CHEST

Preserved Ratio Impaired Spirometry Prevalence, Risk Factors, and Outcomes

A Systematic Review and Meta-Analysis

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BACKGROUND: The prevalence of chronic respiratory diseases is increasing globally. There is evidence that those with spirometric impairment and no signs of obstruction (termed preserved ratio impaired spirometry [PRISm]) have an increased risk of morbidity and mortality compared with those with normal lung function. Several gaps remain in characterizing PRISm.

RESEARCH QUESTION: What are the prevalence, risk factors, and clinical outcomes associated with PRISm globally?

STUDY DESIGN AND METHODS: In this systematic review, a comprehensive search using MEDLINE, Web of Science, Cumulative Index to Nursing and Allied Health Literature, and Cochrane Central Register of Controlled Trials databases was conducted to include epidemiologic studies; there were no language or data restrictions. Two reviewers independently screened citations and shortlisted full-text articles according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, and data were extracted. Quality was assessed with the Effective Public Health Practice Project tool.

RESULTS: A total of 52 studies met the inclusion criteria, and 33 studies were included in the meta-analysis. Pooled PRISm prevalence was 12% (95% CI, 0.10-0.15) with greater prevalence in low- and middle-income countries (LMICs) compared with high-income countries (19% vs 11%). Comorbid diabetes was a significant risk factor associated with PRISm, but the data for female sex and smoking were mixed. PRISm was associated with increased all-cause (OR, 1.41; 95% CI, 1.08-1.83; $P = .02$), cardiovascular (OR, 1.84; 95% CI, 1.31-2.58; $P < .01$), and respiratory (OR, 1.82; 95% CI, 1.08-3.05; $P = .03$) mortality. PRISm was not associated with a reduced rate of lung cancer diagnosis ($P = .46$). Quality assessment analysis found that 34.6% (n = 18) of studies were rated "strong," 42.3% (n = 22) "moderate," and 23.1% (n = 12) "weak." Studies conducted in LMICs had lower quality ratings.

INTERPRETATION: Our findings show that individuals with PRISm have an increased risk of all-cause, cardiovascular, and respiratory mortality. Recognizing and targeting modifiable PRISm risk factors may reduce the growing burden of PRISm and transition to obstructive lung disease globally. Additional studies in LMICs are needed to assess unique exposures and disease trajectories relevant to these populations. CHEST 2025; 167(6):1591-1614

KEY WORDS: mortality; pre-COPD; preserved ratio impaired spirometry; prevalence; risk factors

ABBREVIATIONS: CRD = chronic respiratory disease; EPHPP = Effective Public Health Practice Project; HIC = high-income country; LMIC = low- and middle-income country; PRISm = preserved ratio impaired spirometry; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses

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Take-Home Points

Study Question: What are the prevalence, risk factors, and mortality associated with preserved ratio impaired spirometry (PRISm) globally?

Results: In this systematic review (N = 52) and meta-analysis of a subset of 33 studies, the pooled prevalence of PRISm was 12%, ranging from 4.5% to 45.7% globally, with a disproportionately higher prevalence in low- and middle-income countries. Significant risk factors associated with PRISm included older age and comorbid diabetes. PRISm was associated with increased mortality, with a 41% increase in odds of all-cause, 84% increase in cardiovascular, and 82% increase in respiratory mortality.

Interpretation: In this study, PRISm was associated with an increased risk of all-cause, cardiovascular, and respiratory mortality. Targeting modifiable risk factors of PRISm may reduce the growing burden of PRISm and transition to obstructive lung disease globally.

Chronic respiratory diseases (CRDs) are among the most common noncommunicable diseases and the third leading cause of death globally.[1-3] Despite the implementation of highly effective strategies to diagnose, treat, and manage CRDs, their prevalence continues to rise.[4] The primary cause of CRD deaths, COPD, is clinically diagnosed using spirometry and is defined as a reduction in the ratio of FEV_1 to FVC.[1] However, emerging evidence suggests that both functional abnormalities and substantial respiratory symptoms exist among those with impaired spirometry although they do not meet the criteria for COPD.[5-7] This population has incremental and proportional reductions in FEV_1 and FVC, which can lead to a normal FEV_1/FVC ratio despite underlying impairment of pulmonary function.[8]

Although the epidemiology of other CRDs, including COPD, are well studied, there are fewer data related to preserved ratio impaired spirometry (PRISm) globally. The reported prevalence of PRISm has a high degree of variability across settings.[6] Longitudinal studies surrounding PRISm have also identified female sex, tobacco use, truncal fat mass, and comorbid cardiovascular and respiratory conditions as risk factors.[5-7,9-13] However, these studies have produced conflicting risk factors varying by country and population. PRISm additionally has been associated with poor health outcomes, including increased rates of mortality, hospitalization, and dyspnea, and decreased health-related quality of life, lung function, and physical performance.[5-7,9-14] However, research is limited on PRISm, with few longitudinal studies because individuals with PRISm are often excluded from COPD-related research. A gap remains in characterizing the natural history and longitudinal progression of PRISm.

The objective of the current systematic review was to describe and quantify the prevalence, risk factors, and clinical outcomes of people with this newly defined clinical condition labeled PRISm based on the current published literature.

Study Design and Methods

The review was conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[15] The study selection criteria were guided by the Population, Intervention, Comparisons, Outcome and Study design framework.[16] Inclusion criteria for studies reporting individuals aged $>$ 18 years, clinical diagnosis of PRISm in any setting, and data related to prevalence, risk factors, and/or outcomes of PRISm are outlined in e-Table 1. The standard definition of PRISm was defined as $FEV_1 < 80\%$ predicted and an FEV_1/FVC ratio ≥ 0.7 on spirometry consistent with the Global Initiative for Chronic Obstructive Lung Disease guidelines.[8] Retrospective and prospective quantitative study designs were considered such as randomized controlled trials, cohort, case-control, cross-sectional, and quasi-experimental studies. For studies including participants diagnosed with COPD, data from participants with PRISm were extracted.

Search Strategy, Study Selection, and Data Extraction

A comprehensive search strategy was developed by using MEDLINE, Web of Science, Cumulative Index to Nursing and Allied Health Literature, and Cochrane

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Central Register of Controlled Trials databases to identify relevant studies; there were no language or data restrictions. MeSH and free text terms were developed and combined, including truncation commands (using root words to capture alternative word endings), proximity operators (for words within a chosen distance of each other), and Boolean logic operators (OR and AND) to ensure maximum yield. Titles and abstracts were searched with terms including "preserved ratio impaired spirometry, prevalence, incidence, proportion, rate, risk factor, tobacco use, smoking, BMI, physical activity, exercise, education, income, school, exacerbation, wheeze, dyspnea, sex, gender, female, male, women, men, race, ethnicity, underweight, overweight, obesity, comorbidity, hypertension, asthma, thyroid, renal, heart disease, kidney, chronic renal disease, diabetes, outcome, morbidity, mortality, lung function, quality of life, forced expiratory volume, EQ-5D, trajectory, pulmonary function, respiratory function, hospitalization, death, symptom, dyspnea, transition, exacerbation, progress, miss, work, or productivity." A full search strategy is provided in e-Table 2. Electronic searches were executed on January 31, 2024. Additional papers were located through hand-searching of citations and reference list tracking.

After exporting all electronic search results and deduplication, 2 reviewers (N. M. R. and C. S. C.) independently screened all the remaining titles and abstracts based on the eligibility criteria, and disagreements were resolved with discussion. Reviewers independently screened full-text articles for eligibility of inclusion into the review. Reasons for exclusion of the full-text studies after screening were noted. After identifying studies included for narrative review, reviewers identified a subset of studies to perform meta-analysis by removing studies reporting overlapping participants from cohort studies as described in Figure 1. Reviewers chose a single study for each cohort study with the greatest number of participants over the longest follow-up period to include in the meta-analysis. Relevant data were extracted from the full-text articles by using a piloted data extraction form. For studies that did not report data in the text or tables, estimates were extracted from graphs or calculated using the available data.

Quality Assessment

Quality assessment of all included studies was independently performed by 2 reviewers (N. M. R. and C. S. C.) using the Effective Public Health Practice Project tool (EPHPP) tool for all the quantitative studies (randomized controlled trials, quasi-experimental studies, and cross-sectional studies).[17,18] The EPHPP tool is used to evaluate selection bias, study design, control of confounders, blinding, data collection and methods, withdrawals and dropouts, intervention integrity, and analysis.[18] Cumulative assessment was reported as strong, moderate, or weak; this tool has performed better than other quality appraisal tools.[19]

Data Synthesis

Data were extracted from the included studies' demographic data and outcomes related to cause-specific mortality and lung cancer diagnosis. Among the subset of studies selected for meta-analysis, the weighted prevalence of PRISm was determined by calculating the crude frequency of PRISm in each study and as a pooled prevalence estimate of included studies per established methods in meta-analyses.[20] Additional stratification of PRISm prevalence was reported according to continent with associated heterogeneity evaluated by I^2 and P values.[21] Random-effects meta-analysis was conducted to estimate the pooled ORs associated with risk factors and mortality among individuals with PRISm compared with non-PRISm participants. Effect estimates to evaluate risk factor and mortality outcomes were log-transformed, and 95% CIs were used to calculate associated SEs. We assessed between-study heterogeneity with I^2 statistics consistent with standard meta-analysis methodology in prior studies.[22] High heterogeneity was considered if I^2 was $> 75\%$. When high levels of heterogeneity were found, subset analyses were performed to further investigate the influence of heterogeneity. Due to high levels of heterogeneity, we opted for a combined meta-analysis and narrative synthesis framework for the synthesis. Also evaluated was the influence of publication bias by using an Egger test and associated funnel plot.[23] We report 95% CIs and two-sided P values with .05 threshold for statistical significance.

All statistical analyses were conducted in R version 4.3.0 (R Foundation for Statistical Computing).

Results

A total of 195 records were initially identified. After elimination of 87 duplicate citations, 108 records remained. Both reviewers (N. M. R. and C. S. C.) screened the titles and abstracts and excluded 33 irrelevant records. Full texts of the remaining 75 papers

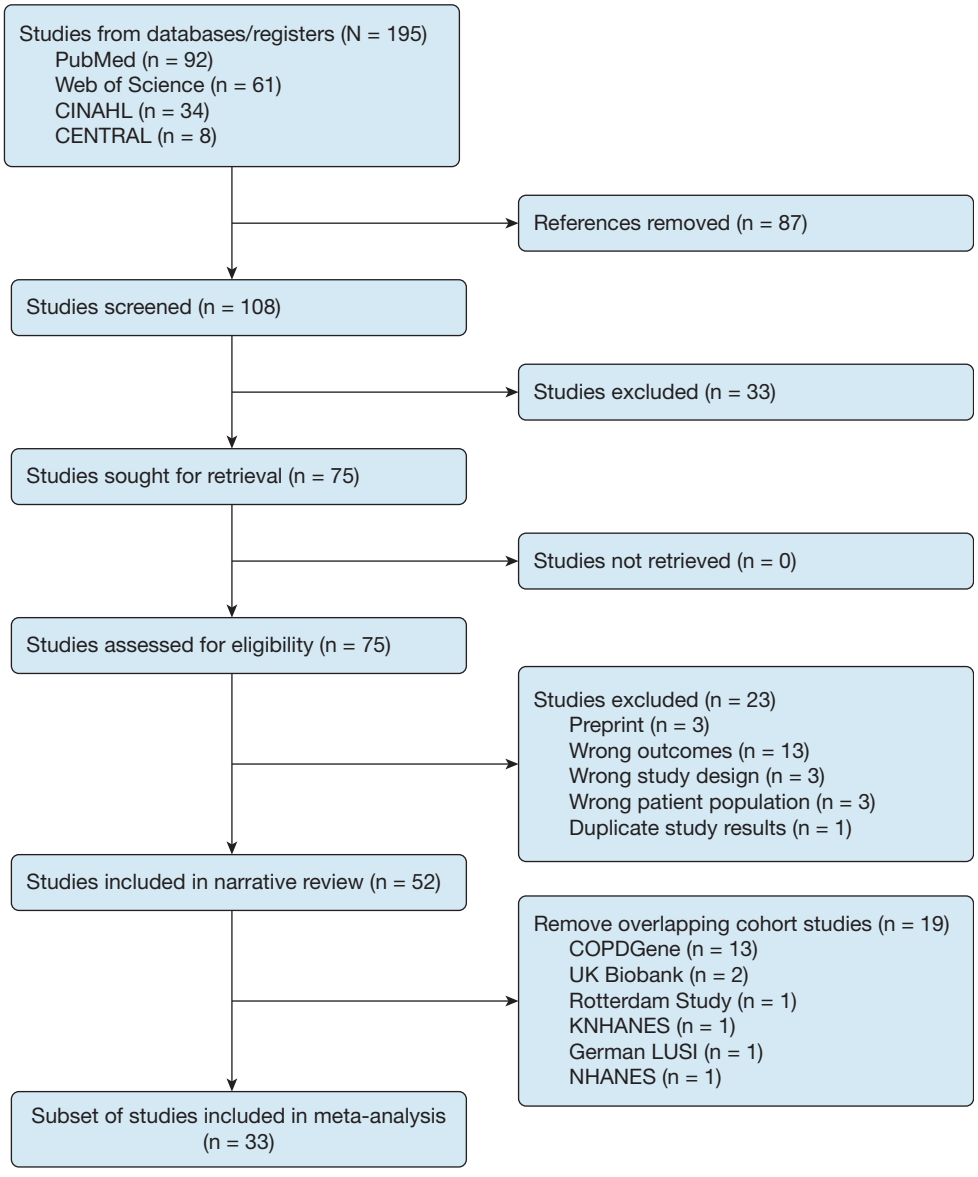

Figure 1 – *Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram detailing the systematic review search strategy and results. CENTRAL = Cochrane Central Register of Controlled Trials; CINAHL = Cumulative Index to Nursing and Allied Health Literature; COPDGene = Genetic Epidemiology of COPD; KNHANES = Korea National Health and Nutrition Examination Survey; LUSI = German Lung Cancer Screening Intervention Study; NHANES = National Health and Nutrition Examination Assessment.*

were evaluated for eligibility, of which 23 were excluded. Ultimately, 52 full-text studies met the inclusion criteria for narrative review, and a subset of 33 studies were identified for meta-analysis as reported in the PRISMA diagram in Figure 1.

Table 1[5,6,9-14,24-67] lists all studies included (N = 52) in this review along with key findings related to study characteristics and PRISm prevalence, risk factors, and outcomes and is stratified by study setting. Table 2 and e-Table 3 summarize the characteristics of all studies. Twenty studies were conducted in North America (Canada and United States),[5,6,10,13,51-59,61-66,68] 22 from Asia (China, India, Japan, and South Korea),[12,14,24-43] 9 from Europe (Denmark, Germany, the Netherlands, and the United Kingdom),[9,11,44-50] and 1 study was a multi-country study conducted in 4 South American countries (Brazil, Chile, Uruguay, and Venezuela) and North America (Mexico).[67]

The majority (86.5% [n = 45]) of included studies were conducted in high-income countries (HICs) compared with seven studies in low- and middle-income country (LMIC) settings. Included studies were published in

TABLE 1] Overview of Included Studies for Narrative Review Summarizing Key Study Characteristics, PRISm Prevalence, Risk Factors, and Outcomes Stratified By Study Continent Setting

Author, Year	Setting	Study Design	Study Dates	Study Population	Recruitment	PRISm Prevalence	Risk Factor	Outcome
Asia								
Park et al, 2018[24]	South Korea Mixed urban and rural	Cross-sectional study	2006-2012	≥ 40 y KNHANES and KNHANES-matched HIRA cohort data	Community members	11.7%	Not reported	Not reported
Heo et al, 2020[12]	South Korea Mixed urban and rural	Cross- sectional study	2008-2013	≥ 40 y KNHANES	Community members	11.5%	Not reported	Not reported
Anami et al, 2021[14]	Japan Mixed urban and rural	Cross- sectional study	2014-2019	≥ 60 y	Community members	12.0%	Hypertension, pulmonary disease, % FVC % predicted,[a] knee extension strength, sit-up test score, one-leg stance test[a]	Not reported
Heo et al, 2021[25]	South Korea Mixed urban and rural	Cohort study	2014-2015	... -KALC-R	Clinic patients	21.3%	Not reported	Non-small cell lung cancer survival, small cell lung cancer survival
Kaise et al, 2021[26]	Japan Urban	Cross-sectional study	September 2018-July 2019	40-70 y	Clinic patients	16.7%	Not reported	Not reported
Kim et al, 2021[27]	South Korea Mixed urban and rural	Cross-sectional study	2007-2015	≥ 50 y KNHANES	Community members	8.9%	Hypertension,[a] diabetes,[a] hypercholesterolemia,[a] obesity,[a] stroke, ischemic heart disease,[a] chronic renal disease,[a] thyroid disease,[a] chronic hepatitis, liver cirrhosis, anemia, rheumatoid arthritis, osteoarthritis, osteoporosis, depression, cancer	Not reported
Tamaki et al, 2021[28]	Japan Urban	Cross- sectional study	September 2018-July 2019	> 40 y OCEAN	Clinic patients	16.7%	Not reported	Not reported
Baidya et al, 2022[29]	India Urban	Cohort study	2014-2016	≥ 18 y	Clinic patients	45.7%	Age, female sex,[a] BMI < 18.5 kg/m^2,[a] tobacco use, past TB diagnosis, diabetes, CD4 level at HIV diagnosis, average CD4 count, ART duration at month 36, average viral load, high IL-6 level, elevated D-dimer, high IL-10 level,* high TNF-α levels, sCD163 level, sCD14 level, CRP	Not reported

(Continued)

TABLE 1] *(Continued)*

Author, Year	Setting	Study Design	Study Dates	Study Population	Recruitment	PRISm Prevalence	Risk Factor	Outcome
Ding et al, 2022[30]	China Urban	Cross-sectional study	October 2014-September 2017	> 40 y	Hospitalized patients	23.3%	Not reported	Not reported
Kanetake et al, 2022[31]	Japan Mixed urban and rural	Cohort study	Period 1: 2014-2016; Period 2: 2017-2019	…	Clinic patients	9.7%	Not reported	Progression from PRISm to COPD
Lu et al, 2022[32]	China Urban	Cohort study	February 2020-February 2021	…	Clinic patients	26.3%	Smoking,[a] inspiratory MLD,[a] lumen,[a] PRM^{SAD}[a]	Not reported
Ogata et al, 2022[33]	Japan Urban	Cohort study	June 2017-December 2021	> 40 y	Clinic patients	13.2%	Not reported	All-cause mortality
Shiraishi et al, 2022[34]	Japan Mixed urban and rural	Cross-sectional study	Not reported	≥ 40 y	Clinic patients	9.5%	PSE presence, CLE presence, increasing age,[a] male sex, BMI, > 20 pack-years of smoking, current smoking status	Not reported
Washio et al, 2022[35]	Japan Rural	Cohort study	2012-2017	≥ 40 y The Hisayama Study	Community members	9.9%	Not reported	All-cause mortality, cardiovascular mortality, cancer mortality, respiratory-related mortality, development of airflow limitation
Zhao et al, 2022[36]	China Urban	Cross-sectional study	July 2019-December 2020	40-80 y ECOPD cohort	Community members	8.8%	CT air trapping,[a] impulse oscillometry-defined small airway disease,[a] pre- and post-BD spirometry-defined small airways disease[a]	Not reported
Kogo et al, 2023[37]	Japan Mixed urban and rural	Cohort study	2008-2010 and follow-up 2013-2015	30-74 y Nagahama Study	Community members	4.5%	Any respiratory symptoms, mMRC ≥ 1,* mMRC ≥ 2,[a] cough, sputum production	Development of COPD
Miura et al, 2023[38]	Japan Urban	Cross- sectional study	2007-2015	35-65 y	Clinic patients	7.5%	Male sex,* increased age,* increased BMI,[a] ever smoking with > 10 pack-years of tobacco use,[a] asthma[a]	Development of airflow obstruction in 5 y
Shin et al, 2023[39]	South Korea Mixed urban and rural	Cohort study	2007-2012	≥ 40 y KNHANES	Hospital-based patients	9.7%	Not reported	Not reported

(Continued)

TABLE 1] *(Continued)*

Author, Year	Setting	Study Design	Study Dates	Study Population	Recruitment	PRISm Prevalence	Risk Factor	Outcome
Sin et al, 2023[40]	South Korea Mixed urban and rural	Cohort study	Recruit: 2001-2002; mortality data following	40-69 y KoGES Ansan and Ansung study	Community recruited by mail, letters, telephone, media, and community leaders	6.3%	Not reported	All-cause mortality, cardiovascular mortality
Zhang et al, 2023[41]	China Urban	Cohort study	May 2018-October 2018; May 2021-October 2021	40-75 y PIFCOPD	Community members	18.7%	OSA,[a] waist-to-hip ratio,[a] current smoking,[a] nasal allergy symptoms[a]	Not reported
Im et al, 2024[42]	South Korea Urban	Cohort study	2003-2020	≥ 40 y	Clinic patients	25.3%	Not reported	5-year rate of CAC progression
Zhang et al, 2024[43]	China Mixed urban and rural	Cross-sectional study	2005-2006	35-70 y	Community members	28.6%	Increased age,[a] male sex,[a] increased BMI,[a] family history of CVD,[a] secondary school completion, post-secondary school completion, diabetes, hypertension, hyperuricemia, FEV_1, FVC, PEF, FEV_1/FVC,[a] self-reported chest pain, self-reported breathlessness, total cholesterol, triglycerides, HDL-C, LDL-C	Not reported
Europe								
Wijnant et al, 2020[9]	Netherlands Urban	Cohort study	Phase 1: 2009-2014; Phase 2: 2014-2016 followed until December 30, 2018	≥ 45 y Rotterdam Study	Not reported	7.1%	Not reported	All-cause mortality, cardiovascular mortality
He et al, 2021[44]	United Kingdom Mixed urban and rural	Cohort study	2002-2013	> 50 y ELSA	At homes recruited households	20.3%	Not reported	All-cause mortality, respiratory mortality, and CVD mortality
Higbee et al, 2022[11]	United Kingdom Mixed urban and rural	Cohort study	2006-2010; 2014-2020	40-69 y UK Biobank	Clinic patients	10.9%	Age, female sex,[a] formerly smoked, currently smokes,[a] overweight,[a] obesity,[a] asthma,[a] stroke,[a] angina,[a] MI,[a] breathlessness[a]	Mortality
Kaaks et al, 2022[45]	Germany Urban	RCT	2007-2016	50-69 y LUSI study	Community members	15.7%	Not reported	Lung cancer diagnosis, all-cause mortality

(Continued)

TABLE 1] *(Continued)*

Author, Year	Setting	Study Design	Study Dates	Study Population	Recruitment	PRISm Prevalence	Risk Factor	Outcome
Xiao et al, 2022[46]	Netherlands Urban	Cohort study	2009-2016	≥ 45 y Rotterdam Study	Community members	6.3%	Not reported	Lacunar infarcts
Cortés-Ibáñez et al, 2023[47]	Germany Urban	RCT	2007-2016	50-69 y LUSI study	Community members, population registers	15.8%	GDF-15,[a] IL-6,[a] CRP, NT-proBNP	Not reported
Li et al, 2023[48]	United Kingdom Mixed urban and rural	Cohort study	2006-2010	37-73 y UK Biobank	Clinic patients	22.6%	Not reported	All-cause mortality, cardiovascular mortality respiratory mortality, MI, unstable angina, coronary heart disease, ischemic stroke, any stroke, diabetic retinopathy, diabetic kidney disease
Marott et al, 2023[49]	Denmark Urban	Cohort study	2003 with 15-year follow up	20-100 y Copenhagen General Population Study	Community members from general population registry	5.7%	Not reported	All-cause mortality, ischemic heart disease or heart failure morbidity, respiratory disease morbidity, cardiac mortality, respiratory mortality
Zheng et al, 2023[50]	United Kingdom Mixed urban and rural	Cohort study	2006-2010 and follow-up 2014-2020	40-69 y UK Biobank	Community members from health system service register	11.5%	Not reported	Major adverse cardiovascular event, MI, heart failure, stroke, CVD mortality, transition to airflow obstruction, transition to normal lung function

(Continued)

TABLE 1] *(Continued)*

Author, Year	Setting	Study Design	Study Dates	Study Population	Recruitment	PRISm Prevalence	Risk Factor	Outcome
North America								
Wan et al, 2014[5]	United States Mixed urban and rural	Cohort study	2007-2012, with 5-year follow-up	45-80 y COPDGene	Clinic patients	12.3%	Increased pack-years of tobacco use,[a] decreased resting oxygen saturation,[a] decreased 6-minute walk distance (per 100 feet),[a] increased mMRC dyspnea score,[a] decreased TLC %,[a] increased percent emphysema,[a] increased segmental wall area percent,[a] peripheral vascular disease,[a] physician diagnosed asthma,[a] diabetes,[a] African-American race,[a] higher BMI,[a] current tobacco use,[a] coronary artery disease comorbidity, increased age,[a] male sex, hyperlipidemia[a]	Not reported
Kinney et al, 2016[51]	United States Mixed urban and rural	Case-control study	2007-2012	45-80 y COPDGene	Clinic patients	...	Incident diabetes[a]	Not reported
Charokopos et al, 2021[52]	United States, multi-center Mixed urban and rural	RCT	2002-2007; followed for outcomes until December 31, 2009	55-74 y National Lung Cancer Screening Trial	Community members	18.3%	Not reported	Lung cancer diagnosis
Parekh et al, 2020[53]	United States Mixed urban and rural	Cohort study	2008-2011; follow-up 2012-2016 Vitals statistics until July 2017	45-80 y COPDGene	Clinical patients	21.0%	Not reported	Not reported
Pompe et al, 2020[54]	United States Mixed urban and rural	Cohort study	2008-2011; 5-year follow-up	45-80 y COPDGene	Clinic patients	11.9%	Not reported	Not reported
Strand et al, 2020[55]	United States Mixed urban and rural	Cohort study	2008-2011 with longitudinal follow-up	45-80 y COPDGene and SPIROMICS	Community members	12.1%	Not reported	Not reported
Pompe et al, 2021[56]	United States Mixed urban and rural	Cohort study	Not reported	45-80 y COPDGene	Clinic patients	9.9%	Not reported	Not reported

(Continued)

TABLE 1] *(Continued)*

Author, Year	Setting	Study Design	Study Dates	Study Population	Recruitment	PRISm Prevalence	Risk Factor	Outcome
Schwartz et al, 2021[6]	United States Rural	Cohort study	1997-2018	18-80 y	Clinic patients	24.3%	Young age,[a] male sex,[a] higher BMI,[a] White race, Hispanic race, higher pre-BD FEV_1,[a] TLC, RV/TLC ratio, active smoking,[a] referral to obstructive diagnosis,[a] referral to other diagnosis,[a] referral diagnosis to other respiratory symptoms,[a] referral diagnosis restrictive disease[a]	Not reported
Wan et al, 2021[13]	United States Mixed urban and rural	Cohort study	1971-2011 with intermittent breaks	18-84 y NHLBI pooled cohorts: SHS; MESA; JHS	Community members	8.5%	Female sex,[a] age 45-64 y,[a] age ≥ 65 y,[a] American Indian/Alaska Native race, Black race, East Asian/Pacific Islander race, Hispanic or Latino race, currently smokes,[a] formerly smoked,[a] higher pack-years of tobacco use,[a] BMI < 18.5 kg/m^2,[a] BMI 25-29.9 kg/m^2,[a] BMI > 30 kg/m^2,[a] less than high school education, high school graduation, some college completion, hypertension,[a] diabetes,[a] congestive heart failure,[a] coronary heart failure,[a] coronary heart disease,[a] stroke,[a] eGFR 30-59 mL/min/1.73m^2, eGFR < 30 mL/min/1.73m^2 (compared with ≥ 60)[a]	All-cause mortality, respiratory-related mortality, coronary heart disease-related mortality, respiratory-related events, coronary heart disease related events
Koo et al, 2022[57]	United States Mixed urban and rural	Cohort study	2008-2011; Phase 2: 2012-2016; data freeze March 2020	45-80 y COPDGene	Community members	12.0%	Not reported	Not reported
Macdonald et al, 2022[58]	United States Mixed urban and rural	Cohort study	2008-2011; Phase 2: 2012-2016 follow-up until March 2020	45-80 y COPDGene	Clinic patients	12.0%	Not reported	Any acute respiratory event, severe acute respiratory event

(Continued)

TABLE 1] *(Continued)*

Author, Year	Setting	Study Design	Study Dates	Study Population	Recruitment	PRISm Prevalence	Risk Factor	Outcome
Ragland et al, 2022[59]	United States Mixed urban and rural	Cohort study	2008-2011; with 5-10 year follow up	45-80 y COPDGene	Community members	12.4%	Not reported	Not reported
Strand et al, 2022[60]	United States Mixed urban and rural	Cohort study	2007-2012	45-80 y COPDGene	Community members	14.4%	Not reported	Not reported
Wan et al, 2022[10]	United States Mixed urban and rural	Cohort study	Phase 1: 2008-2011; Phase 2: 2012-2016; Phase 3: 2017-2022	45-80 y COPDGene	Community members	10.4%	Not reported	Predictor of significant transition in lung function
Chen et al, 2023[61]	United States Mixed urban and rural	Cross-sectional study	2007-2012	18-79 y NHANES	Community members	7.0%	Not reported	Not reported
Diaz et al, 2023[62]	United States Mixed urban and rural	Cohort study	Phase 1: 2007-2011; Phase 2: 2017-2021; outcomes until August 2022	45-80 y COPDGene	Clinic patients	12.9%	Not reported	10-year mortality
Krishnan et al, 2023[63]	Canada Urban	Cohort study	2005-2016; follow up 2009-2019	> 40 y CanCOLD	General population	6.1%	Not reported	CVD
Labaki et al, 2023[64]	United States Mixed urban and rural	Cohort study	Jan. 2009-June 2011; until 2020 for vital status	45-80 y	Community members	12.5%	Higher Pi10[a]	All-cause mortality
Li et al, 2023[65]	United States Mixed urban and rural	Cohort study	2007-2012	> 20 y NHANES	Community members	17.3%	Not reported	All-cause mortality, cardiovascular mortality
Tran et al, 2023[66]	United States Mixed urban and rural	Cohort study	2007-2012 with 5-year follow up	45-80 y COPDGene	Clinic patients	13.6%	Not reported	Diagnosis of obstructive lung disease at 5-year follow up

(Continued)

TABLE 1] *(Continued)*

Author, Year	Setting	Study Design	Study Dates	Study Population	Recruitment	PRISm Prevalence	Risk Factor	Outcome
South America								
Perez-Padilla et al, 2023[67]	Chile, Uruguay, Brazil, Mexico, Venezuela Urban	Cohort study	2002-2004 and follow up for 5-9 y	≥ 40 y PLATINO Study	Community members	5.0%	Not reported	Mortality, survival, exacerbations in the past year

ART = antiretroviral therapy; BD = bronchodilator; CAC = coronary artery calcification; CanCOLD = Canadian Cohort Obstructive Lung Disease; COPDGene = Genetic Epidemiology of COPD; CD4 = cluster of differentiation 4 (T-cell count in HIV); CLE = centrilobular emphysema; CRP = C-reactive protein; CVD = cardiovascular disease; ECOPD = Early Chronic Obstructive Pulmonary Disease Cohort; eGFR = estimated glomerular filtration rate; ELSA = English Longitudinal Study of Aging; GDF-15 = growth differentiation factor 15; HDL-C = high-density lipoprotein cholesterol; HIRA = Health Insurance Review and Assessment; JHS = Jackson Heart Study; KALC-R = Korean Association for Lung Cancer Registry; KNHANES = Korea National Health and Nutrition Examination Survey; KoGES = Korean Genome and Epidemiology Study; LDL-C = low-density lipoprotein cholesterol; LUSI = Lung Cancer Screening Intervention; MESA = Multi-Ethnic Study of Atherosclerosis; MI = myocardial infarction; MLD = mean lung density; mMRC = modified Medical Research Council; Nagahama Study = Nagahama Cohort for Comprehensive Human Bioscience; NHANES = National Health and Nutrition Examination Assessment; NHLBI = National Heart, Lung, and Blood Institute; NT-proBNP = N-terminal pro-B-type natriuretic peptide; OCEAN = Okinawa COPD Case Finding Assessment Study; PEF = peak expiratory flow; PIFCOPD = Predictive Value of Combining Inflammatory Biomarkers and Rapid Decline of FEV_1 for COPD; PLATINO = Proyecto LatinoAmericano de Investigación en Obstrucción Pulmonar (Latin-American Pulmonary Obstruction Investigation Project); PRISm = preserved ratio impaired spirometry; PRM^{SAD} = parametric response mapping small airway disease; PSE = parasepta emphysema; RCT = randomized controlled trial; RV/TLC = residual volume/total lung capacity; SHS = Strong Heart Study; SPIROMICS = Subpopulations and Intermediate Outcome Measures in COPD Study; TLC = total lung capacity; TNF-α = tumor necrosis factor-α.
[a]Significance at threshold is $P < .05$.

English from 2014 to 2023. Most studies described participants from mixed urban and rural settings (63.5% [n = 33 studies]) and recruited community members from non-health care settings (52.8% [n = 28]). Included studies were cohort (n = 36), cross-sectional (n = 12), randomized controlled trial (n = 3), and case-control (n = 1) study designs and primarily prospective in nature (n = 33). The majority of studies included participants aged 40 to 80 years; few studies included participants aged < 40 years[6,29,37,43,48,49,61,68] due to populations previously studied with risk factors related to obstructive lung disease.

PRISm Prevalence

In the meta-analysis (N = 33), PRISm prevalence ranged from 4.5% to 45.7% among included studies, and the pooled prevalence was 12% (95% CI, 0.10-0.15) with high heterogeneity ($I^2 = 100\%$; $\chi^2 = 0.46$; $P < .001$) (Fig 2). PRISm prevalence was higher in LMIC settings compared with HIC settings (19% vs 11%). In subgroup analysis per region, PRISm prevalence also varied by continent, with Asia having the highest prevalence at 14% (95% CI, 0.10-0.19). South America had the lowest PRISm prevalence at 5.0% (95% CI, 0.04-0.06), which consisted of 1 included study. The prevalence of PRISm in North America was 12% (95% CI, 0.07-0.18) and 10% (95% CI, 0.06-0.16) in Europe. PRISm prevalence was further stratified per study design, with PRISm prevalence 12% (95% CI, 0.8, 0.18) in cross-sectional studies, 12% (95% CI, 0.09, 0.16) in cohort studies, and 17% (95% CI, 0.08, 0.32) in randomized controlled trials (Fig 3).

Risk Factors

Included studies analyzed risk factors for PRISm related to sociodemographic factors, lung function, symptoms, comorbidities, biomarkers, and imaging findings.

The reported sociodemographic risk factors were sex, age, race, tobacco use, BMI, height, weight, income status, and educational attainment. Female sex had higher odds (OR, 1.22; 95% CI, 0.97-1.54; $P = .09$) of PRISm compared with male participants (e-Fig 1), but this was not statistically significant. However, the association between sex and PRISm varied by setting with statistical significance as a predictor of PRISm in North America ($P < .01$). On narrative review, increasing age was associated with significantly increasing odds of PRISm by 6% to 24% in 2 studies ($P < .01$).[38,43] However, a cohort study among rural US participants found that increasing age was associated

TABLE 2] Characteristics of Studies Included in Narrative Review

Characteristic	No. of Studies (N = 52)	Description
Publication year	NA	2014-2024
Study dates of included participants	NA	1971-2022
Income of country[a]		
Low- and middle-income	7 (13.5%)	NA
High income	45 (86.5%)	NA
Continent study setting[a]		
North America	20 (38.5%)	NA
South America	0	NA
Europe	9 (17.3%)	NA
Africa	0	NA
Asia	22 (42.3%)	NA
Multi-continent	1 (1.9%)	The multi-country study included 4 countries in South America and 1 country in North America
Rurality of study setting		
Urban	17 (32.7%)	NA
Rural	2 (3.8%)	NA
Mixed	33 (63.5%)	NA
Study design		
Cross-sectional	12 (23.1%)	NA
Case-control	1 (1.9%)	NA
Cohort	36 (69.2%)	NA
Randomized controlled trial	3 (5.8%)	NA
Timing of data collection		
Prospective	33 (63.5%)	NA
Retrospective	7 (13.5%)	NA
Not applicable (cross-sectional studies)	12 (23.1%)	NA
Sampling methods		
Healthcare Setting (ie, hospital, clinic)	23 (44.2%)	NA
Community members	28 (53.8%)	NA
Not reported	1 (1.9%)	NA
Cohort name (if applicable)		
CanCOLD	1 (1.9%)	NA
COPDGene	14 (26.9%)	NA
Copenhagen General Population Study	1 (1.9%)	NA
ECOPD	1 (1.9%)	NA
ELSA	1 (1.9%)	NA
German LUSI	2 (1.9%)	NA
Hisayama Study	1 (1.9%)	NA
KALC-R	1 (1.9%)	NA
KNHANES	2 (3.8%)	NA
KNHANES and HIRA (matched)	1 (1.9%)	NA
KoGES Ansan and Ansung study	1 (1.9%)	NA
Nagahama Study	1 (1.9%)	NA
NHANES	2 (3.8%)	NA

(Continued)

TABLE 2] *(Continued)*

Characteristic	No. of Studies (N = 52)	Description
NLST	1 (1.9%)	NA
OCEAN Study	1 (1.9%)	NA
PIFCOPD	1 (1.9%)	NA
PLATINO	1 (1.9%)	NA
Rotterdam Study	2 (3.8%)	NA
UK BioBank	3 (5.8%)	NA
SHS, MESA, and JHS pooled cohorts	1 (1.9%)	NA

CanCOLD = Canadian Cohort Obstructive Lung Disease; COPDGene = Genetic Epidemiology of COPD; ECOPD = Early Chronic Obstructive Pulmonary Disease Cohort; ELSA = English Longitudinal Study of Aging; HIRA = Health Insurance Review and Assessment; JHS = Jackson Heart Study; KALC-R = Korean Association for Lung Cancer Registry; KNHANES = Korea National Health and Nutrition Examination Survey; KoGES = Korean Genome and Epidemiology Study; LUSI = Lung Cancer Screening Intervention; MESA = Multi-Ethnic Study of Atherosclerosis; NA = not applicable; Nagahama Study = Nagahama Cohort for Comprehensive Human Bioscience; NHANES = National Health and Nutrition Examination Assessment; NLST = National Lung Cancer Screening Trial; OCEAN = Okinawa COPD Case Finding Assessment Study; PIFCOPD = Predictive Value of Combining Inflammatory Biomarkers and Rapid Decline of FEV_1 for COPD; PLATINO = Proyecto LatinoAmericano de Investigación en Obstrucción Pulmonar (Latin-American Pulmonary Obstruction Investigation Project); SHS = Strong Heart Study.

[a]Clinical sites income of country status was defined by the 2022 World Bank Country and Lending Groups (World Bank, 2022). Multi-country studies with multiple clinical sites that included at least 1 low- and middle-income country were classified in the low- and middle-income country category.

with decreased odds of PRISm (OR, 0.92; 95% CI, 0.88-0.97; $P = .03$)[6]; similarly, a study among people living with HIV in India similarly found that age was protective of PRISm (OR, 0.62; 95% CI, 0.44-0.88).[29] Among the 20 studies reporting ever tobacco use for participants with PRISm, ever smoking had no significant change in odds (OR, 1.30; 95% CI, 0.95-1.78; $P = .10$) of PRISm compared with participants who reported never smoking (e-Fig 2). Increasing BMI and weight were associated with increased odds of PRISm in 6 included studies.[5,6,10,11,38,43] However, an urban cohort study among people living with HIV receiving antiretroviral therapy in India found that BMI $\leq$ 18.5 kg/m^2 was associated with increased odds of PRISm (OR, 3.02; 95% CI, 1.06-8.57; $P = .03$).[29]

Studies related to PRISm explored comorbidities such as asthma, diabetes, hypertension, obesity, hyperlipidemia, coronary artery disease, heart failure, pulmonary TB, stroke, pulmonary vascular disease, chronic kidney disease, thyroid disease, liver disease, anemia, depression, cancer, and rheumatologic disease (Tables 1 and 2). Among 19 studies including data on comorbid diabetes and PRISm, comorbid diabetes had increased odds (OR, 1.73; 95% CI, 1.29-2.31; $P < .01$) of PRISm compared with participants without diabetes (e-Fig 3). Three studies reported an increased association of asthma with PRISm,[5,11,38] and similarly, hyperlipidemia, hypertension, and stroke were associated with increased odds of PRISm in 2 studies for each risk factor.[5,10,11,27] A number of studies reported symptoms related to PRISm, including dyspnea, wheezing, sputum production, and chest pain; these features were quantified by using the St. George's Respiratory Questionnaire and modified Medical Research Council dyspnea score. PRISm was associated with an increasing modified Medical Research Council dyspnea score in 2 studies.[5,37] Higbee et al[11] reported that those with PRISm had a 2-fold increase in breathlessness (OR, 2.0; 95% CI, 1.91-2.14; $P < .01$) compared with those without. Nasal allergy symptoms was similarly associated with PRISm in a study by Zhang et al.[41] PRISm was additionally associated with decreased oxygen saturation at rest and shorter 6-minute walk distance.[5] Few studies reported risk factors related to CT imaging findings such as percent emphysema and airway wall thickness Pi10. Likewise, few studies explored biomarkers, including C-reactive protein, tumor necrosis factor-α, IL-6, or IL-10, related to PRISm. Increasing levels of IL-6 and growth differentiation factor 15 were associated with PRISm ($P < .01$), as were decreasing levels of IL-10 (OR, 0.76; 95% CI, 0.59-0.99; $P = .04$).[29,47]

In a subgroup analysis, we further evaluated PRISm risk factors stratified according to continent. In North America, female sex had 1.41 increased odds of PRISm (OR, 1.41; 95% CI, 1.13-1.76) (e-Fig 4). However, in South America, Perez-Padilla et al[67] found that female sex was associated with 83% decreased odds of PRISm (OR, 0.17; 95% CI, 0.11-0.25). Even after stratifying tobacco use analysis by continent, tobacco use was not associated with statistically significant odds of PRISm in Asia, North America, and Europe; these results were limited by high heterogeneity, however (e-Fig 5). The association between comorbid diabetes and PRISm was consistent across continents, with Europe carrying the

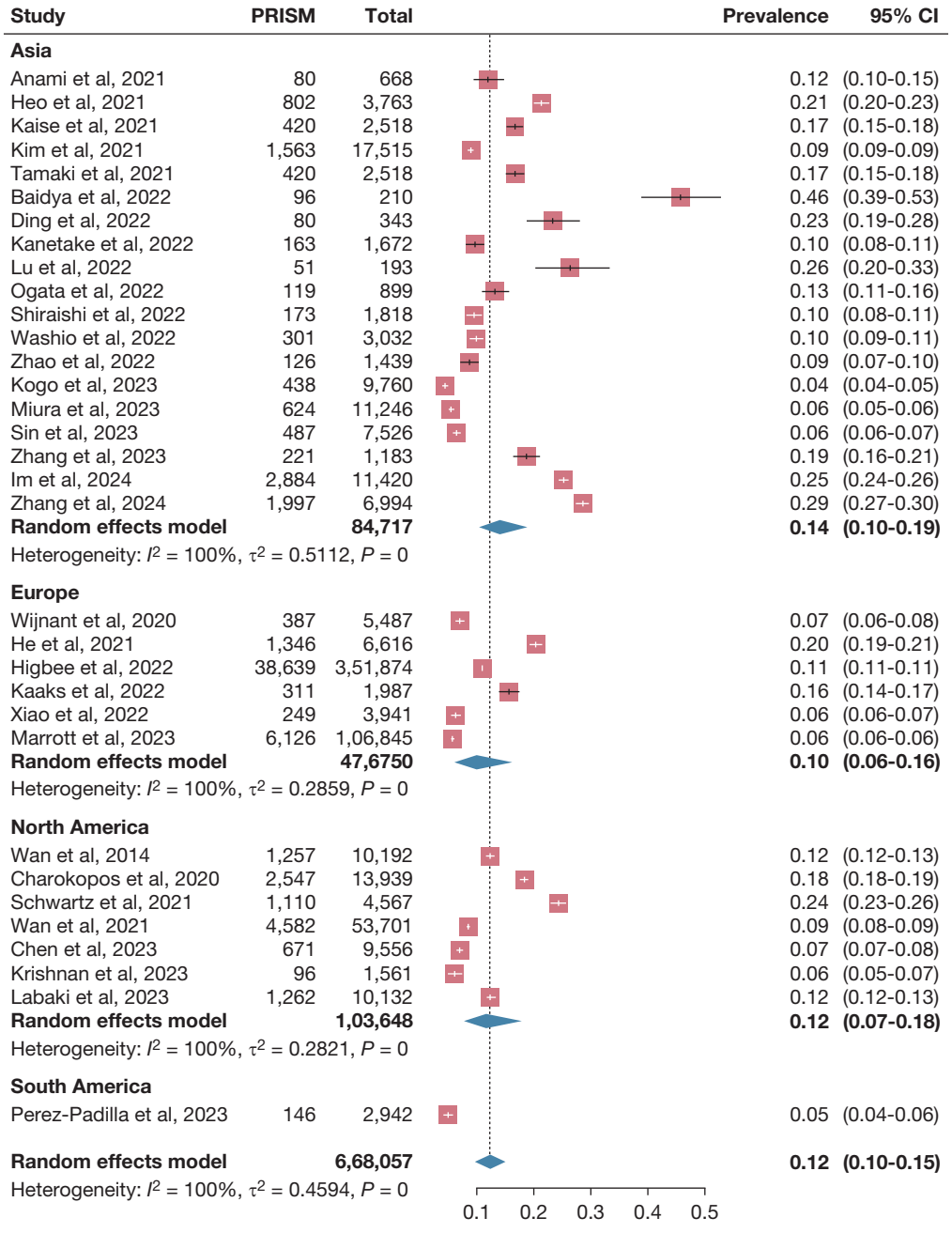

Figure 2 – *Forest plot of results for prevalence of PRISm in the global population stratified according to continent. PRISm = preserved ratio impaired spirometry.*

greater odds of PRISm (OR, 2.02; 95% CI, 1.37-2.99) compared with other regions (e-Fig 6).

Outcomes

The included studies reported outcomes related to mortality, respiratory function, transition to airflow obstruction, cardiovascular events, and comorbid diagnoses. PRISm mortality, including all-cause mortality, cardiovascular-related mortality, respiratory-related mortality, all-cancer mortality, and lung cancer mortality, were analyzed. PRISm was associated with increased odds (OR, 1.41; 95% CI, 1.08-1.83; $P = .02$) of all-cause mortality among 10 included studies (Fig 4). PRISm also was associated with increased odds of cardiovascular mortality (OR, 1.84; 95% CI, 1.31-2.58; $P < .01$) among 7 studies. PRISm carried 1.8 times increase in odds (OR, 1.82; 95% CI, 1.08-3.05; $P = .03$) of respiratory-related mortality among four studies.

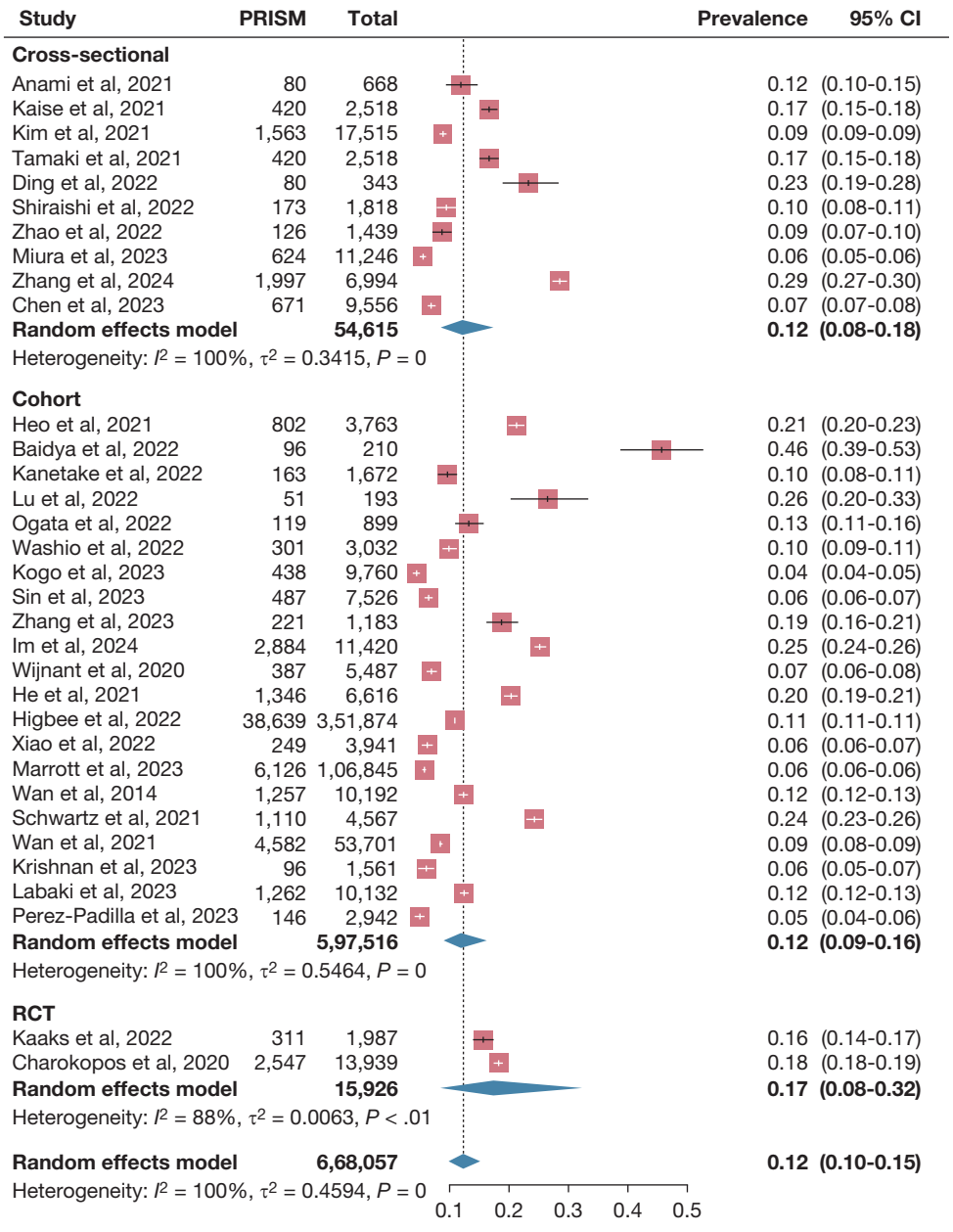

Figure 3 – *Forest plot of the PRISm prevalence stratified according to study design. PRISm = preserved ratio impaired spirometry. RCT = randomized controlled trial.*

Included studies analyzed respiratory outcomes, which were respiratory events, lung function, exacerbation frequency, and transition to airflow obstruction or COPD. These studies also explored lung cancer diagnosis, myocardial infarction, cardiovascular disease, stroke, lacunar infarcts, and diabetic-related disease as comorbidities. We found that PRISm was not significantly associated with a change in odds of lung cancer diagnosis (OR, 1.28; 95% CI, 0.39-4.19; $P = .46$) among 3 studies compared with the non-PRISm group (Fig 4). When stratifying the non-PRISm group into COPD and normal spirometry, the odds of lung cancer diagnosis changed. Compared with patients with COPD, PRISm was associated with lower odds of lung cancer diagnosis (OR, 0.86; 95% CI, 0.78-0.95; $P < .001$). In contrast, compared with patients with normal spirometry, PRISm was associated with higher odds of a lung cancer diagnosis (OR, 1.37; 95% CI, 1.24-1.50; $P < .001$).

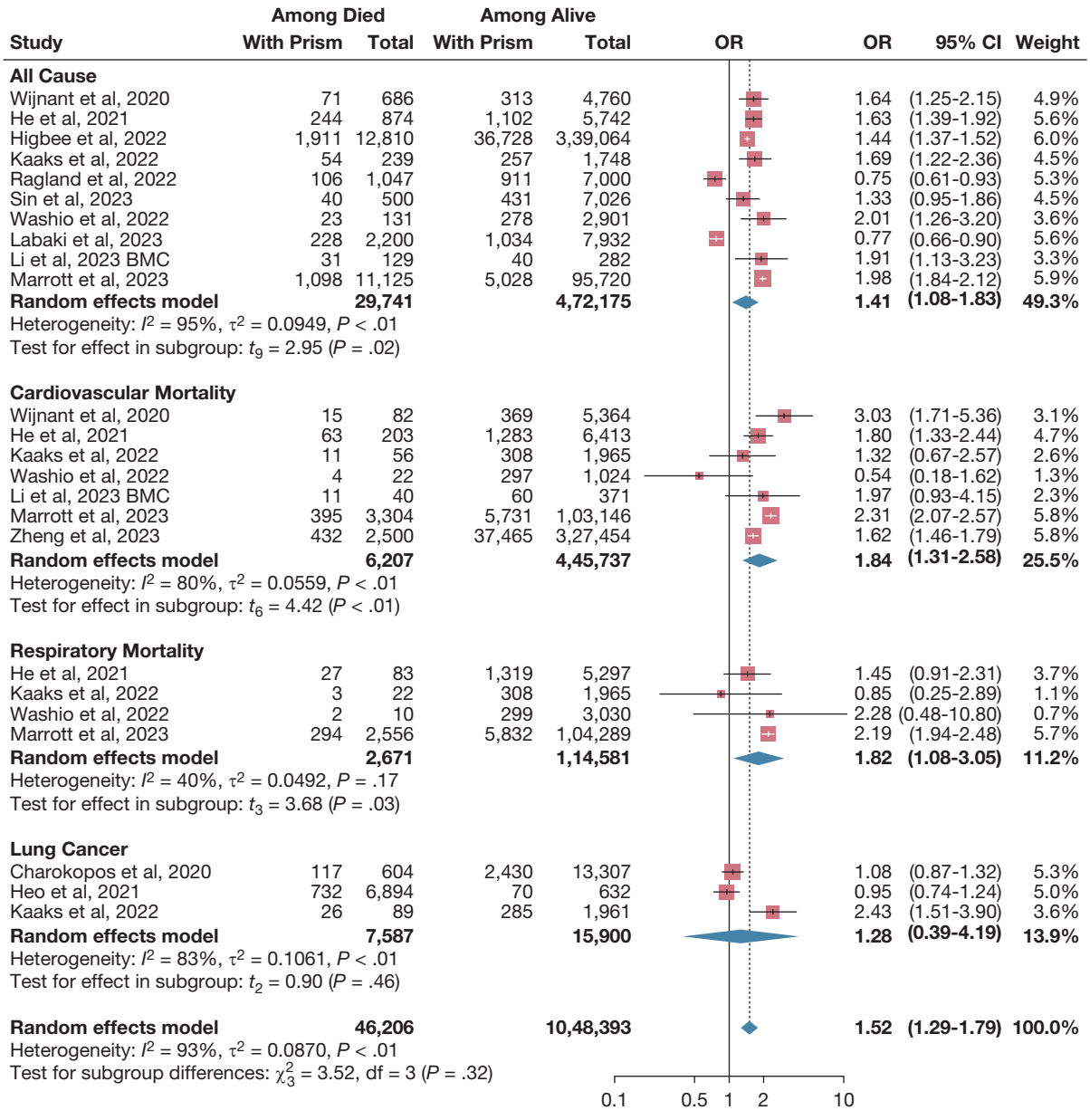

Figure 4 – *Forest plot of the association between PRISm and outcomes, including all-cause mortality, cardiovascular mortality, respiratory mortality, and lung cancer diagnosis outcomes among the included studies. PRISm = preserved ratio impaired spirometry.*

Quality Assessment: Among all studies (N = 52), we performed a quality assessment evaluation by using the EPHPP quality assessment tool. We found that 34.6% (n = 18) were rated "strong," 42.3% (n = 22) were rated "moderate," and 23.1% (n = 12) were rated "weak" (Figure 5).[5,6,9-14,24-66] The majority of studies were rated moderate quality study design due to a substantial portion of cross-sectional and cohort studies. Similarly, most were rated weak quality in the withdrawal and dropouts subcategory. Many included studies had moderate selection bias due to recruiting hospital and clinic-based participants with moderate participant uptake. Among included studies conducted in LMIC settings, most studies were rated weak to moderate for selection bias, and many studies were rated moderate study design. The global rating in LMIC-based included studies was moderate or weak.

We further assessed bias of PRISm prevalence and OR estimates through construction of funnel plots (e-Figs 7, 8). We found high precision with moderate bias, likely due to publication bias and heterogeneity (Egger test, t = 0.804; P = .428). The Egger test does not indicate the presence of funnel plot asymmetry.

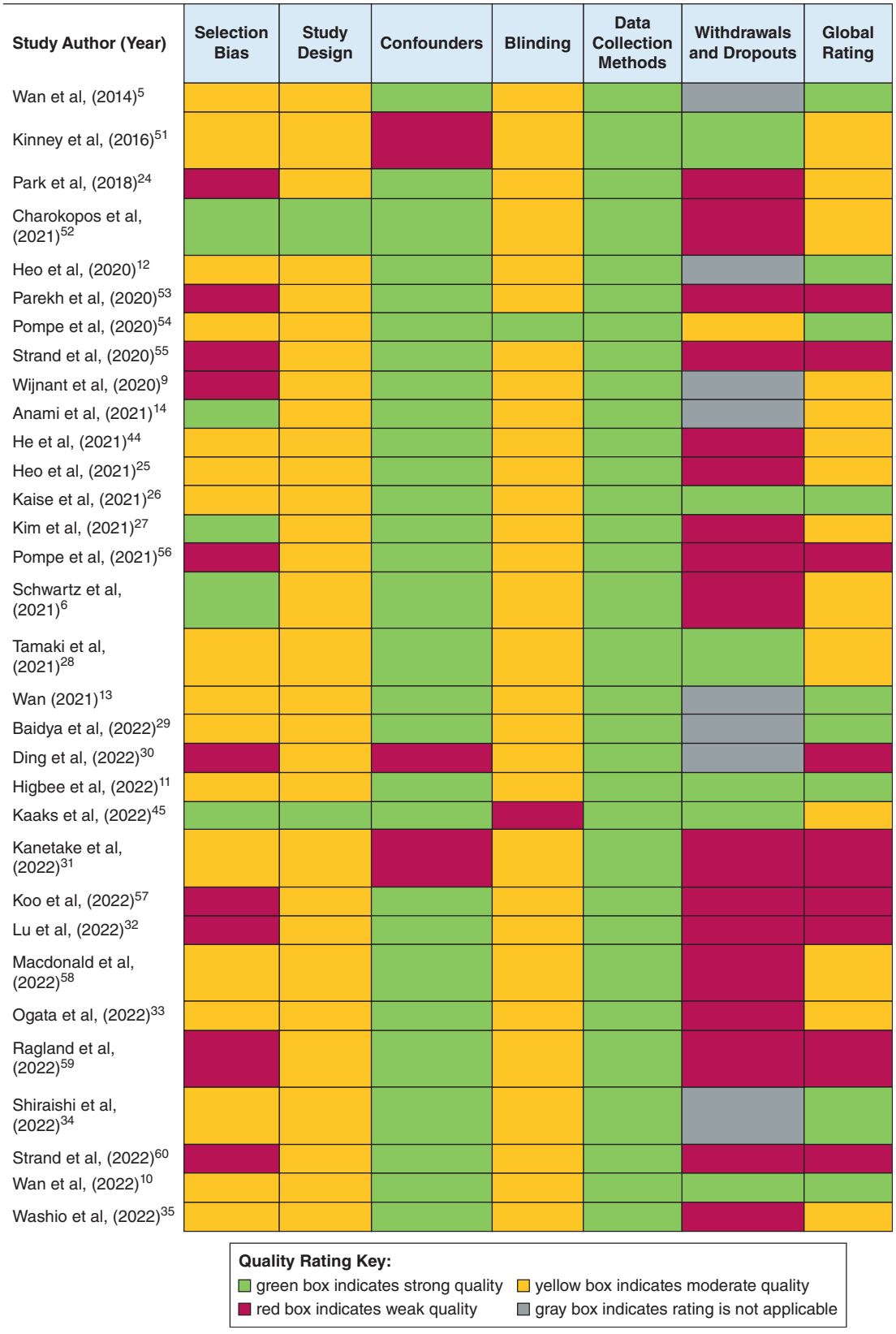

Figure 5 – *Quality assessment evaluation using the EPHPP quality assessment tool for quantitative studies (N = 52). EPHPP = Effective Public Health Practice Project.*

Figure 5 – *Continued*

Discussion

In this systematic review, we found a pooled 12% prevalence of PRISm, disproportionately affecting LMIC settings compared with HIC settings. A pooled analysis of 9 US general population cohorts by Wan et al[13] found a 8.5% prevalence of PRISm, but our findings point to a likely unrecognized higher global burden of PRISm. Of note, prevalence may fluctuate to some degree due to use of differing reference equations accompanied by varying cutoffs, influencing PRISm prevalence estimates. Moreover, prior research has shown that the prevalence of PRISm varies according to setting, race, and age.[7,69] Our results align with this finding, noting a higher prevalence of PRISm in LMICs rather than HICs. However, these results are limited because only 7 (13.5%) studies were conducted in LMICs, and these studies had varying quality. Differences in prevalence likely result from unique nonmodifiable risk factors, environmental exposures, health care resources, and behaviors specific to each population. For this reason, there have been continued calls to include cohorts in LMICs.[70] Therefore, diversifying global cohort studies to include underrepresented populations in research is needed to better understand and quantify the global burden of PRISm.

We found that sociodemographic risk factors, including older age, higher BMI, comorbid asthma, and comorbid diabetes, were risk factors associated with PRISm. Further research is needed to study the influence of sex and tobacco use on PRISm. Data surrounding the influence of age on PRISm prevalence have been mixed, varying by setting, exposure status, and subpopulations (ie, people living with HIV), which may be affected by

the known association of increasing age and COPD.[29,38,43] We found the association of PRISm with female sex to be weak and not significant ($P = .09$) in our meta-analysis, but prior literature has found variable associations between sex and PRISm in both HICs and LMICs.[13,71] The differing exposure to biomass, nutritional status, occupational status, or tobacco use may further contribute to sex differences in PRISm. However, these results should be interpreted with caution. In contrast, there was a moderate significant association of PRISm with comorbid diabetes ($P < .01$), which may be attributed to confounding with obesity.

As is evident in our findings, tobacco use may be marginally associated with increasing PRISm diagnosis, but more data are needed.[5,35,63] Specifically, in North America, there were 3 studies evaluating tobacco use as a PRISm risk factor, with high heterogeneity further highlighting the need for larger population-based studies. Although the pathophysiology surrounding tobacco use and PRISm is unknown, researchers speculate that individuals with PRISm may transition to COPD, asserting that PRISm is a step in the pathway to fixed airway obstruction.[72] Casaburi and Crapo[73] note, however, that the current body of research surrounding PRISm among nonsmokers is lacking, specifically the risk of PRISm progression to restriction or COPD. Understanding the implications of PRISm risk according to smoking status may further implicate trajectory and prognosis in terms of mortality. Additional longitudinal cohort studies including nonsmokers may increase understanding of the relationship between tobacco use and PRISm development.

Obesity may also negatively affect lung function through metabolic effects of increased adipose tissue or chest restriction due to central obesity.[74] Data surrounding the influence of non-cardiovascular and non-respiratory comorbid conditions on PRISm are limited. Moreover, further research is needed to understand how comorbid conditions, biomarker levels, education, and unique exposures such as biomass exposure and prior TB infection affect PRISm. Understanding these PRISm risk factors may influence preventative, diagnostic, and treatment approaches.

Published literature has established COPD as a predictor of mortality.[75] We found that PRISm was also associated with increased odds of all-cause, cardiovascular, and respiratory mortality. However, PRISm is not significantly associated with odds of lung cancer diagnosis compared with COPD but increased odds compared with normal spirometry. Similar findings were reported in a systematic review by Yang et al,[76] with increased risk of all-cause, cardiovascular disease, and respiratory-related mortality among eight included studies, likely due to systemic inflammation that has been associated with PRISm.[77]

The relatively high rates of tobacco use (≥ 15 pack-years), older age, a greater number of comorbid conditions, and surveillance may also influence higher mortality rates in these study populations. We expand on these data with more robust inclusion criteria and a data set updated to 2024. Also, the prior study excluded people living with HIV, an underrepresented population with an established higher risk of obstructive lung disease.[78] The association between PRISm and comorbid conditions such as obesity, diabetes, and asthma and exposures such as ever tobacco use may increase the risk of mortality in PRISm. Comorbid diabetes and increasing BMI have been linked to increased cardiovascular mortality, but the influence of PRISm on lung function and airway architecture impairment may further affect mortality. Likewise, the increased respiratory mortality associated with PRISm may be due to the lung function decline associated with PRISm trajectory and transition to COPD, which was reported among 23% of participants in the Rotterdam study.[9] In addition, a high proportion of tobacco use among the included participants may further increase mortality due to the known causal relationship between smoking and mortality; however, the relationship between lung cancer diagnosis and PRISm and etiology is not completely understood and requires further study. Further research is also needed to understand the impact of PRISm on outcomes, including quality of life measures and respiratory symptoms.

Quality assessment analysis revealed that the majority of studies were rated moderate quality due to a high frequency of cross-sectional and cohort studies. Quality rating was also negatively influenced by selection bias with clinically recruited participants. Studies in LMIC settings were weak to moderate in quality due to selection bias and study design. The limited representation of studies conducted in LMICs is due to multi-level health system barriers, spirometry access and under-utilization, and trained personnel; these factors may further disproportionately affect LMIC populations, where the largest proportion of burden of CRD exists.[2] This highlights a need for high-quality research studies, including cohort studies with general population sampling.

Strengths and Limitations

To our knowledge, this is the first systematic review examining risk factors and outcomes associated with PRISm globally. A strength of this systematic review is the robust methodology by searching multiple electronic databases and gray literature with no date or language restrictions and utilization of Cochrane methodology and PRISMA reporting guidelines to limit selection bias. Many included studies consisted of large community-based populations, increasing the generalizability of results.

A limitation of the current study includes the inability to perform a meta-analysis on a greater number of risk factors and outcomes related to PRISm due to high heterogeneity of results, study designs, and few studies reporting each variable. PRISm prevalence varied by study design due to high heterogeneity. In addition, the majority of studies were performed in HICs in North America and Europe rather than LMICs, where a substantial burden of CRDs exists. Furthermore, there were few published studies describing PRISm relative to the prevalence of the condition, likely due to increased likelihood of publishing positive rather than negative results (publication bias) and greater access to publication in HICs. Although many studies were secondary analyses of established cohorts, with 14 included studies from the Genetic Epidemiology of COPD (COPDGene) study, we minimized this bias by choosing the largest sample size and longest follow-up period of each cohort to include in the meta-analysis. This reduced over-representation of participants from the same cohorts. Further research is needed to analyze risk factors and outcomes of PRISm with prospective study designs and performance in LMIC settings.

Another limitation to this study was the availability of aggregate data rather than individual participant data in each study, limiting subgroup analysis by sex and various risk factors. For this reason, we report crude associations with PRISm. In addition, although a substantial portion of the studies were cohort studies, only 3 of the included studies were randomized controlled trials.

Interpretation

CRDs such as COPD have been robustly characterized globally. However, the body of literature surrounding PRISm is limited. PRISm has a rising global burden with reduced quality of life and increased mortality. Understanding risk factors of PRISm may allow clinicians to stratify patient populations by identifying higher risk characteristics and behaviors. We therefore suggest a comprehensive approach to evaluating high-risk patients with respiratory symptoms with spirometry, particularly in LMICs. Recognizing this undiagnosed population at risk for obstructive lung disease is vital in reducing the growing incidence of CRDs around the world. Additional high-quality studies are needed to further characterize prevalence, modifiable and nonmodifiable risk factors, and outcomes related to PRISm.

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