



Original article

Association between early history of asthma and COPD diagnosis in later life: a systematic review and meta-analysis

Michael Asamoah-Boaheng ^{1,*} Lily Acheampong,¹ Eric Y Tenkorang,² Jamie Farrell,¹ Alwell Oyet³ and William K Midodzi¹

¹Department of Medicine, Clinical Epidemiology Unit, Faculty of Medicine, Memorial University of Newfoundland, St. John's, Canada, ²Department of Sociology, Memorial University of Newfoundland, St. John's, Canada and ³Department of Mathematics and Statistics, Memorial University of Newfoundland, St. John's, Canada

*Corresponding author. Department of Medicine, Clinical Epidemiology Unit, Faculty of Medicine, Rm 4M129-Medical Education Center, Memorial University, St John's, NL A1B 3V6, Canada. E-mail: masamoahboah@mun.ca

Editorial decision 26 August 2018; Accepted 6 September 2018

Abstract

Background: Whereas most studies have reported prior history/diagnosis of asthma as an independent risk factor for Chronic Obstructive Pulmonary Disease (COPD) development in later life, no systematic review and meta-analysis has been conducted to synthesize these observational studies. The aim of this review is to investigate associations between prior history of asthma and later development of COPD.

Methods: We conducted a comprehensive search in PubMed, CINAHL and EMBASE for studies related to prior history of asthma and COPD diagnosis. Articles were screened for relevance by two independent reviewers. Methodological quality was independently assessed and data extracted for qualitative and quantitative review. We explored heterogeneity and performed a publication bias check.

Results: From the 1260 articles retrieved, 9 were included in the qualitative review and 7 in the meta-analysis. History of asthma was associated with developing COPD in later life (Inverse Variance Random-effects model, odds ratio: 7.87, 95% confidence interval: 5.40–11.45, $p < 0.00001$).

Conclusions: Studies with high methodological quality provided sufficient evidence to suggest that individuals with previous history of asthma have an increasing likelihood of developing COPD in later life.

Key words: Chronic Obstructive Pulmonary Disease, prior asthma, risk factor, meta-analysis, random-effects model

Key Messages

- No systematic reviews and meta-analysis have been conducted on the association between prior history of asthma and Chronic Obstructive Pulmonary Disease (COPD) diagnosis.
- We examined the association between previous history of asthma (childhood and adulthood asthma) and subsequent development of COPD.
- We found previous history of asthma was significantly associated with increasing likelihood of developing COPD in later life.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a progressive lung disease that limits normal airflow in the bronchial tubes, resulting in chronic cough, breathlessness and exercise intolerance.^{1,2} The condition is projected to be the third leading cause of death worldwide by 2020.^{3,4} Tobacco smoking is widely accepted as the main cause of COPD and has been linked to the gradual damage to the parenchymal cells of the lungs over time, leading directly to poor quality of life in people with the disease.^{5,6} Evidence, suggests, however, that 25–45% of patients with COPD have never smoked and a proportion of smokers (10–20%) actually develop it.^{7,8} These figures raise questions of other possible factors driving COPD cases. It has been reported that early-childhood experiences may influence the normal growth and development of lungs and subsequently pose a risk for COPD in later adult life.⁹ Impaired lung development during childhood and adolescence resulting from recurrent infections, premature gestation, atopy, bronchial hyper-responsiveness and asthma has been associated with failure to attain maximum lung function in adult life.⁹ In addition, there is recent evidence of the role of prior or existing history of early asthma in the subsequent development of COPD. Many epidemiological studies have demonstrated that asthma diagnosis in early life could be a risk factor for COPD regardless of smoking history or status.^{10–12} However, to the best of our knowledge, there have been no systematic reviews and meta-analyses of studies in this important area. Accordingly, this study was conducted to review the evidence of the association between prior asthma and later COPD diagnosis.

The purpose of this review was to systematically identify, select and summarize the literature linking prior history of asthma and subsequent development of COPD. To this end, we analysed the results from independent studies quantitatively and produced a single and more precise estimate of the extent of the association using meta-analysis. The review addressed the following question: for a general population of individuals aged 5 years and older,

does prior history of asthma compared with no prior history of asthma increase the risk of developing COPD in later life?

Methods

We used systematic and explicit methods to review the existing literature to identify, select and critically appraise potentially relevant studies related to the question of interest. We used the recommended Preferred Reporting Item for Systematic Review and Meta-analysis (PRISMA) and Meta-analyses of Observational Studies in Epidemiology (MOOSE) checklists to conduct and report the systematic review and meta-analysis of the selected studies.¹³ The methods are summarized below.

Literature search

Our literature search was conducted using MEDLINE (PubMed), EMBASE, CINAHL. The search included articles and review articles published from inception to September 2017. The search criteria included keywords and MeSH terms and a combination of the two. MeSH terms included 'Pulmonary Disease, Chronic Obstructive', 'asthma' and 'risk factors'; keywords included 'chronic obstructive pulmonary disease', 'asthma', 'child', 'history', 'previous' and 'risk factors'. The search focused on studies conducted on humans with no restriction on language. The reference lists of articles were screened to identify additional studies. Some experts and study authors were contacted and asked about any additional studies (both published and unpublished). The comprehensive search started on 10 September and ended on 2 October 2017. The final search string used in PubMed, EMBASE and CINAHL is shown in [Supplementary Appendix 1](#), available as [Supplementary data](#) at *IJE* online.

The initial literature search included cohort, case-control and cross-sectional studies. Studies investigating patients with and without previous history of asthma (whether childhood or adult-onset) as the exposure of

interest were included. Likewise, studies and reviews were included if COPD was mentioned as one of the outcomes (preferably the primary outcome). Our exclusion criteria included case series and case reports, studies that did not include asthma as one of the exposure variables and studies that did not include COPD as one of the outcomes.

Studies were included in the quantitative synthesis (meta-analysis) if they investigated the association between previous history of asthma and COPD diagnosis, were cohort and case-control studies, published measures of association such as hazard ratios (HRs) and odds ratios (ORs), and had a 95% confidence interval (CI) for their estimates.

Study selection and quality assessment

Two reviewers (MAB, LA) independently provided quality assessment of the articles at all stages. The titles and abstracts yielded by the databases in the initial search were read or scanned. After their relevance was assessed, selected articles were further screened. Nine were extracted from the final screening (four cohort studies, four case-control studies and one cross-sectional study). The quality of the studies was assessed using the US Preventive Services Task Force (USPSTF) Quality Rating Criteria assessment of bias for cohort and case-control studies. Using the USPSTF assessment of bias tool, each author independently assessed and graded each of the nine studies as good, fair or poor. Before evaluating the individual studies, an independent reviewer was called to black out the names of the authors, study title and institution of affiliation to ensure blinding. Any disagreement in assessing the articles was resolved by reaching consensus.

Data extraction

We developed a standardized form using generic items to assist in the data-extraction process. The entire process of data extraction was concurrently performed by two independent reviewers; any recognized differences, such as definition of cases, were reconciled by mutual agreement. The form was piloted on three selected studies before its incorporation. Using the standardized form as a guide, the two reviewers extracted the following information from the selected studies: authors' surnames and year of publication, participants, COPD diagnosis in the exposed and unexposed group, exposure variables, outcomes, results and adjusted confounders (see [Table 1](#)). We estimated the relative association measure (ORs) and their corresponding 95% CI, *p*-values and the adjusted results.

Statistical analysis

The principal summary measure for the seven studies included in the meta-analysis was the OR. The Review

Manager (RevMan version 5.3) and Comprehensive Meta-Analysis (CMA) software were used for data analysis at the quantitative synthesis stage. We employed a random-effects model with a generic inverse variance method, as we suspected heterogeneity across the studies because of differences in asthma diagnosis, study type and patient population. We used a funnel plot to determine the presence or absence of publication bias in the review through visual inspection; more specifically, we conducted Egger's and Begg's tests to look for funnel plot asymmetry/small-study effect to quantitatively assess the publication bias. Finally, we conducted sensitivity analysis to assess the robustness of the results of the meta-analysis in the presence of differences in the studies' results.

Results

Summary of included studies

Our initial literature search using the three electronic databases yielded 1258 articles (PubMed = 422, EMBASE = 765, CINAHL = 71). Two articles were obtained from other sources (scanning reference lists of articles = 2). After removing duplicates using the referenced manager software, we were left with 1200 articles. The titles and abstracts of 1200 articles were screened for relevance by two reviewers (M.A.-B., L.A.); after screening, 27 articles were retrieved and downloaded for full-text review. When all 27 full-text articles had been assessed, 18 articles were excluded because they did not meet the inclusion/exclusion criteria, leaving 9 articles for the qualitative assessment (see [Figure 1](#)). The nine selected articles comprised four cohort studies, four case-control studies and one cross-sectional study. The year of publication for the selected studies ranged from 2007 to 2017. The studies were conducted in a number of European countries as well as Japan, New Zealand, Australia, China and the USA [i.e. the European Community Respiratory Health Survey (ECRHS) study includes a number of centres, of which only one is from Norway]. The length of follow-up ranged from 20 to 50 years. The main measure of association reported in the studies was ORs. The majority provided tables of patient characteristics at the levels of baseline and multivariate analysis. Most adjusted for important confounders, such as age, sex, smoking status, maternal smoking and exposure to air pollution. We reviewed all nine studies qualitatively and seven studies quantitatively.

Qualitative review

The total quality score for each paper is reported in [Table 2](#). Overall, those selected for review were of 'fair' quality. Only one out of the nine selected papers was

Table 1. Summary of findings of studies included in the review for investigating the association between prior history of asthma and COPD

Article	Study type/design	Patient/population	Exposed group	Non-exposed group	Outcomes assessed	Results	Adjusted variables
Omori <i>et al.</i> (2017) ¹⁴	Prospective study	A total of 9896 participants within the age range 35–60 years were included	Remitted asthma ($n = 287$), adult-onset asthma ($n = 354$), childhood-adulthood asthma ($n = 101$)	Healthy controls (without asthma, $n = 9154$)	Airflow obstruction objectively measured as: FEV1/FVC < 0.7 and FEV1	Remitted asthma was independently associated with airflow obstruction, OR: 2.87 (95% CI: 1.66–4.96), B: -2.4 (-3.09, -1.71)	Adjusted for age, sex, current smoking and pack years (per 10)
Aanerud <i>et al.</i> (2015) ¹⁵	Prospective cohort study	Randomly selected adults aged 20–44 years from the European Community Respiratory Health Survey (ECRHS) I (1991–93) survey in 25 countries	Early asthma independent of smoking (<10 years), late asthma independent of smoking (>10 years)	Never smokers without diagnosis of asthma	Airway obstruction objectively measured as FEV1/FVC < 0.7	Early asthma independent of smoking was associated with airway obstruction (AO): OR: 21.0 (95% CI: 12.7–35.0). Late asthma was also associated with AO: OR: 11.2 (95% CI: 6.8–18.6)	Adjusted for potential confounders such as age, sex, country, education, body mass index, height, smoking and sample design
Hirayama and Lee (2015) ¹⁶	Case-control study	300 COPD patients aged 50–75 years and 400 controls/adults residing in the same communities as the cases were recruited	278 patients (244 men, 34 women)	340 (272 men, 68 women)	Diagnosis of COPD confirmed by spirometry after bronchodilation with FEV1/FVC < 0.7	Childhood asthma was significantly associated with the risk of COPD adj. OR [95% CI as 3.32 (1.05–10.45)]	Adjusted for age, gender, cumulative smoking exposure, education level, body mass index, alcohol drinking status, lifelong physical fitness, residential location and marital status
Chan-Yeung <i>et al.</i> (2007) ¹⁷	Case-control study	289 patients with COPD were recruited from outpatient clinic	Patients with COPD	Healthy controls from two sources	COPD	Several risk factors were assessed and smoking was found to be associated with COPD	Adjusted for sex, childhood wheezy bronchitis groups, childhood hay fever or eczema, smoking status
Tai <i>et al.</i> (2014) ¹⁰	Longitudinal prospective cohort study	401 Patients recruited from the 1957 birth cohort at age 7 years and reviewed regularly to the age of 50 years from the 30 000 grade 2 Melbourne Asthma Study. At age 50 years, 346 of the surviving cohort participated in the current study	113 children with asthma, 83 with severe asthma and 178 with intermittent asthma	Children without the symptoms of wheeze at age 7 years (105 non-asthmatics)	Outcomes assessed included: asthma remission, current asthma and COPD	Children with severe asthma 32 times higher risk of developing severe asthma after adjusting for important covariates. OR: 32 (95% CI: 3.4–269)	Adjusted for sex, childhood wheezy bronchitis groups, childhood hay fever or eczema, smoking status

(Continued)

Table 1. Continued

Article	Study type/design	Patient/population	Exposed group	Non-exposed group	Outcomes assessed	Results	Adjusted variables
Tsuda <i>et al.</i> (2009) ¹⁸	Case-control study	9493 patients older than 65 years registered in the hospital database were recruited	Never smokers with COPD (<i>n</i> = 49)	Smokers with COPD (<i>n</i> = 98)	Clinically relevant COPD	Patients with history of asthma were significantly associated with COPD, OR: 29.4 (95% CI: 10.1–85.4)	Adjusted for female sex, age, body mass index, age at initial diagnosis, smoking history, extrinsic allergy, second-hand smoke
Svanes <i>et al.</i> (2010) ¹⁹	Mixed design (cross-sectional study and cohort study)	Participants aged 20–44 years from general population of study in the European Community Respiratory Health Survey (ECRHS)	Childhood disadvantage factors: maternal and paternal asthma, childhood asthma and childhood respiratory infections	Subjects without any of the childhood disadvantage factors	FEV1 and COPD	COPD increased with increasing childhood disadvantage ≥ 3 factors, men: OR 6.3 (95% CI: 2.4–17), women: OR 7.2 (95% CI: 2.8–19)	Adjusted for age, height, smoking, education, social class and country
Shirtcliffe <i>et al.</i> (2012) ²⁰	Cross-sectional study	A total of 3500 subjects were gathered from the Wellington Respiratory Survey and divided between the ages of 25 and 75 years	Childhood asthma	Non-asthmatics	GOLD lung function criteria for defining COPD	Childhood asthma was strongly associated with GOLD-defined COPD	Adjusted for age, atopy, hospitalized under age 2 years, sex, Maori and pack years (per 10)
Tagiyeva <i>et al.</i> (2016) ²¹	Prospective cohort study	A cohort of children aged 10–15 years recruited and followed up to age 60–65 years	Childhood asthma = 38, 53 with childhood wheezy bronchitis	239 control subjects	FEV1, FVC, COPD	Childhood asthma was associated with an increased risk of COPD, OR 6.37 (95% CI: 3.73–10.94) and childhood wheezy bronchitis, OR 1.81 (95% CI: 1.12–2.91)	Adjusted for sex, age, history of ever smoking and Scottish Index of Multiple Deprivation

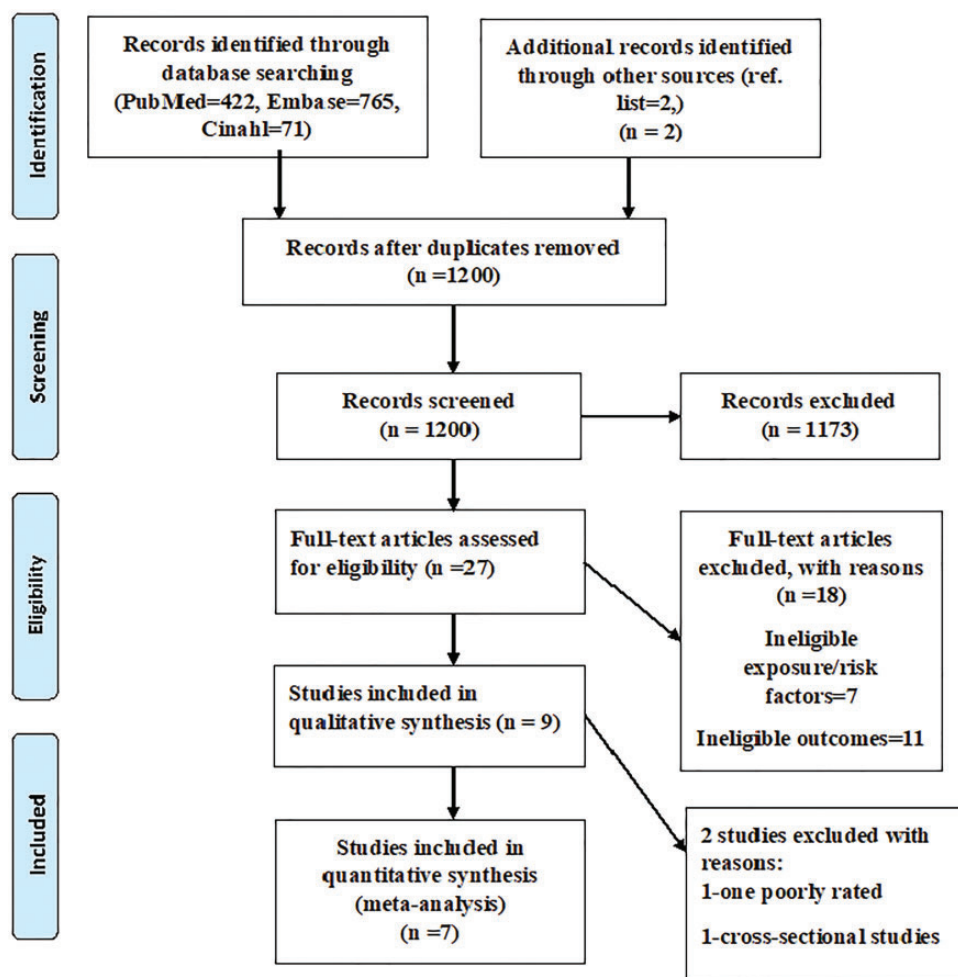


Figure 1. Preferred reporting items for systematic reviews and meta-analyses flow diagram of search strategy and article selection.

graded as ‘poor’ and this was due to very high drop-out rates (>50%), which were not accounted for.¹⁷ For longitudinal studies, the domain ‘maintenance of comparable groups’ was generally assessed as ‘fair’ across studies. Retrospective studies (case-control and cross-sectional) mostly had a ‘fair assessment’ for one particular USPSTF domain: ‘measurement of exposure accurate and applied equally to each group.’ The fair assessment here was due to the recall nature of exposure measurement (history of asthma). The criteria and the study type made it impossible for these studies to objectively measure the exposure variable, since it was entirely based on recall. Overall, the risk of bias was minimal across studies, as potential confounding factors (smoking status and history, age, maternal smoking and exposure to air pollution) were clearly identified and adjusted for in all selected papers.

In all studies, COPD was ascertained with spirometry using the 2001 version of the Global Obstructive Lung Disease (GOLD) criteria defined by spirometric data of post-bronchodilator $FEV_1/FVC < 0.7$ as well as $FEV_1 < 80\%$ predicted.²² The longitudinal studies used medical

records and the retrospective studies used self-reports. In all studies, the outcome was measured as development of COPD but they differed slightly in their definition of COPD in terms of the use of post and pre bronchodilator. Seven defined COPD using the GOLD-approved definition of a spirometric finding of $FEV_1/FVC < 0.7$ after the use of a bronchodilator, whereas two other studies used a pre-bronchodilator value of $FEV_1/FVC < 0.7$, rather than the post-bronchodilator value used by most studies.^{14,19} However, the 2014 GOLD criteria report that the degree of airflow limitation (which measures FEV_1 before and after bronchodilator or corticosteroids) is no longer recommended.²³ In all, nine studies provided an objective measure of COPD diagnosis using spirometry and based on the GOLD standard before and after the use of a bronchodilator.

Studies found some evidence of a positive association between prior history of asthma and development of COPD in later life. Although the extent of the association was significant, the precision of their estimates was unclear, as CIs were very wide. This could be attributed to

Table 2. Assessment of potential bias of studies for inclusion in the synthesis using USPSTF Quality criteria for cohort studies and case control studies

Article	Assembly of comparable groups	Maintenance of comparable groups	No important differential loss to follow-up or overall high loss to follow-up	Measurements: equal reliable, valid (includes masking of outcome assessment)	Clear definition of intervention	All-important outcomes considered	Analysis: Adjustment for potential confounders	Overall assessed quality
Aanerud <i>et al.</i> (2015) ¹⁵	Good	Good	Good	Good	Good	Good	Good	Good
Tai <i>et al.</i> (2014) ¹⁰	Good	Fair	Fair	Good	Good	Good	Good	Good
Tagiyeva <i>et al.</i> (2016) ²¹	Good	Fair	Fair	Good	Good	Good	Good	Good
Svanes <i>et al.</i> (2010) ¹⁹	Fair	Unclear	Good	Good	Good	Good	Fair	Fair
Assessment of potential bias of studies for inclusion in the synthesis using USPSTF Quality criteria for case-control								
Article	Accurate ascertainment of cases	Non-biased selection of cases/controls	Response Rate	Diagnostic testing procedures applied equally to each group	Measurement of exposure accurate and applied equally to each group	Appropriate attention to potential confounding variable	Overall assessed quality	
Hirayama and Lee (2015) ¹⁶	Good	Good	Good	Good	Fair	Good	Good	
Tsuda <i>et al.</i> (2009) ¹⁸	Fair	Unclear	Fair	Good	Fair	Fair	Fair	
Omori <i>et al.</i> (2017) ¹⁴	Good	Good	Fair	Good	Fair	Fair	Fair	
Chan-Yeung <i>et al.</i> (2007) ¹⁷	Good	Unclear	Poor	Unclear	Fair	Fair	Poor	
Shirtcliffe <i>et al.</i> (2012) ²⁰	Good	Fair	Fair	Unclear	Unclear	Good	Fair	

the smaller sample sizes for both the exposed and unexposed groups. Studies with smaller sample sizes tend to provide very large effects estimates and are less powered. Therefore, the prediction of the true effects in these studies could have been over-estimated.

Quantitative review (meta-analysis)

We performed meta-analysis on seven studies comprising four cohort studies and three case-control studies after we assessed their quality using the USPSTF quality assessment of bias tool. These seven studies were generally rated as 'fair' and 'good'. All seven studies used the OR as the main summary measure for the effects estimate. We used a generic inverse variance method to estimate the contribution of each study (expressed in weights) to the pooled effect. The log (OR) for all studies was transformed back and the effects estimate of all studies was calculated as an OR. [Supplementary Table 1](#), available as [Supplementary data](#) at *IJE* online, presents the summary of the studies in the quantitative review. Although 7 studies were included, slightly different exposure variables were extracted and considered as separate studies, resulting in a total of 10 studies.

Effect of prior history of asthma on patients' likelihood of developing COPD

[Figure 2](#) shows the forest plot of the 10 studies summarizing the effect of prior history of asthma on the likelihood of developing COPD. The forest plot indicated that patients with a prior history of asthma (such as childhood asthma, adult-onset asthma) were 7.23 times more likely to develop COPD, with a 95% CI of 5.05–10.33 and p -value < 0.00001 . This means early diagnosis of asthma could be a significant risk factor for developing COPD.

However, the average summary effect was not consistent across studies, and there was substantial heterogeneity ($I^2 = 66\%$, $p = 0.001$) among the 10 studies. This suggests that results were not similar from study to study. The studies might have differed by study type, methodological quality and other sources of heterogeneity. To identify the source(s) of the heterogeneity, we conducted a subgroup meta-analysis stratified by the study-quality ratings of 'fair' and 'good'.

Subgroup analysis

Via subgroup analysis, we were able to identify the source or cause of heterogeneity. [Figure 3](#) shows the subgroup analysis by quality-assessment grading. The first subgroup was made up of studies graded as 'good', followed by the second subgroup 'fair'. The studies graded and classified as 'good' had a pooled OR 7.87 with a 95% CI of 5.40–11.45 and $p < 0.00001$. The meta-analysis of the first subgroup indicated that individuals with a prior history of asthma had an increased likelihood of developing COPD compared with individuals without any history of asthma (7.87 times more likely to develop COPD). Studies in this subgroup were generally homogeneous ($I^2 = 26\%$, $p = 0.25$) and their results were similar. The pooled-effects estimate was consistent across studies graded 'good'.

The second subgroup synthesized studies graded as 'fair'. The forest plot gave a pooled effect estimate/average estimate (OR) of 6.62 with a 95% CI of 3.7–11.86 and $p < 0.00001$. Meta-analysis of this combined effect also showed individuals with a prior history of asthma had an increased likelihood of developing COPD. Nonetheless, results in this subgroup were not similar, making the pooled effects inconsistent across studies (highly heterogeneous at $I^2 = 79\%$, $p = 0.0002$). The combined-effects estimate for studies with 'fair' methodological quality cannot

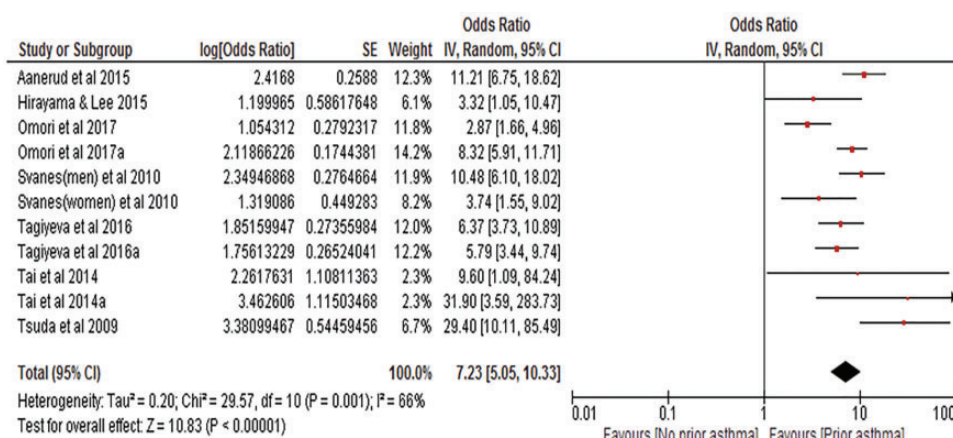


Figure 2. Forest plot of assessing whether a prior history of asthma increases the likelihood of developing COPD.

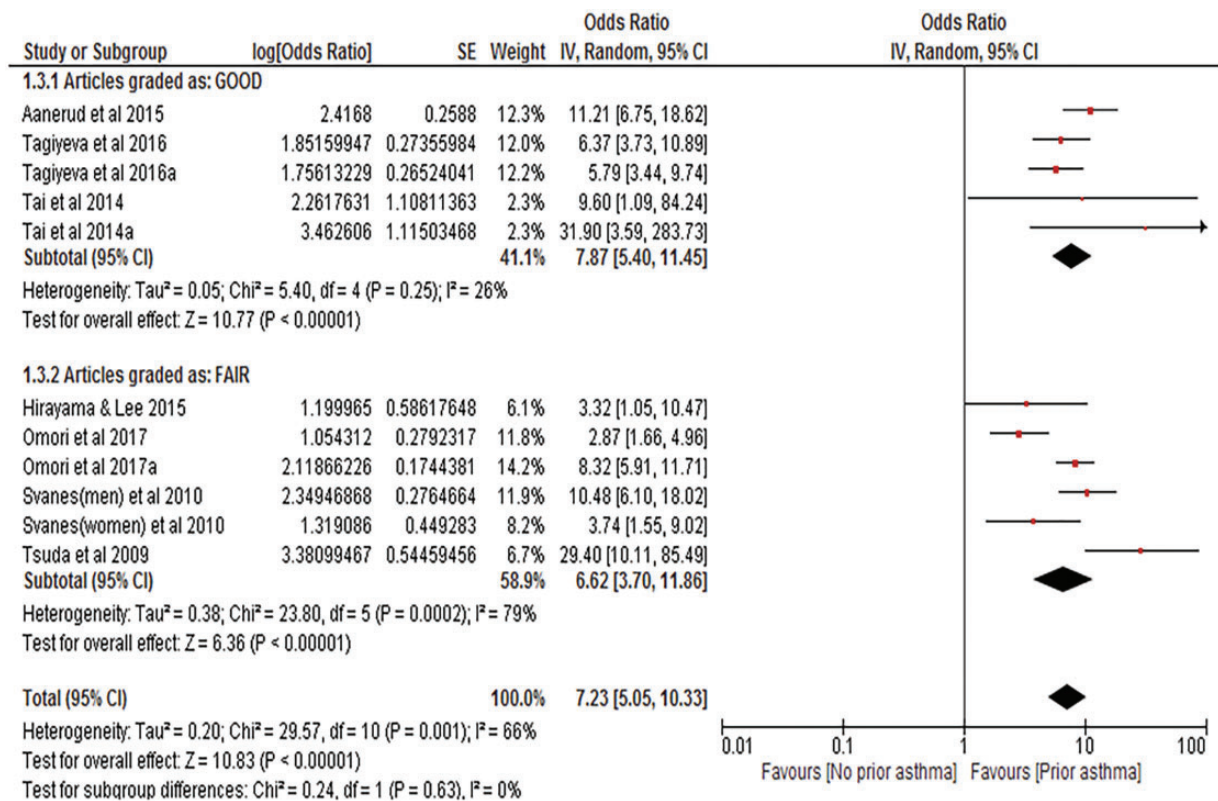


Figure 3. Forest Plot assessing whether a prior history of asthma increases the likelihood of developing COPD (subgroup analysis by study quality).

be used, as these studies are entirely different from each other; the wider CI and higher heterogeneity render the precision of the effects estimate uncertain.

Figure 3 shows the test of subgroup differences between the two subgroups. The forest plot revealed that the two subgroups were similar, hence their pooled-effects estimates were similar with no substantial heterogeneity ($I^2 = 0\%$, $p = 0.63$). The combined effect for the association between prior history of asthma and development of COPD was OR: 7.23 (95% CI: 5.05–10.33, $p < 0.00001$).

Publication bias

The funnel plots shown in Figure 4 and Supplementary Figure 2, available as Supplementary data at IJE online, were employed to visually assess and detect publication bias. A visual inspection of the two funnel plots showed some level of symmetry, indicating no possibility of publication bias.

Egger’s and Begg’s tests for checking publication bias

Egger suggests that we assess publication bias or small-study effect by using precision (the inverse of the standard error) to predict the standardized effect (effect size divided by the standard error). From Supplementary Table 2, available as

Supplementary data at IJE online, the intercept (β_0) is 0.28688, 95% CI: -2.50302 to 3.07678 , with $t = 0.23261$, $df = 9$. The one-tailed p -value is 0.41063 and the two-tailed p -value is 0.82127. Results from Egger’s test indicate no substantial publication bias. Similarly, the Begg and Mazumdar rank correlation recorded a one-tailed p -value of 0.50000, indicating no publication bias in this review.

Sensitivity analysis

The considerable heterogeneity identified in the ‘fair’ study-quality subgroup was explained by sensitivity analysis. We performed a meta-analysis by excluding some studies in the subgroup with larger effects estimates (OR greater than 8.00). Studies excluded were Omori *et al.* (2016a), Svanes (men) *et al.* (2009) and Tsuda *et al.* (2009). Results from the remaining studies were similar from study to study ($I^2 = 0\%$, $p = 0.88$), with very precise effects estimates (OR: 3.12, 95% CI: 2.03–4.80, $p < 0.00001$) (see Supplementary Figure 1, available as Supplementary data at IJE online).

Discussion

The purpose of this study was to systematically summarize the available literature on the association between prior history of

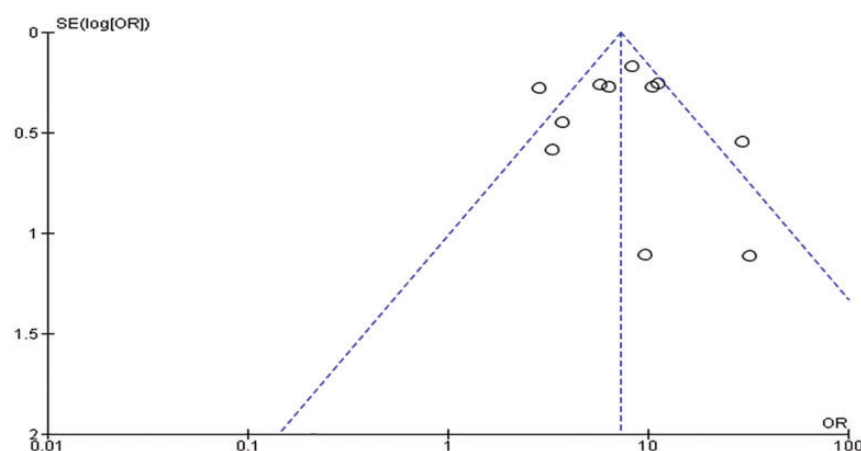


Figure 4. Publication bias check for assessing whether a prior history of asthma increases the likelihood of developing COPD.

asthma and subsequent development of COPD. To the authors' knowledge, this is the first comprehensive systematic review and meta-analysis of this topic. In a population aged 5 years and older, prior history of asthma was found to be significantly associated with development of COPD in later life.

We adhered to strict priori inclusion and exclusion criteria for all studies. We excluded cross-sectional studies at the quantitative synthesis stage, as they do not present the best evidence compared with other higher levels of evidence such as case-control and cohort studies to answer the question of interest. A priori, COPD was chosen as the outcome measure, and we excluded studies not reporting COPD as an outcome. The USPSTF Quality Rating Criteria assessment of bias tool confirmed that the selected studies had low risk of bias. The evidence we obtained was of good strength, had low risk of bias and was considered sufficient to draw broad conclusions on the association between asthma history and COPD development in later life.

As COPD continues to be a global burden, efforts are being made to identify all risk factors and the necessary interventions to reduce the disease burden. In the past decade, an increasing number of epidemiological studies have noted the growing prevalence of COPD among non-smokers in developed countries. The risk of acquiring COPD from smoking was assessed as 45 and 44% in the Swedish OLIN and the US NHANES III studies, respectively; in other words, more than half of all COPD cases are unrelated to smoking.⁷ Our findings provide good evidence that having asthma at some point in an individual's life, regardless of the person's age, smoking status and occupational exposure, puts them at risk of developing COPD about seven times more likely than someone who has never had asthma. Our study findings agree with the narrative review by Tai (2015)²⁴ and are stronger than this previous work because of our comprehensive search for studies and use of quantitative synthesis.

Poorly controlled asthma is thought to be a progressive disease that can advance from a fully reversible bronchospasm to permanent airflow obstruction of the airways. Airway inflammation and remodelling have been seen in some young children and adolescents with asthma and have been hypothesized to be linked to the development of an irreversible airflow obstruction and a Forced Expiratory Volume in 1 second (FEV₁) decline—a characteristic of COPD. To date, this hypothesis has not been verified, and more research is needed to unravel the complex relationship between asthma and COPD.

This review highlights the need for research investigating whether asthma medication might reduce the risk for such development. Patients with asthma should also be educated on the need to avoid other risk factors of COPD, such as smoking, as this might increase their likelihood of developing the disease.

Strength and limitations

One of the strengths of our study was the fact that studies of 'good' methodological quality provided ample evidence of the association between prior history of asthma and later development of COPD. Any differences could be attributed to chance or random error. In addition, we included articles adjusted for potential confounders and we obtained adjusted estimates of the effects. Finally, COPD as the primary outcome was objectively measured in all studies in the quantitative synthesis. Limitations of this study were: (i) studies with slightly different exposures were not included; (ii) the inclusion of studies of 'fair' methodological quality with substantial heterogeneity made pooling of a common effects estimate impossible. We attributed this later limitation to the inability of most studies to objectively measure asthma from infancy to adulthood; most were based on recall. Differences in study

type introduced heterogeneity across studies in the synthesis stage. Some retrospective and prospective studies also differed in the duration of their follow-up.

Conclusion

Our findings demonstrated evidence of a positive association between prior history of asthma and COPD. Studies with high methodological quality (operationalized here as 'good') provided considerable evidence that prior history of asthma independently of tobacco smoking and other factors is associated with the development of COPD in the life course. Future work should include more studies with low risk of bias, considering studies that present the best evidence to improve the precision of the effects estimates.

Supplementary Data

Supplementary data are available at *IJE* online.

Acknowledgements

We acknowledge the effort of Michelle Swab, a librarian at the Health Science Library at the Memorial University of Newfoundland, for her effort and assistance in performing an exhaustive literature search. M.A.-B. was supported by the Deans Doctoral Award; student's award at Faculty of Medicine, Memorial University of Newfoundland. M.A.-B., L.A., E.Y.T., J.F., A.O. and W.K.M. conceived the study and designed the study protocol; M.A.-B. and L.A. developed the search strategy as well as conducted the search for studies. M.A.-B., L.A., E.Y.T., J.F., A.O. and W.K.M. conducted the screening and study selection. Data extraction was performed by M.A.-B. and L.A. Data analysis and interpretation were carried out by M.A.-B., L.A., E.Y.T., J.F., A.O. and W.K.M. M.A.-B., L.A., E.Y.T., J.F., A.O. and W.K.M. drafted the manuscript and critically revised the manuscript for intellectual content. M.A.-B. is the guarantor of the paper. All authors read and approved the final version of the manuscript. All references have been checked for accuracy and completeness.

Conflict of interest: Authors declare no competing interests and that this study has not been published previously in a similar form.

References

- Williams B, Chang A, Landefeld C, Ahalt C, Conant R, Chen H. *Current Diagnosis and Treatment: Geriatrics* 2E. New York: McGraw-Hill Education Medical, 2014.
- The Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2017 [Internet]. GOLD 2017. <http://www.goldcopd.org> (10 October 2017, date last accessed).
- Evans J, Chen Y, Camp PG, Bowie DM, McRae L. Estimating the prevalence of COPD in Canada: reported diagnosis versus measured airflow obstruction. *Health Rep* 2014;25:3.
- Murray CJ, Lopez AD, World Health Organization, World Bank & Harvard School of Public Health. The Global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020: summary / edited by Christopher J. L. Murray, Alan D. Lopez. Geneva: World Health Organization, 1996. <http://www.who.int/iris/handle/10665/41864>
- de Marco R, Accordini S, Antò JM *et al.* Long-term outcomes in mild/moderate chronic obstructive pulmonary disease in the European community respiratory health survey. *Am J Respir Crit Care Med* 2009;180:956–63.
- Fletcher C, Peto R. The natural history of chronic airflow obstruction. *Br Med J* 1977;1:1645–48.
- Salvi SS, Barnes PJ. Chronic obstructive pulmonary disease in non-smokers. *Lancet* 2009;374:733–43.
- Siafakas NM, Tzortzaki EG. Few smokers develop COPD: why? *Respir Med* 2002;96:615–24.
- Bakke PS. Factors affecting growth of FEV₁. *Monaldi Arch Chest Dis* 2003;59:103–07.
- Tai A, Tran H, Roberts M, Clarke N, Wilson J, Robertson CF. The association between childhood asthma and adult chronic obstructive pulmonary disease. *Thorax* 2014;69:805–10.
- Silva GE, Sherrill DL, Guerra S, Barbee RA. Asthma as a risk factor for COPD in a longitudinal study. *Chest* 2004;126:59–65.
- Burrows B, Knudson RJ, Lebowitz MD. The relationship of childhood respiratory illness to adult obstructive airway disease 1–3. *Am Rev Respir Dis* 1977;115:751–60.
- Liberati A, Altman DG, Tetzlaff J *et al.* The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* 2009;6:e1000100.
- Omori K, Iwamoto H, Yamane T *et al.* Clinically remitted childhood asthma is associated with airflow obstruction in middle-aged adults. *Respirology* 2017;22:86–92.
- Aanerud M, Carsin AE, Sunyer J *et al.* Interaction between asthma and smoking increases the risk of adult airway obstruction. *Eur Respir J* 2015;45:635–43.
- Hirayama F, Lee AH. Association between childhood asthma and chronic obstructive pulmonary disease in later life. *Asia Pac J Public Health* 2015;27:NP1273–79.
- Chan-Yeung M, Ho AS, Cheung AH *et al.* Determinants of chronic obstructive pulmonary disease in Chinese patients in Hong Kong. *Int J Tuberc Lung Dis* 2007;11:502–07.
- Tsuda Y, Noguchi T, Mochizuki H *et al.* Patients with mild-to-moderate asthma may develop clinically significant chronic obstructive pulmonary disease. *Respirology* 2009;14:529–36.
- Svanes C, Sunyer J, Plana E *et al.* Early life origins of chronic obstructive pulmonary disease. *Thorax* 2010;65:14–20.
- Shircliffe P, Marsh S, Travers J, Weatherall M, Beasley R. Childhood asthma and GOLD-defined chronic obstructive pulmonary disease. *Intern Med* 2012;42:83–88.
- Tagiyeva N, Devereux G, Fielding S, Turner S, Douglas G. Outcomes of childhood asthma and wheezy bronchitis: a 50-year cohort study. *Am J Respir Crit Care Med* 2016;193:23–30.
- Global Initiative for Chronic Obstructive Lung Disease. *Global Strategy for the Diagnosis, Management, and Prevention of*

- Chronic Obstructive Pulmonary Disease. NHLBI/WHO Report, NHLBI Document N2701. Bethesda, MD, USA: National Institutes for Health, 2001.*
23. The Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD), The pocket guide, updated in 2014, Available from: <http://www.korektorzdrowia.pl/wp-content/uploads/gold-2014.pdf> (5 July 2018, date last accessed).
24. Tai A. Childhood asthma and chronic obstructive pulmonary disease: outcomes until the age of 50. *Curr Opin Allergy Clin Immunol* 2015;15:169–74.

Association of early history of asthma and COPD diagnosis in later life: A systematic Review and Meta-analysis.

Michael Asamoah-Boaheng^{1*}, MPhil, Lily Acheampong¹, BSc, Eric Y Tenkorang², PhD, Jamie Farrel³, MD, Alwell Oyet⁴, PhD, William K Midodzi¹, PhD.

¹Department of Clinical Epidemiology, Faculty of Medicine, Memorial University of Newfoundland, Canada, ²Department of Sociology, Memorial University of Newfoundland, Canada, ³Faculty of Medicine, Memorial University of Newfoundland, Canada, ⁴Department of Mathematics and Statistics, Memorial University of Newfoundland, Canada.

Appendix S1- Search string in the three databases

Database	Search string
PubMed	("Pulmonary Disease, Chronic Obstructive"[Mesh] OR COPD[tiab] OR "chronic obstructive pulmonary disease"[tiab]) AND ("Asthma"[Mesh] OR asthma*[tiab]) AND (child*[tiab] OR history[tiab]) AND (relationship[tiab] OR association[tiab] OR "Risk Factors"[Mesh] OR "risk factor"[tiab] OR "risk factors"[tiab])
Embase	('chronic obstructive lung disease'/de OR copd:ab,ti OR 'chronic obstructive pulmonary disease':ab,ti) AND ('asthma'/exp OR asthma*:ab,ti) AND (child*:ab,ti OR history:ab,ti OR previous*:ab,ti) AND ('risk factor'/exp OR 'risk factor':ab,ti OR 'risk factors':ab,ti)
Cinahl	(MH "Pulmonary Disease, Chronic Obstructive+" OR TI COPD OR AB COPD OR TI "chronic obstructive pulmonary disease" OR AB "chronic obstructive pulmonary disease") AND (MH "Asthma+" OR TI asthma OR AB asthma) AND (TI child* OR AB child* OR TI history OR AB history OR TI previous* OR AB previous*) AND (MH "Risk Factors" OR TI "risk factor" OR AB "risk factor" OR TI "risk factors" OR AB "risk factors")

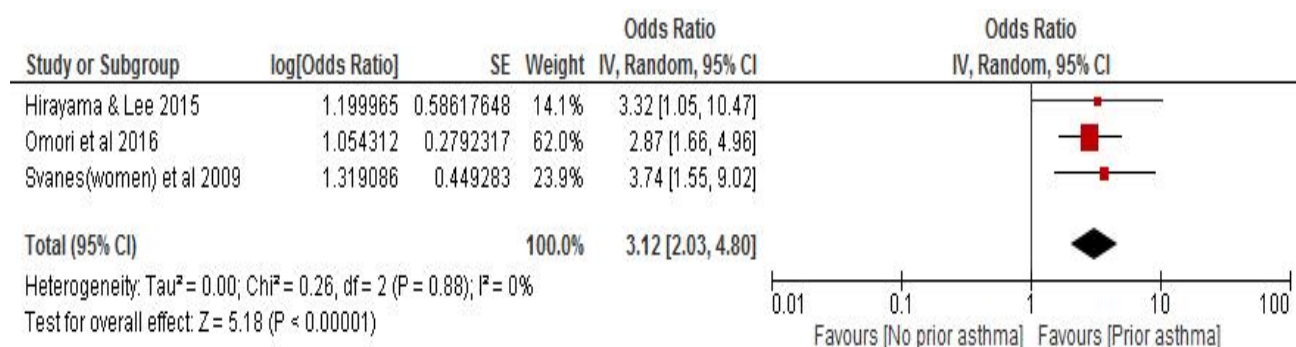


Figure S1- Forest plot of sensitivity analysis after removing studies with odds ratio greater than 8.00

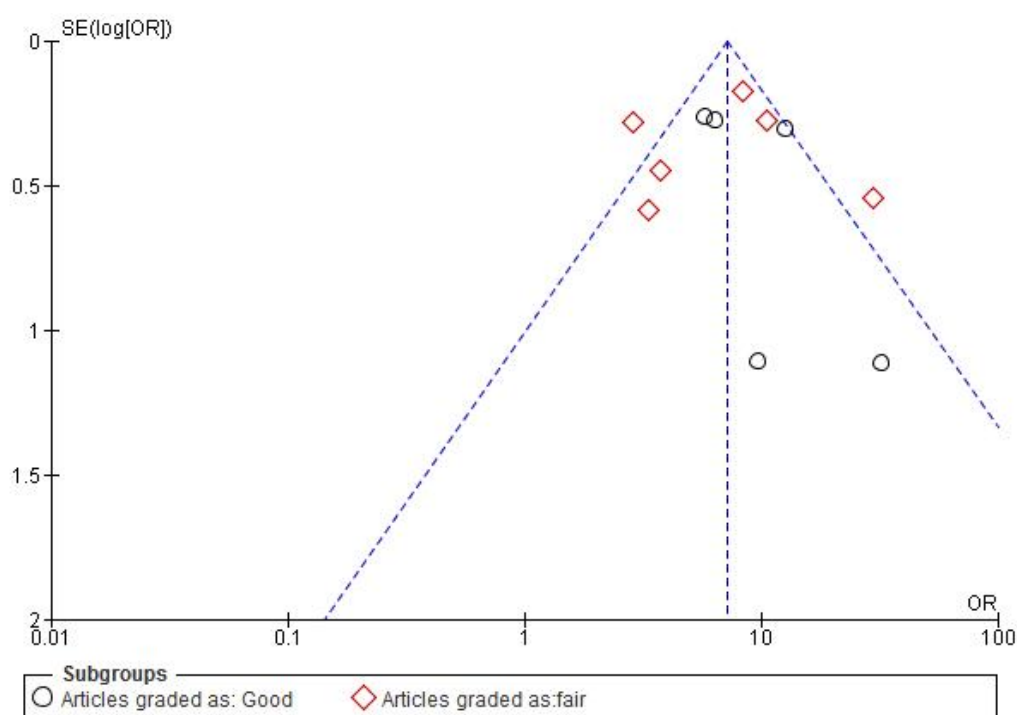


Figure S2- Publication bias check for assessing whether a prior history of asthma increases the likelihood of developing COPD (Subgroup analysis by Study Quality Grading)

Table S1: Summary studies included in meta-analysis

Article	Exposure variable	Study type	Exposed group		Unexposed group		Results
			Events	Total	Events	Total	
Aanerud et al (2015)	Late-onset asthma (>10 years, never-smokers)	Cohort	118	425	192	425	OR: 11.21, 95% CI (6.75-18.60)
Tai et al (2014)a	Severe asthma	Cohort	15	34	1	48	OR: 31.9,95%CI(3.4-269)
Tai et al (2014)	Asthma	Cohort	8	49	1	48	OR: 9.6,95%CI(1.0-77)
Tagiyeva et al (2016)a	Childhood asthma(1964 wheeze group)			135		820	OR: 5.79,95%CI(3.44-9.73)
Tagiyeva et al (2016)	Childhood asthma(2001 wheeze group)			135		637	OR: 6.37,95%CI(3.73-10.9)
Hirayama and Lee, 2015	Childhood asthma	Case control	17	268	8	336	OR:3.32, 95%CI(1.05, 10.45), p=0.04
Tsuda et al (2009)	History of asthma	Case control	30	49	5	98	OR:29.4, 95%CI(10.1, 85.4)
Omori et al (2016)	Remitted Childhood asthma	Case control	15	287	199	9154	OR:2.87, 95%CI(1.66, 4.96), p=<0.001
Omori et al (2016)a	Adult-onset asthma	Case control	51	354	199	9154	OR: 8.32, 95% CI(5.91,11.71), p=<0.001
Svanes(men) et al (2009)	Childhood asthma	Mixed(cross sectional &cohort		0		0	OR: 10.48, 95% CI: (6.10 to 18.03), p=<0.001
Svanes(women) et al (2010)	Childhood asthma	Mixed(cross sectional &cohort		0		0	OR: 3.74, 95% CI: (1.55 to 9.02),P=0.003

Table S2: Test for funnel plot asymmetry

Egger's regression	
Intercept	0.28688
Standard error	1.23329
95% lower limit (2-tailed)	-2.50302
95% upper limit (2-tailed)	3.07678
t-value	0.23261
df	9.00000
P-value (1-tailed)	0.41063
P-value (2-tailed)	0.82127
Begg and Mazumdar rank correlation	
Kendall's S statistics (P-Q)	-1.00000
Kendall's tau without continuity correction	
Tau	-0.01818
z-value for tau	0.07785
P-value (1 tailed)	0.46897
P-value (2-tailed)	0.93795
<i>Kendall's tau with continuity correction</i>	
Tau	0.00000
z-value for tau	0.00000
P-value (1 tailed)	0.50000
P-value (2-tailed)	1.00000