

# “What are my chances of developing COPD if one of my parents has the disease?” A systematic review and meta-analysis of prevalence of co-occurrence of COPD diagnosis in parents and offspring

Lok Sze Katrina Li<sup>1</sup>  
Catherine Paquet<sup>2</sup>  
Kylie Johnston<sup>1</sup>  
Marie T Williams<sup>3</sup>

<sup>1</sup>School of Health Sciences, Sansom Institute for Health Research, University of South Australia, Adelaide, South Australia, <sup>2</sup>Center for Population Health Research, Sansom Institute for Health Research, University of South Australia, Adelaide, South Australia, <sup>3</sup>Alliance for Research in Exercise, Nutrition and Activity (ARENA), Sansom Institute for Health Research, University of South Australia, Adelaide, South Australia, Australia

**Introduction:** Intergenerational associations in chronic obstructive pulmonary disease (COPD) have been well recognized and may result from genetic, gene environment, or exposure to life course factors. Consequently, adult offspring of parents with COPD may be at a greater risk of developing COPD. The aim of this study was to review the prevalence of co-occurrence of COPD in adult offspring with one or both parents having COPD independent of specific genetic variations.

**Methods:** In total, five databases were searched for original studies in which prevalence of COPD was reported in both offspring (children) and one or both parents. Studies were excluded if COPD was not clearly defined, COPD was linked to specific genetic variations, COPD was combined with other chronic respiratory conditions, or estimates included other first-degree relatives. Data extraction (ie, sample characteristics, prevalence of COPD, and odds ratio [OR] if reported) was completed by two independent reviewers. A meta-analysis of prevalence and OR was conducted, where possible.

**Results:** Of the 3,382 citations, 129 full texts were reviewed to include eight studies (six case-control, one cross-sectional, and one cohort) reflecting either prevalence of COPD in offspring of parents with COPD (descendent approach, n=3), which ranged from 0% to 17.3%, or prevalence of people with COPD reporting positive parental history of COPD (antecedent approach, n=5), for which the pooled prevalence was 28.6%. Offspring of people with COPD had 1.57 times greater odds (95% confidence interval = 1.29–1.93;  $P < 0.001$ ) of having COPD compared with people not having a parental history of COPD.

**Conclusion:** The prevalence of COPD in adult offspring of people with COPD is greater than population-based estimates, and the ORs indicate a higher risk in this group. This offers clinicians a potential strategy for opportunistic screening, early identification, and intervention in this at-risk group.

**Keywords:** COPD, intergenerational, prevalence, systematic review

Correspondence: Lok Sze Katrina Li  
School of Health Sciences, Sansom Institute for Health Research, University of South Australia, GPO Box 2471, Adelaide, 5000, South Australia, Australia  
Tel +61 8 830 21284  
Email lok\_sze\_katrina.li@mymail.unisa.edu.au

## Introduction

Chronic obstructive pulmonary disease (COPD) is a common condition and is estimated to become the third leading cause of death by 2030.<sup>1,2</sup> Globally, the prevalence of COPD has been estimated to be between 9% and 10%.<sup>3</sup> Although COPD is a progressive disease, early intervention strategies such as optimizing medication,

exercise, and pulmonary rehabilitation have been shown to reduce the rate of disease progression and improve symptom control in people diagnosed with COPD.<sup>4–8</sup> The high prevalence of undiagnosed COPD has been reported internationally.<sup>9,10</sup> Underdiagnosis of COPD is problematic as symptoms of COPD may hinder an individual's daily activities.<sup>11,12</sup> Generalized population level screening for COPD is controversial and, currently, is not recommended for asymptomatic individuals as it is unclear whether early detection improves clinical outcomes.<sup>13</sup> Individuals may, however, present asymptomatic because of modification in activities that trigger symptoms.<sup>14</sup> Targeted case findings in the community and in primary care commonly focus on people with recognized COPD risk factors or exposures such as smokers and consider them as an at-risk population.<sup>15,16</sup>

Although cigarette smoking is a key risk factor for COPD development, not all COPD cases can be explained by smoking.<sup>17</sup> Lifetime exposure to smoke or pollution has been shown to increase a person's risk of developing COPD.<sup>18,19</sup> In addition, early life factors such as low birth weight, prematurity, nutrition, childhood respiratory illness, and exposure to passive smoking are associated with reduced lung function in later life.<sup>20–24</sup>

Familial or intergenerational associations for chronic respiratory disease have been observed with an increased risk of chronic bronchitis in people with family members having bronchitis.<sup>25,26</sup> Strong familial associations have been reported for increased respiratory symptoms or conditions including wheezing, asthma, and lung cancer among twins and individuals living in the same household.<sup>23,27–29</sup> Currently, although alpha-1-antitrypsin deficiency is the only robustly defined inherited form of COPD that can explain familial aggregation of COPD,<sup>30</sup> <3% of people with COPD have this deficiency.<sup>31</sup> Intergenerational associations overlap with the risk factors associated with the development of COPD, including smoking behavior of parents and offspring, educational achievement, lung function, and conditions or diseases such as asthma and lung cancer.<sup>29,32–35</sup> Concepts, knowledge, and behaviors about health can be transmitted from one generation to the next.<sup>36</sup> Thus, offspring of people with COPD are considered as an at-risk group for the development of COPD, as they may be exposed to a greater number of these intergenerational factors that could trigger or have a cumulative effect that shapes the trajectory of lung health.<sup>37</sup>

Apart from studies that focus on associations between genetic forms of COPD, specific genes, and lung function in families,<sup>38,39</sup> there seem to be little direct data concerning

the likelihood or specific risk of COPD in offspring of parents with COPD. The odds of having COPD have been shown to be 1.7–2.7 times higher in people with family history of COPD (all first-degree relatives included) than in those without family history.<sup>40,41</sup> Adult offspring of people with COPD might present with a different risk profile as they are more likely to cohabitate during formative early life periods. It is hypothesized that offspring of people with COPD through exposure to intergenerational and life course factors will have higher rates or an increased risk of COPD compared with people without a parental history of COPD. The overall aim of this systematic review was to collate the reported evidence for co-occurrence and risk of COPD, especially in adult offspring with one or both parents having COPD independent of specific genetic variations.

The following were the two objectives of this review:

1. To report the prevalence of COPD in offspring of people with COPD and/or prevalence of a positive parental history of COPD in people with COPD.
2. To report the strength of the association between parental and offspring COPD status.

## Methods

This review was designed and reported according to the recommendations in the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines, and the protocol was registered (PROSPERO no: CRD42015025228).<sup>42</sup>

## Study selection

Electronic databases (ie, Medline, CINAHL, EMBASE, SCOPUS, and Cochrane Library) were systematically searched from inception to mid-September 2015. Search terms (Table 1) were adapted from previous systematic reviews on COPD and the effects of family history.<sup>5,8,23,29</sup> Two researchers independently performed the systematic search

**Table 1** Search strategy

Databases	Search terms
Medline	"COPD" OR exp "pulmonary disease, chronic obstructive" OR "emphysema" OR "chronic bronchitis" OR "obstructive lung disease" OR
EMBASE	"chronic obstructive pulmonary disease" OR "COAD" AND
CINAHL	"familial aggregation" OR "familial risk" OR "familial transmission" OR "heredity" OR "adult child" OR
SCOPUS	"intergenerational" OR "inheritance" OR "family adj3 history" OR "parental adj3 COPD" OR "adult child" OR
Cochrane library	OR "adult son" OR "adult daughter" OR "offspring"

following a prospectively planned search protocol that was developed with the aid of an academic librarian.

## Inclusion and exclusion criteria

Studies were included if data were reported or could be inferred for the prevalence of COPD, chronic bronchitis, and/or emphysema (through self-report, physician-diagnosed, spirometry-diagnosed, or symptom profile) in parents and adult offspring of people with COPD. No year or language limits were set for inclusion of studies in this review.

Studies were excluded: 1) if they did not define family history or specifically report offspring/parents within first-degree relative groups (due to possible inclusions of other family members such as siblings); 2) if they reported specific lung function parameters without a COPD classification definition; 3) if COPD, emphysema, or chronic bronchitis was combined with other respiratory conditions; 4) if data were limited to familial investigation of known genetic variations in COPD (alpha-1-antitrypsin deficiency); and 5) if studies were on participants from specific occupations/living environment (eg, coal miners, coke oven workers, and living close to asbestos factory).

## Screening of studies

Two reviewers independently screened the titles and abstracts of citations returned from searches. Full texts of studies were reviewed by two independent reviewers for inclusion or exclusion. Reasons for excluding the studies were recorded, and discrepancies were discussed until consensus was reached. Reference lists of relevant articles were searched, and citation tracking was performed to retrieve any potential additional citations.

## Data extraction and appraisal of methodological bias

By using a predetermined template (Table S1), two reviewers independently extracted data from the included studies with disagreements resolved by consensus. A ten-item methodological appraisal checklist for studies reporting prevalence data was used.<sup>43</sup> Interpretations specific to the review questions (Table S2) were used by two independent reviewers; when consensus was not reached, then a third reviewer was consulted. No studies were excluded on the basis of the methodological bias.

## Data analysis

Study design, participant characteristics, and the method of COPD diagnosis were descriptively reported. Studies were

collated and analyzed separately: 1) studies that considered people with confirmed COPD and the prevalence of COPD in their offspring (descendent approach); and 2) studies that considered prevalence of positive parental history of COPD in people with confirmed COPD (antecedent approach). If odds ratios (ORs) were not reported in the study but sufficient data were provided, then the ORs were calculated. The prevalence and ORs were compiled from the reported statistics or calculated when sufficient information was provided, the pooled prevalence and OR were calculated, and forest plots were created by using MedCalc for Windows, Version 15.11.4 (MedCalc Software, Ostend, Belgium).  $I^2$  statistics were used to assess the heterogeneity of the studies. The random-effects model was used due to the high level of heterogeneity between the studies.

## Results

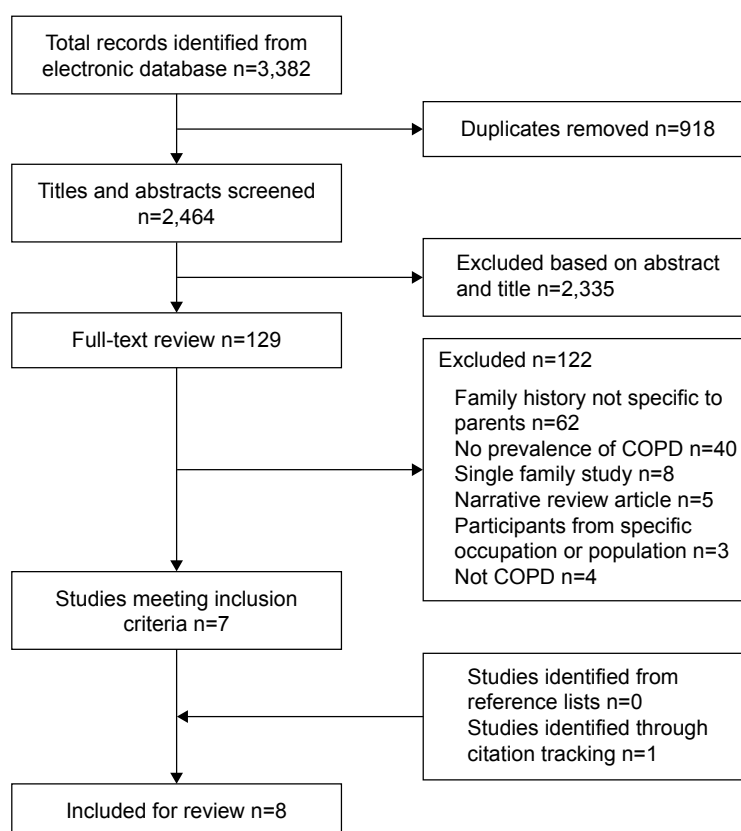
### Search results

One hundred and twenty-nine full-text articles were reviewed (including 18 non-English articles; Figure 1). Studies were excluded for two main reasons: first (51% of the excluded studies), despite reporting data for family history of COPD in people with COPD, studies either did not define family history as a parental history<sup>44,45</sup> or reported a pooled analysis of family history that included various combinations of siblings, parents, offspring, and first-degree relatives.<sup>46,47</sup> Second (33% of the excluded), studies reported on the prevalence of respiratory problems/symptoms or on measures of lung function in offspring of people with COPD without a reference to a COPD classification.<sup>48–50</sup>

Seven studies were included after full-text review, and one additional study was identified through citation tracking, resulting in a total of eight studies eligible for inclusion in this review.

### Study characteristics

All the included studies were observational in design. Of the eight studies, three studies reported on the prevalence of COPD in offspring of people with COPD (descendent approach, Table 2), with a total of 204 cases and 161 controls in two case-control studies and 5,054 participants in a cross-sectional study,<sup>51–53</sup> and five studies reported on the prevalence of a parental history of COPD in people with COPD (antecedent approach, Table 3), with 1,545 cases and 1,995 controls in four case-control studies and 80,214 participants in a cohort study.<sup>54–58</sup> None of the studies included in this review were primarily designed as prevalence studies, and all the studies included had a variable risk of bias when appraised using the prevalence appraisal checklist (Table S2).<sup>43</sup>



**Figure 1** Flow chart for identification of studies.

**Abbreviation:** COPD, chronic obstructive pulmonary disease.

**Table 2** Summary of studies reporting on COPD prevalence in offspring of people with COPD (descendent approach)

	Higgins and Keller, <sup>53</sup> 1975	Khoury et al, <sup>51</sup> 1985	Amra et al, <sup>52</sup> 2015
Country of data collection	US	US	Iran
Study design	Cross-sectional	Case-control	Case-control
Total number of index cases	5,054 <sup>a</sup>	150 cases, 107 controls	54 cases, 54 controls
Case/control cohort	Residents of Tecumseh between 1962 and 1965	Cases: COPD Control: nonpulmonary patient	Cases: offspring of people with severe COPD Controls: matched in age, sex, and height
Demographics of parents	Not reported	Not reported	Not reported
Diagnosis of parents	Chronic bronchitis (symptoms)	COPD (medical records)	COPD (medical records)
COPD severity of parents	Not reported	Not reported	Severe (based on GOLD)
Demographics of offspring (COPD)	50.3% male Male, age (years): <16, n=1,779; age =16–39, n=660; age =40+, n=105 Female, age (years): <16, n=1,779; age =16–39, n=621; age =40+, n=110	Offspring of COPD parents 44.8% male Mean age =27.4 years	Offspring of COPD parents 65.8% male Mean age =34.3 years
Diagnosis of offspring	Chronic bronchitis (symptoms)	Chronic bronchitis (symptoms) Airway obstruction <sup>b</sup>	Abnormal pulmonary function <sup>c</sup>
Prevalence of COPD in offspring of people with COPD	Male: 17.3% (16–39 years); 16.7% (40+ years) Female: 6.6% (16–39 years); 8.3% (40+ years)	14.9% (with chronic bronchitis) 6% (with airway obstruction)	0%
Severity of offspring OR	Not reported Number of offspring in each age category with parental history and OR not reported (unable to calculate OR)	Not reported OR =2.1 (reported chronic bronchitis) OR =6.4 (reported airway obstruction)	Not applicable Number of parents in matched offspring control group and OR not reported (unable to calculate OR)

**Notes:** <sup>a</sup>Original study had 9,226 subjects in total, there were 5,054 offspring participants with one or more parent assessed; <sup>b</sup>FEV<sub>1</sub> <68% of FVC; <sup>c</sup>FEV<sub>1</sub>/FVC <0.7.

**Abbreviations:** COPD, chronic obstructive pulmonary disease; FEV<sub>1</sub>, forced expiratory volume in 1 s; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; OR, odds ratio.

**Table 3** Summary of studies reporting prevalence of parental history of COPD in people with COPD (antecedent approach)

	<b>Mostovoï,<sup>54</sup> 1987</b>	<b>Silverman et al,<sup>55</sup> 1998</b>	<b>McCloskey et al,<sup>56</sup> 2001</b>	<b>Hersh et al,<sup>57</sup> 2011</b>	<b>Zöller et al,<sup>58</sup> 2015</b>
Country of data collection	Ukraine	US	UK	US	Sweden
Study design	Case-control	Case-control	Case-control	Case-control	Cohort study
Total number of index cases	530 cases, 760 controls	44 cases, 20 controls	150 cases, 439 controls	821 cases, 776 controls	80,214
Case/control cohort	Case: chronic bronchitis Control: healthy persons	Case: severe early onset COPD Control: current or ex-smokers	Case: severe COPD Control: matched for age, sex, and smoking	Case: COPD GOLD Stage II or higher Control: smokers	Cohort: Swedish-born adoptees born between 1932 and 2004
Demographics of parents	Not reported	Not reported	Parents who underwent spirometry 23.7% male Mean age: 75.9±9.8 years	Not reported	Not reported
Diagnosis of parents	Chronic bronchitis (self-reported by offspring)	Chronic bronchitis, emphysema or COPD (self-reported by offspring)	COPD (spirometry and self-reported by offspring)	COPD (self-reported by offspring)	COPD (medical records) ICD7-10 codes
COPD Severity of parents	Not reported	Not reported	Not reported	Not reported	Not reported
Demographics of offspring (COPD)	Not reported	20.4% male Mean age: 47.2±5.6 years; Mean pack-years: 38.8±22.5	46% male Mean age: 52.3±6.9 years	51.8% male Mean age: 64.2±8.4 years, Mean pack-years: 53.2±26.3	49.8% male in total population 43% male with COPD events
Diagnosis of offspring	Chronic bronchitis (Chest x-ray, clinical information)	COPD (spirometry)	COPD (spirometry GOLD)	COPD (spirometry GOLD)	COPD (medical records) ICD7-10 codes
Prevalence of positive parental COPD history in people with COPD	14.5%	58%	44% (spirometry performed on living parents n=38) (self-reported) Male offspring: mother with COPD 32%; father with COPD 37%; Female offspring: mother with COPD 29%; father with COPD 33%	43%	14.3% (biological parents) 11.7% (adoptive parents)
Severity of offspring	Not reported	Severe	Severe	GOLD Stage II or higher	Not reported
Odds ratio	OR =1.95 (crude calculated)	OR =7.9 (95% CI =2.0–30.9) (reported; unadjusted)	No control group for parents, unable to calculate OR	OR =1.69 (crude, calculated) OR =1.68 (95% CI =1.32–2.13; fully adjusted <sup>a</sup> )	OR =1.41 (crude calculated, biological parents) OR =1.21 (crude calculated, adoptive parents)

**Note:** <sup>a</sup>Includes demographic covariates, parental history of COPD, parental history of smoking, and childhood environmental tobacco smoke exposure.

**Abbreviations:** CI, confidence interval; COPD, chronic obstructive pulmonary disease; ICD, International Statistical Classification of Diseases and Related Health Problems; GOLD, Global Initiative for Chronic Obstructive Lung Disease; OR, odds ratio.

## Prevalence

The prevalence of COPD in offspring of one or more parents with a diagnosis of COPD ranged from 0% to 17.3% in studies that used a descendent approach (Table 2). Studies that used the antecedent approach reported prevalence estimates ranging from 11.7% to 58% in people with COPD with a parental history of COPD (Table 3).

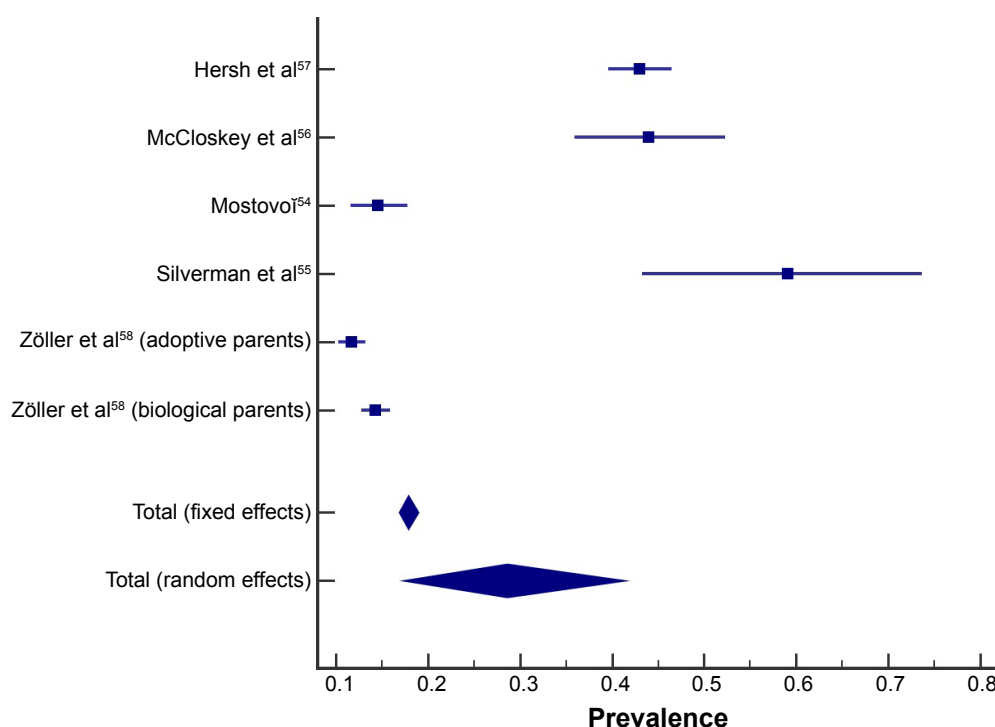
## Pooled prevalence estimate

A pooled prevalence of COPD in offspring of people with COPD could not be calculated across the three studies that

employed the descendent approach (Table 2), as one study reported prevalence of COPD in offspring for different age groups and a second study essentially excluded offspring with respiratory conditions.<sup>52,53</sup>

The calculated pooled prevalence of people with COPD with a positive parental history of COPD (antecedent approach) was 28.6% (random-effects model, 95% confidence interval [CI] =17.4–41.3; Table 3, Figure 2). One study provided prevalence of COPD in both biological and adoptive parents of people with COPD (both included in the





**Figure 2** Pooled prevalence of people with COPD with positive parental COPD history.

**Abbreviation:** COPD, chronic obstructive pulmonary disease.

pooled prevalence calculation).<sup>58</sup> Evidence of heterogeneity between the studies was found ( $I^2=98.8\%$ ;  $P<0.0001$ ). A study by Silverman et al (1998) included a specific group of participants (severe early-onset COPD).<sup>55</sup> When excluding Silverman et al (1998), the prevalence of people with COPD with a positive parental history of COPD was 24.0% (random-effects model, 95% CI =13.2–36.8;  $I^2=99.0\%$ ;  $P<0.0001$ ).<sup>55</sup>

## Pooled OR

Of the eight included studies, three studies reported an OR (of the increased likelihood of offspring of people with COPD to develop COPD),<sup>51,55,57</sup> two studies reported enough information to calculate comparable ORs,<sup>54,58</sup> and three studies did not provide sufficient information for OR calculation.<sup>52,53,56</sup> A study by Khoury et al reported the prevalence of chronic bronchitis and airway obstruction in the offspring of people with COPD.<sup>51</sup> However, this study defined airway obstruction (forced expiratory volume in 1 s [FEV<sub>1</sub>]/forced vital capacity [FVC] <68%) differently from the conventional ratio used for COPD diagnosis (FEV<sub>1</sub>/FVC <70%).<sup>1</sup> To maintain consistency across diagnosis methods through the studies, only the data on chronic bronchitis from the study by Khoury et al were used in the pooled analysis.<sup>51</sup>

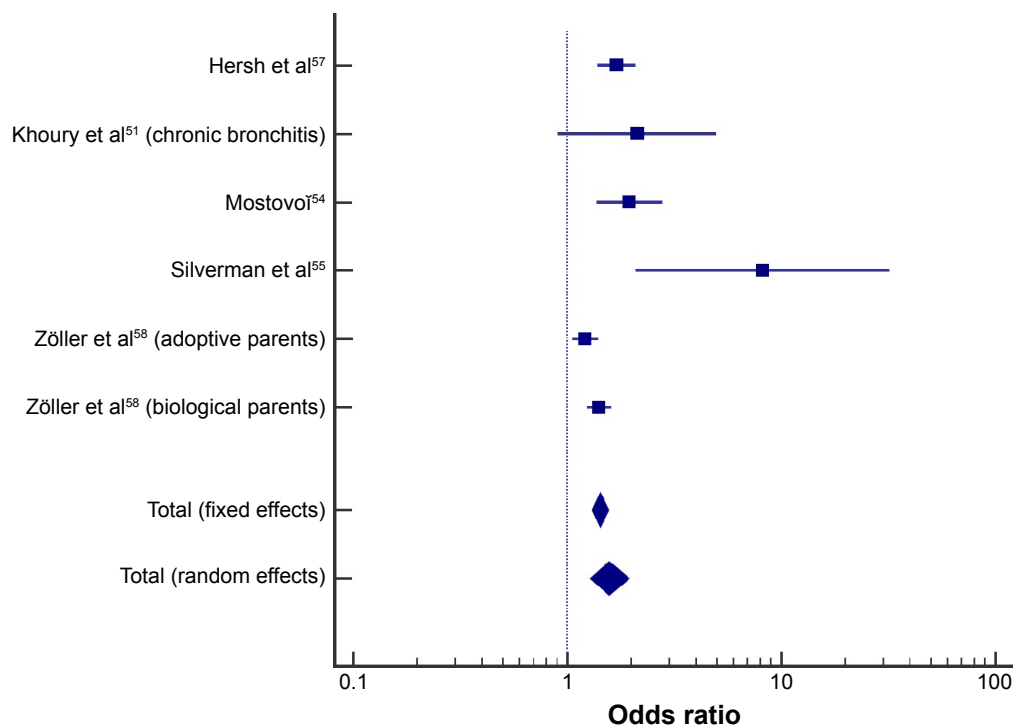
Meta-analysis of crude OR from five studies indicated that offspring of people with COPD had 57% higher odds

of having COPD compared with people without a parental history of COPD (random-effects model, pooled OR =1.57; 95% CI =1.29–1.93;  $P<0.001$ ; Figure 3). Evidence of heterogeneity between studies was found ( $I^2=72\%$ ;  $P=0.0029$ ). When the study by Silverman et al (in severe early-onset COPD) was excluded from the pooled analysis,<sup>55</sup> the heterogeneity decreased ( $I^2=66\%$ ;  $P=0.0198$ ), and offspring of people with COPD had 50% higher odds of having COPD compared with people without a parental history of COPD (random-effects model, pooled OR =1.50; 95% CI =1.26–1.77).

## Discussion

This review specifically focused on the co-occurrence of COPD in parents and offspring. The pooled prevalence of people with COPD and a positive parental history of COPD was 28.6%, and offspring of people with COPD had 1.57 times greater odds of having COPD compared with people without a parental history of COPD. Although there is evidence to support familial associations in lung function decline in parent and offspring pairs,<sup>59</sup> this review identified a paucity of studies (especially recent publications) that provided or enabled an estimate of the prevalence of COPD, especially in offspring of people with COPD, to be obtained.

Due to the inconsistencies in the definition of family history and reporting of outcome measures, only a small



**Figure 3** Summary of effects of positive parental COPD history on offspring COPD (unweighted).

**Abbreviation:** COPD, chronic obstructive pulmonary disease.

number of studies met the inclusion criteria of this review. Lower values for pulmonary function in offspring of COPD probands compared with reference or non-COPD probands have been reported,<sup>49,60,61</sup> but in the absence of categorizing offspring with or without COPD or sufficient information to calculate COPD prevalence within offspring, these studies were excluded.

Variation in the original intent of the included studies resulted in differences in study design, source and nature of participants, and classification of COPD. Index cases in the case-control studies varied from people with chronic bronchitis to people with severe early-onset COPD,<sup>54,55</sup> whereas index cases in the control groups varied from matched individuals to smokers.<sup>52,57</sup> Apart from two older studies (published in 1975 and 1987), all other studies employed spirometry to classify COPD in offspring;<sup>53,54</sup> only one study directly assessed both parents and offspring with spirometry.<sup>56</sup> Parental COPD history was self-reported by participants in all but one of the antecedent studies,<sup>54–57</sup> with the remaining study using medical records to identify COPD in parents and offspring.<sup>58</sup> High prevalence of undiagnosed COPD has been reported worldwide;<sup>10,62</sup> thus, identifying COPD by self-report or medical record screening may be an underestimation and not reveal the true prevalence of positive parental COPD history.<sup>11,59</sup>

Three of the eight studies used a descendent approach and reported a wide range of COPD prevalence (0%–17.3%) in

offspring of people with COPD.<sup>51–53</sup> Amra et al represent an outlier within this group as none of the offspring (n=54) met spirometric criteria for COPD ( $FEV_1/FVC < 0.7$ ).<sup>52</sup> However, young mean age of offspring (34.3 years) and exclusion criteria applied to offspring cases (smokers, employed in high-risk jobs for the respiratory system, or had a pulmonary disease) biased the case group toward including only those with lower risk profile for COPD. The other two studies reported prevalence ranging between 6% and 17.3% which was higher than contemporaneous published prevalence estimates of COPD in the general population for a comparable age-group (4% in 25–44 years).<sup>51,53,63</sup>

Across five studies that used the antecedent approach, between 11.7% and 58.0% of people with COPD reported a positive parental history.<sup>54–58</sup> No comparable reviews or population-based data were found to compare these estimates of parental history of COPD; however, this prevalence appears high when compared to the estimate of prevalence of COPD in the general population (9%–10%).<sup>3</sup> Studies that recruited participants with moderate-to-severe COPD reported a relatively higher positive parental history of COPD (43%–58%) and alluded that the increased risk of COPD in families was likely to be the result of genetic factors.<sup>55–57</sup> Although there are ongoing studies on genome-wide association exploring genotypes of COPD, there remain unanswered questions on COPD heritability and susceptibility.<sup>64</sup>

Another possible explanation for the higher prevalence of positive parental COPD history reported by participants with more severe COPD may be an increased awareness of respiratory problems in their immediate family and greater vigilance or likelihood of reporting.<sup>65</sup>

The risk of developing COPD in people with a parental history of COPD (OR =1.57) was comparable to those exposed to passive smoking (OR =1.48), maternal smoking (OR =1.7), and childhood pneumonia (OR =1.4) and lower compared with the effects of personal smoking in the development of COPD (OR =6.3).<sup>18,66–68</sup> Further epidemiological studies are required to promote understanding of the mechanism of interactions between various risk factors and differentiate shared lifestyle factors from true genetic risk in parents with COPD and their adult offspring.

Early identification of those at a risk of developing COPD is commonly based on modifiable behavior such as smoking or symptom profiles. Smokers are a common target population in COPD case-finding studies as smoking cessation is a well-recognized early intervention that slows the progression of the disease.<sup>16,69,70</sup> As universal screening of asymptomatic individuals for COPD is not recommended,<sup>13</sup> offspring of people with COPD may be considered as an at-risk group due to their shared genetic and environment factors, which presents an opportunity for case finding. By capitalizing on the increased prevalence and the risk of developing COPD in adult offspring of people with confirmed COPD, health practitioners working with people with COPD could use opportunistic screening of adult offspring to enable early lifestyle intervention strategies such as smoking cessation, physical activity, appropriate pharmacologic support, and pulmonary rehabilitation to reduce the rate of lung function decline, improve symptom control, and improve quality of life.<sup>7,71,72</sup>

## Limitations

This review included studies that were published over a 40-year period (1975–2015). The two oldest studies included in this review reported on the prevalence of COPD in offspring of people with COPD, and unsurprisingly the diagnostic criteria used differed from the current standard.<sup>1,51,53</sup> Diagnostic criteria and terminology for COPD have changed over time.<sup>73</sup> As no time limit was set for the systematic search strategy, studies were eligible for inclusion in this review if participants were classified as having emphysema, chronic bronchitis, or COPD. The prevalence of co-occurrence of COPD reported in this review may differ from the present day due to changes in the definition of COPD, lifestyle,

and increased education and health promotion on the health consequences of smoking.<sup>74</sup>

A critical appraisal checklist for studies reporting on prevalence data was used even though the included studies were not specifically designed to report prevalence.<sup>43</sup> As no studies were excluded from the review, modifications were required to adapt the checklist to determine the representativeness of the study sample and interpretation of the results specific to the review question.

Meta-analysis was performed despite significant heterogeneity among the studies. The pooled prevalence and OR calculated provided a summary of the available evidence but may not be generalizable due to the heterogeneity and limited populations of the included studies.

## Conclusion

Although familial associations with COPD have been generally well recognized, the results of this review indicate that there were few studies that specifically reported on the co-occurrence of COPD diagnosis in both parents and offspring. Nevertheless, the findings of this review indicate that offspring of people with COPD are at an increased risk of developing COPD. Targeted screening in this at-risk group (adult offspring of people with COPD) may lead to opportunities to capitalize on familial links and promote early identification and intervention.

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## Author contributions

All the authors (LSKL, CP, KJ, and MTW) contributed substantially to the study design, data collection, data analysis and interpretation, and the writing and critical revision of the manuscript.

## Disclosure

The authors report no conflicts of interest in this work.

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## Supplementary materials

**Table S1** Data extraction table

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Publication details

Author

Year

Study method

Country of data collected

Study design

Comparator

Sample size (if case-control study, number of cases and controls)

Sampling method

Study inclusion criteria

Study exclusion criteria

Participant flow (descendent/antecedent approach)

Data on parents

Demographics

Method of COPD diagnosis

Severity of COPD

Data on offspring

Demographics

Method of COPD diagnosis

Severity of COPD

COPD parents

Total number of COPD parents

Number of COPD parents with COPD offspring

Non-COPD parents

Total number of parents without COPD

Number of parents without COPD, offspring with COPD

Statistical analysis

Odds ratio (if reported)

Covariates (if any) used to adjust the prevalence and/or odds ratio estimates

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**Abbreviation:** COPD, chronic obstructive pulmonary disease.

**Table S2** Methodology quality assessment of the included studies

	Higgins and Keller <sup>1</sup>	Khoury et al <sup>2</sup>	Mostovoi <sup>3</sup>	Silverman et al <sup>4</sup>	McCloskey et al <sup>5</sup>	Hersh et al <sup>6</sup>	Amra et al <sup>7</sup>	Zöller et al <sup>8</sup>
1. Was the sample representative of the target population?	Unclear	Unclear	Unclear	Yes	Yes	No	No	Yes
2. Were study participants recruited in an appropriate way?	Unclear	Unclear	Unclear	Yes	Yes	Unclear	Unclear	Yes
3. Was the sample size adequate?								
a. Did the authors conduct a sample size calculation to determine an adequate sample size?	No	No	No	No	No	No	No	No
b. Estimating an expected prevalence of 10% with 2.5% precision, <sup>9</sup> did the study have adequate sample size?	Yes	No	No	No	No	Yes	No	Yes
4. Were the study subjects and the setting described in detail?								
a. Did the study provide sufficient details on the subjects?	No	Yes	No	Yes	Yes	Yes	Yes	Yes
b. Did the study provide sufficient details on the setting?	Yes	Yes	No	Yes	Yes	No	Unclear	Yes
5. Was the data analysis conducted with sufficient coverage of the identified sample?								
a. Did the authors describe the reasons for nonresponse and compare people in the study to those not in the study, particularly with regard to their sociodemographic characteristics?	Yes	No	No	Yes	Yes	Yes	No	Yes
b. Could the nonresponders have led to an underestimate of prevalence of the disease or condition under investigation?	No	Unclear	Unclear	No	No	Yes	Yes	No
c. If reasons for nonresponse appear to be unrelated to the outcome measure and the characteristics of nonresponders are comparable to those in the study, the researchers may be able to justify a more modest response rate	Unclear	Unclear	N/A	N/A	N/A	Unclear	Unclear	Unclear
6. Were objective, standard criteria used for the measurement of the condition?								
Parents?	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Offspring?	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
7. Was the condition measured reliably?								
Parents?	Yes	Unclear	Unclear	Unclear	Unclear	Yes	Unclear	Yes
Offspring?	Yes	Unclear	Yes	Yes	Unclear	Yes	Unclear	Yes
8. Was there appropriate statistical analysis?	No	Yes	Unclear	Yes	Yes	No	No	Yes
9. Are all important confounding factors/subgroups/differences identified and accounted for?								
Prevalence?	Yes	No	No	Unclear	Yes	No	Unclear	No
Odds ratio?	N/A	No	N/A	Yes	Yes	Yes	N/A	No
10. Were subpopulations identified using objective criteria?								
Prevalence?	Yes	No	No	No	No	No	N/A	Yes
Odds ratio?	N/A	No	N/A	yes	Yes	Yes	N/A	Yes

**Note:** <sup>9</sup>Calculated by using the formula suggested in the Joanna Briggs Institute reviewers' manual.<sup>9</sup>

**Abbreviation:** N/A, not applicable.

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