n < 100) to determine if the overall effect is stable and not driven by smaller, potentially less precise studies.

Country(ies) involved China.

Keywords COPD cognitive frailty risk factors.

Contributions of each author
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