Identifying risk factors for developing COPD and adult-onset asthma: an umbrella review

Supplementary materials

PRISMA checklist

Full search strategy

Amendments to protocol

Supplementary Table S1 – Full characteristics of all included studies regarding adult-onset asthma

Supplementary Table S2 – Full characteristics of all included studies regarding COPD

PRISMA checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	p.1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	/
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	p.2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	p.3
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	p.3
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	p.3
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	p.3
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	p.3
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	p.3
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	p.3
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	/
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	p.3
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	p.4
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	/
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	/
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	p.4

Section and Topic	Item #	Checklist item	Location where item is reported
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	p.3
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	/
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	/
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	p.3
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	p.3
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	p.4
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	p.4
Study characteristics	17	Cite each included study and present its characteristics.	p.5/6/7/8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	p.5/6/7/8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	P.14/15/Supplementary material
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	p.9/10/11/12
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	p.9/10/11/12
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	/
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	/
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	p.5/6/7/8
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	p.4
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	p.16/17
	23b	Discuss any limitations of the evidence included in the review.	p.17
	23c	Discuss any limitations of the review processes used.	p.17

Section and Topic	Item #	Checklist item	Location where item is reported
	23d	Discuss implications of the results for practice, policy, and future research.	p.18
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	p.3
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	p.3
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Supplemental information
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	/
Competing interests	26	Declare any competing interests of review authors.	/
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	/

Amendments to protocol

As compared to the registered protocol on PROSPERO, the following was changed;

- Lung cancer was omitted due to feasibility
- The title was changed, due to the removal of lung cancer
- The review question, inclusion criteria, and search strategy were all amended to remove lung cancer
- The second screening was done by a second reviewer for 10% instead of for all articles

Search strategy

"asthma"[Title] OR "COPD"[Title] OR "chronic obstructive pulmonary disease"[Title] OR "emphysema"[Title] OR "COAD"[Title] OR "Chronic obstructive airway disease"[Title] OR "chronic obstructive lung disease"[Title] OR "chronic bronchitis"[Title] OR “Pulmonary Disease, Chronic Obstructive/epidemiology”[MeSH] OR “Pulmonary Disease, Chronic Obstructive/etiology”[MeSH] OR “Asthma/epidemiology”[MeSH] OR “Asthma/etiology”[MeSH]

AND "risk"[Title/Abstract] OR "determinant"[Title/Abstract] OR “predictor”[Title/Abstract] OR “risk factors”[MeSH]

AND “systematic review” [Title/Abstract] OR “meta-analysis”[Title/Abstract] OR “meta analysis”[Title/Abstract]

AND "English"[Language]

Supplementary Table S1 – Full characteristics of all included studies regarding adult-onset asthma

Author, year	Number studies included	Total n participants	Review year range	Study setting (pop, age range)	Risk factor(s)	Meta-analysis (y/n)	Main findings	JBI Score	Adult-onset asthma (diagnosis)	Quantitative measure
Wang, Zhou & Zhi, 2023	3 on asthma in adults	35,467	2020-2021	1 in Europe, 1 in North America, 1 in Middle East. Age range 18-65	Exposure to greenness	Not for studies in adults	Results are contradictory. Of the 3 studies, 1 showed greenness exposure increased asthma risk, 1 showed exposure to greenness not associated with asthma but with poor lung function, and 1 showed green space and home gardening to be protective factors against asthma	10	Not specified	Not given
Mikkelsen et al., 2022	17	4,333,364	2016-2021	16 in Europe, 1 in South America. Age range 18+, one study 16+	Various. Body mass index, puberty timing, linoleic acid, vitamin b12, folate, iron, smoking, alcohol consumption	Yes, not for all risk factors	A higher BMI and early puberty increase asthma risk. Lifetime smoking, alcohol consumption, late puberty, and linolic acid seem to be protective factors. Vitamin B12, iron, and folate intake are not significant.	7	Yes	Summary risk ratio, BMI: 1.05 per kg/m2 increase in BMI 95%CI 1.03,1.07), Puberty: early vs average 1.10 (95%CI 1.04,1.15), late vs average 0.93 (95%CI 0.90,0.96), vitamin B12 per 100pg/ml 0.99 (95%CI 0.95,1.04), folate per 10 ng/ml 0.80(95%CI 0.43,1.21), Iron per SD increase in iron micromol/L 0.92 (95%CI 0.67,1.25), linoleic acid per SD increased LA 0.89 (95%CI 0.85,0.93), alcohol per 1 unit/week higher intake 0.95(95%CI 0.91,0.99), smoking lifetime 0.97 (95%CI 0.96,0.99)
Macan et al., 2022	22 on asthma in humans	19,740	1996-2016	19 in Europe, 1 in North America, 1 in South America, 1 in both Europe and North America. Age range 18+; Hairdressers	Persulphates	No	Persulphates were associated with asthma in hairdressers, in particular bleaching products.	8	Yes, occupational asthma	Not given
Sio & Chew, 2021	289, 171 in meta-analysis	Not specified	1993-2021	all in Asia, age range unspecified	Wide range	Yes	Most frequently reported asthma risk factors were housing-related factors, including the presence of mold, mold spots, mold odor, cockroach, water damage, and incense burning, the random-effect pooled OR ranged from 1.43 to 1.73. Other risk factors with significant pooled OR for asthma development included male gender (1.30, 95% CI: 1.23–1.38), cigarette smoke exposure (1.44, 95% CI: 1.30–1.60), cigarette smoking (1.66, 95% CI: 1.44–1.90), body mass index (BMI)–related parameters (pooled OR ranged from 1.06 to 2.02), various types of air pollution (NO2, PM10, and O3; pooled OR ranged from 1.03 to 1.22)	8	No, no distiction between childhood and adult asthma	Pooled ORs: housing related factors range from 1.43 to 1.73, male gender 1.30 (95%CI 1.23,1.38), cigarette smoke exposure 1.44(95%CI 1.30,1.60), cigarette smoking 1.66(95%CI 1.44,1.90), BMI related parameters ranging from 1.06 to 2.02 for increased BMI
Romero Starke et al., 2021	14, 12 on asthma	100,975	1996-2021	10 from North America, 2 from Europe. Age range 20-68	Healthcare workers exposed to cleaning and disinfection agents	Yes	The review found a 67% increased risk of new-onset asthma for nurses compared with the nonexposed comparison group and a 43% increased risk of new-onset asthma for nurses who cleaned or disinfected surfaces. Nurses	11	Yes, 6 studies used new-asthma onset, after starting the jon, or as asthma starting since the start of cohort. 4 used current asthma, defined as having had asthma in	Pooled RR of nurses reporting new onset asthma was 1.67 (1.11-2.50). For nurses exposed to cleaning or disenficting surfaces was 1.43 (1.09-1.89). For nurses exposed to intrument

							who cleaned or disinfected instruments had a 34% increased risk of new-onset asthma. Nurses exposed to bleach or glutaraldehyde in the workplace had, respectively, 2.4- and 1.9-times increased risk of asthma than their nonexposed counterparts.		the previous 12 months (2), as ever having had asthma (1), or having asthma at present time (1 study). 2 used work related asthma symptoms.	cleaning/disinfection/sterilization the pooled RR was 1.59 (1.19-2.13).
Yu et al., 2020	13, 5 in adults	2,174	2003-2015	3 in Asia, 2 in Western countries. Age range unknown.	Formaldehyde exposure	Yes	A significantly increased risk of asthma in adults with high concentrations of FA exposure was found. However, this increased risk was not found for exposure to low concentration levels.	11	Unlcear, based on ever having asthma or taking asthma medication currently.	High exposure to FA associated with an increased risk of asthma (OR 1.81 (1.18-2.78)
Chen, Sun & Wu, 2020	36, 27 in adults	49,198	1987-2018	10 in Europe, 4 in Africa, 4 in Asia, 4 Middle East, 2 in North America, 3 Oceania. Age range 18-117	Zinc and selenium levels	Yes, only meta-analysis	The current meta-analysis provides evidence that lower circulating Zn and Se levels are associated with an increased risk of asthma.	10	Unclear whether onset is in adulthood, cases were asthma patients if they were diagnosed according to global initiative for asthma guidelines.	Asthma patients had lower Zn (standardized mean difference = -0.26 (-0.40, -0.13)) and Se (SMD = -0.06 (-0.13, 0.02))
Rodriguez et al., 2019	70, 9 in adults	13,471	2001-2016	3 in Africa, 2 in Europe, 2 in South America, 2 in Asia. Age range unknown, just older than 18	Urban-rural differences	Yes	Overall, these findings provide evidence that urban residence and urbanisation are important determinants of asthma prevalence but do not permit us to identify which aspects of the urbanisation process are most important as determinants of risk due to most of the studies exploring the effects of urbanisation on asthma have used the simple urban–rural approach.	8	Unclear, not mentioned	Doctor diagnosis: OR 1.89 (1.47, 2.41)
Zhang et al., 2019	17		1994-2015	10 in Europe, 5 in Asia, 2 in North America. Age range 15-65	Organic dust exposure	Yes	Based on the studies evaluated, our meta-analysis results prompt that organic dust exposure is a risk factor inducing asthma, although precise analysis focus on specific organic dust materials is still warranted.	9	No, seems more about prevalence	Summary estimates; OR 1.48 (1.26-1.75) for organic dust exposure and asthma. Specifically: paper/wood 1.62 (1.38, 1.90), flour/grain 1.48 (1.11, 1.97), and textile dust 1.50 (1.08, 2.09).
Shen et al., 2018	2 in adults	7,572	2004-2015	2 in Europe. 1 study pop aged 31, 1 study pop aged 20-25	Early life vitamin D deficiency	Yes	No statistaclly significant association	9	Unclear, had to be diagnosed by doctors and required the use of asthma medication	0.57 (0.35, 0.93)
Vincent, Parker & Maier, 2017	21	Unknown	1994-2015	Unknown	Cleaning products	No	The evidence linking exposure to cleaning agents as a risk factor for causing new onset asthma is limited	6	Age of onset not specified	NA
Cong et al., 2017	26, 11 in adults	25,587,163	1996-2015	7 in Asia, 7 in North America, 5 in Oceania, 4 in Europe, 3 in South America, total age range 0-87	Temperature changes	Yes	However, there was no increased risk for adults when the temperature dropped	8	Risk of asthma is defined as asthma incidence or pre-existing asthma onset, which comes from self-reported or hospital/national recorded.	1.002 (0.93, 1.08)
Wiggans, Evans, Fishwick & Barber, 2016	55, 54 in results	191,144	1981-2013	30 in Europe, 6 in Asia, 2 in Middle East, 1 in South America, 7 in North America, 2 in Africa, 5 in Oceania, 1 unkown. Unknown age range	Wood dust	No	Work in this sector was associated with a significantly increased risk of respiratory symptoms and asthma.	8	Varying definition across studies. However, all related to exposure to dust whilst working so assuming all adult-onset	Only 1 with RR: 1.5 (1.25, 1.87) for asthma in woodworkers compared to the general population
Uphoff et al., 2015	183, of which 39 in adults, 25 mixed	14,233,434	1994-2013	15 in Europe, 4 in North America, 2 from Asia, 5 from	Socioeconomic position	Yes	Low SEP is associated with asthma	8	Unclear, some interview based, some doctor diagnosed. Nowhere	1.38 (1.37, 1.39)

				Oceania, 6 from South America, 3 from Africa, 22 unkown, 3 in multiple countries. Age range 18-70+					specified whether the asthma is adult-onset	
Tan et al., 2015	12, of which 5 adult onset	1,958	1992-2012	3 in Europe, 1 in Oceania, 1 in Asia. Age range 33.9-47.4	Risk factors associated with age of onset	Yes	The key findings of this review show that adults with late-onset current asthma are more likely to be female (58-75%), smokers (56%).	8	Yes. 5 studies used active, late-onset asthma. Asthma definitions included survey-reported asthma; physician-diagnosed asthma and spirometrically diagnosed asthma.	Not given
Nurmatov et al., 2015	30 on development of Asthma, 9 in adults	Unknown	1995-2012	6 in Europe, 2 in Asia, 1 in North America. Age range 15-89	Volatile organic compounds	No	The results of the effect on VOC's on the development of asthma are inconsistent.	9	Not specified	Not given
Lieberoth et al., 2014	7	22,996	2000-2013	All in Europe or North America. Age range 18-33, 2 at follow up starting 11 and 13.	Age at menarche	Yes	Early menarche (<12) appears to be associated with increased risk of asthma.	8	Post-menarchal asthma, defined as asthma, either by selfreport of asthma or self-report of diagnosed asthma.	1.37 (1.15, 1.64)
Kakutani et al., 2014	14, 7 in adults	3,329	1996-2007	6 in Europe, 1 in Oceania. Age range 16-72	Arachidonic acid intake	No	The results seem to suggest that ARA exposure is not consistently associated with asthma risk.	8	Mixed; 1 used newly diagnosed adult asthma patients, 4 used physician diagnosis, 1 used interviewer-administered questionnaire, 1 used self-reported questionnaire	Not given
Doust et al., 2014	23, 12 in adults	86,214	1995-2009	2 from Asia, 2 from Africa, 2 from South America, 2 from North America, 1 from Middle East, 1 in Europe, 1 in Oceania, 1 multiple. Age range not mentioned in review, just adults.	Pesticide exposure	No	The results were suggestive of potentially adverse associations between pesticide exposure and an increased likelihood of wheezing symptoms and asthma, with the evidence being stronger for an association in children than in adults.	7	2 specificy adult-onset, rest does not	Mixed OR, ranging from 0.41 (0.15, 1.11) to 2.12 (1.19, 3.75) and 3.67 (1.19, 11.3)
Sharpe et al., 2014	17, 4 in adults	3,910	2001-2012	2 in Oceania, 1 in Asia, 1 in north america. Age range all ages - 45	Exposure to indoor fungi	Yes	Exposure to certein species of fungi might increase the risk of developing asthma. However, current studies do not embrace the full extent of indoor fungal diversity and exposure to other allergenic fungi.	9	In the 4 studies in adults, 2 used wheeze for less than 12 months, spirometry plus bronchial hyperreactivity to methacholine and clinical activity to diagnose asthma, 1 used self-reported questionnaire for receiving medical treatment for bronchial asthma, and 1 used doctor-diagnosed asthma and allergy defined at interview to obtain information on doctor-diagnosed asthma and allergies, asthma symptoms in the past year, and current asthma medication use.	1 gave OR :1.25 (0.99-1.58)
Mu et al., 2014	17, 5 in adults	42,88	1998-2009	5 in Europe, age range unknown	Birth weight	Yes	These results suggest that low birth weight (<2,500 g) is associated with increased risk of asthma both in children and adults and may serve as a mediator between prenatal	9	Unclear what age diagnosis was	1,25 (1.12, 1.39) with birth weight >2500g, 1.25 (1.12, 1.40) compared to birth weight 2500-4000g

							influences and later disease risk; but high birth weight (>4,000 g) was not associated with increased risk of asthma.			
Folletti, Zock, Moscato & Siracusa, 2014	24	79,505	1975-2008	All in westernized countries, age range 20-59	Cleaning work/products	No	Increased risk of asthma or rhinitis has been shown in 79% of included epidemiological studies.	6	Asthma based on symptoms. Age of onset unclear.	OR's mainly between 1.5 and 3
Canova, Jarvis, Walker & Cullinan, 2013	27, 9 in adults	12,502	1994-2011	8 in Europe, 1 in Asia Age range 18+	Domestic paints	No	The variable quality of the exposure assignment and heterogeneous study design makes it difficult to draw firm conclusions on whether domestic paint exposures cause or exacerbate asthma in adults.	7	Not clear	OR for current asthma 1.6 (1.0, 2.5)
Baur, Bakehe & Vellguth, 2012	474 in total, 407 on asthma	Unknown	Up untill June 2012	No information	Workplace irritants	No	There is evidence that long-term exposure to workplace irritant could increase asthma development	7	Occupational asthma; episodes of shorteness of breath due to particular occupational environment and reversible airflow limitation	Not given
Etminan et al., 2009	18, 6 including adults	91,12	2000-2008	4 in Europe, 1 in US, 1 in Africa. Age range till 70 approx. (not given for all studies).	Acetaminophen use	Yes	The results of our review are consistent with an increase in the risk of asthma and wheezing in adults exposed to acetaminophen.	10	Not specified	Pooled OR 1.63 (1.46, 1.77)
Takkouche, González-Barcala, Etminan & Fitzgerald, 2008	32 total, 4 in adults	1,423	1993-2003	Regions not in paper, age >18	Exposure to furry pets	Yes, only meta-analysis	In adults, the evidence regarding either an increased or decreased risk of asthma when exposed to furry pets seems inconclusive and more research is needed	8	Diagnosis of asthma present, age of onset unknown	RR for exposure to cats; 1.22 (0.33, 4.52) & 1.59 (0.35, 7.08), for any pet 1.58 (0.99, 2.54) & 1.70 (1.27, 2.28)
Jaakkola & Knight, 2008	10 in adults	2,486	1975-2006	6 from North America, 4 from Europe. Age range 21-63	Exposure to Phthalates	Yes	Heated PVC fumes possibly contribute to development of asthma in adults.	6	Not specified, however it exposure was based on job category	OR 1.55 (1.18, 2.05)
Beuther & Sutherland, 2007	7	333,102	1999-2004	All in Europe or North America. Age range 18+	BMI	Yes, only meta-analysis	Higher BMI is associated with a dose-dependent increase in the odds of developing asthma in men and women	8	Asthma development in adults	Compared to normal weight, obesity and overweight had an OR of 1.51 (1.27, 1.80). OR normal weight vs overweight 1.38 (1.17, 1.62), normal vs obesity 1.92 (1.43, 2.59)
Jaakkola et al., 2006	19, 2 in adults	5,607	1998-2001	Both in Europe. Age range 20-31	Preterm delivery	Yes	Premature babies seem to have an increased risk of developing asthma later in life. However, the results in adults are inconclusive.	8	Age of onset unknown	OR of 1.86 (0.23, 12.0) and 1.14 (0.92, 1.40)
Flaherman & Rutherford, 2006	12, 2 including adults	8,511	2002-2003	1 in Europe, 1 in North America. Age range 18-31	High childhood BMI	Yes, only meta-analysis	High body weight in childhood seems to increase the risk of asthma later in life. However, in adults results are not conclusive.	7	Both adult onset.	OR of high body weight during middle childhood 1.32 (0.82, 2.4). Effect of high birth weight OR 1.26 (0.88, 1.82).

Supplementary Table S2 – Full characteristics of all included studies regarding COPD

Author, year	N primary studies included	Total n participants	Review year range	Study setting (pop, age range)	Risk factor(s)	Meta-analysis (y/n)	Main findings	JBI Score	Quantitative measure
Njoku et al., 2023	21 on risk factors	27,192	2004-2020	All in Africa, age range 32-60	Various. Biomass burning, smoking, tuberculosis, older age, wheeze, asthma, sex, ethnicity, BMI, living in urban areas, educational level, occupational exposure to dusts gases or fumes	Yes, for risk factors examined in 5 or more studies	Smoking, previous tuberculosis, use of biomass fuels, older age, wheeze, and asthma were associated with increased COPD risk.	9	ORs for previous TB (OR 5.98, 95%CI 4.18,8.56), smoking (OR 2.80, 95%CI 2.19,3.59), use of biomass fuel (OR 1.52, 95%CI 1.39,1.67).
Adeloye et al., 2022	162 in total, unclear how many on risk factors	Unclear	1990-2019	Studies from all continents, distribution unclear. Age range 30-79	Sex, age, smoking status, second-hand tobacco smoke, biomass exposure, occupational exposure to dust or smoke, BMI, previous respiratory illness, socioeconomic status, education level, urban vs. rural	Yes	For almost all included risk factors, associations with COPD were found.	6	Pooled Ors; Male 2.1 (95%CI 1.9,2.3), age per 10 years increase when <50 1.5 (95%CI1.3,1.5), 50-59 2.1(95%CI 1.8,2.6), older than 60 4.2(95%CI 3.1,5.6), smoking status all vs non smokers; current smoker 3.2(95%CI 2.5,4.0), former smoker 2.1(95%CI 1.8,2.4), ever smoker 2.3(95%CI 2.0,2.5), pet 10-unit increase in pack-years if <20 1.3 (95%CI 1.2,1.3), more than 20 pack years 3.2 (95%CI 2.1,4.7), second-hand tobacco smoke 1.2(95%CI 1.0,1.4), biomass exposure 1.4(95%CI 1.2,1.7), occupational exposure to dust or smoke 1.4(95%CI 1.3,1.6), BMI compared to BMI 20-24; <18.5 2.2(95%CI 1.7,2.7), more than 25 0.9 (95%CI 0.8,0.9), child hospital admission for severe respiratory illness 1.9(95%CI 1.5,2.4), family histroy of obstructive airway disease 1.6(95%CI 1.4,1.9), asthma 2.6(95%CI 1.6,4.1), tuberculosis 2.8(95%CI 1.9,4.0), education vs no education; college or higher 0.8(95%CI 0.7,0.9), middle or high school 1.1 (95%CI 0.9,1.2), primary or no education 1.5(95%CI 1.0,2.1), urban 1.2(95%CI 1.0,1.5), rural 1.4(95%CI 1.3,1.6).
Awokola et al., 2022	27	17,566	1997-2019	All in Africa, mean age range between 38 and 80.	Increasing age, biomass exposure ,smoking	Yes	An increased prevalence of COPD was associated with increasing age, smoking and biomass smoke exposure.	10	Pooled OR only for current smoking vs. never smoking 2.20 (95%CI 1.62,2.99)
Pando-Sandoval et al., 2022	20	909,067	2002-2017	In Europe, in North America, in South America, in Asia, and in Africa. All in never smokers.	Exploratory in never-smokers	No	Increased COPD risk was associated with exposure to biomass, occupational exposure and passive smoking to having a history of asthma, tuberculosis or respiratory infections during childhood.	5	Max and min OR per factor: occupation 4.5-1.26, Biomass 3.94-1.09, Passive smoking 3.94-1.31, Asthma 10.621-4.24, Tuberculosis 4.5-3.66, Respiratory infections in childhood 4.80-3.075, Radon 1.03
Budhathoki et al., 2021	13	24,963	2003-2019	All in Nepal, age range unavailable	Gender, literacy rate, occupation, smoking status, primary cooking	Yes	Smoking and traditional firewood cooking were identified as major risk factors	6	Proportions

					methods, ethnicity, marital status, and area of residence				
Chen et al., 2021	20	995,190	2005-2020	All in China, age range unspecified	Various (PM exposure, smoking history, passive smoking history, sex, exposure to biomass burning, childhood respiratory infections, drinking history, residence, and family history)	Yes	All included factors, except drinking history, were found to be risk factors for COPD in the Chinese population	8	Pooled ORs; Exposure to PM2.5 1.73(95%CI 1.16,2.58), smoking history 2.58(95%CI 2.00,3.32), Passive smoking history 1.39(95%CI 1.03,1.87), male sex 1.70(95%CI 1.31,2.22), BMI <18.5 1.73(95%CI 1.32,2.25), BMI >28 0.96(95%CI 0.76,1.22), biomass exposure 1.65(95%CI 1.32,2.06), childhood respiratory infection 3.44(95%CI 1.33,8.90), residence 1.24 (95%CI 1.09,1.42), family history of respiratory disease 2.04(95%CI 1.53,2.71), and drinking history 0.82(95%CI 0.54,1.23)
Duan et al., 2021	30	795,935	2004-2020	4 in Asia, 5 in Oceania, 11 in Europe, 8 in North America, 1 in Middle East, 1 in various countries. Aged older than 40, except for 1 (mean age 36).	Early life exposures	Yes	Childhood respiratory disease, maltreatment, maternal smoking and low birth weight increase the risk of COPD. Furthermore, subgroup analyses revealed that probability was increased for only women with childhood physical abuse, sexual abuse and exposure to intimate partner violence.	11	OR childhood serious respiratory infections 2.23 (1.63, 3.07), childhood asthma 3.45 (2.37, 5.02), maternal smoking 1.42 (1.17, 1.72), child maltreatment 1.30 (1.18, 1.42), low birth weight 1.58 (1.08, 2.32). No association: childhood environmental tobacco smoke exposure 1.30 (0.83, 1.61) or premature birth 1.17 (0.87, 1.58).
van Iersel, Beijers, Gosker & Schols, 2021	89	673,616	1983-2021	33 from Europe, 17 from Asia, 22 from North America, 3 from the Middle East, 1 from Oceania, 2 from South America, 1 from Africa, 1 unknown. Age range unknown	Nutrition	No	The unhealthy Western-style diet is associated with an increased risk of COPD and an accelerated decline of pulmonary function. Consumption of processed meat was associated with higher COPD risk.	8	Not given
Kamal et al., 2021	12	9,986	1994-2013	5 in Europe, 4 in Asia, 2 in South America, 1 in Middle east. Age range unknown, all in women.	Indoor biomass burning	Yes, only meta-analysis	The present meta-data analysis has shown that household air pollutants may be a factor associated with increased risk of COPD in women.	9	OR 3.16 (1.82, 5.49) for women exposed to different fuels
Park et al., 2021	7	2,643,686	2011-2018	Studies from USA, Canada, Europe, and Taiwan, unknown age range	PM2.5, PM10, NO2	Yes	Exposure to higher levels of PM2.5 significantly increased the incidence of COPD. Exposure to NO2 showed a marginal association with the risk of COPD development. No significant association with PM10	10	A 10 µg/m3 increase in PM2.5 associated with pooled HR 1.18 (1.13, 1.23). Same increase NO2 pooled HR 1.07 (1.00, 1.16). PM10 HR 0.95 (0.83, 1.08)
Zhang et al., 2021	30	1,578,449	2000-2019	7 from North America, 18 in Asia, 4 in Europe, 1 in Africa, cases aged 18-89	BMI	Yes	BMI is associated with risk of COPD. Underweight might increase the risk, overweight might reduce the risk.	8	Pooled OR op COPD for underweight group 1.96 (1.78, 2.17). For overweight 0.80 (0.73, 0.87) and for the obestiy group 0.86 (0.73, 1.02).
Parvizian et al., 2020	12	290,747	2007-2019	6 from Europe, 5 from North America, 1 on Middle East. Age range 20-75	Unhealthy dietary patterns	Yes	Consumption of unhealthy dietary patterns was associated with a higher risk of COPD (OR 1.22, 95% CI 0.84–1.76); however, the results were not statistically significant and had high heterogeneity	11	OR 1.22 (0.84–1.76)
Vinnikov et al., 2020	5	18,908	2014-2019	3 in Russia, 1 in Azerbaijan & Kazakhstan, 1 in Kazakhstan	Occupational exposure to vapors, gases, dusts and fumes	Yes	The combined data from three countries included in meta-analysis, showed that occupational exposures, classified with questionnaires, increased the risk of COPD 1.69-fold.	9	OR 1.96 (1.35, 2.85) in Kazakhstan, 1.52 (1.13, 2.05) in Russia.
Xiong et al., 2020	10	54,578	2005-2019	7 from south America, 2 in Asia, 1 in Europe. Age range 31-60+	High altitude	Yes	The study found a higher prevalence of COPD at high-altitudes than those from average data. However, altitude was not found to be an independent risk factor for developing COPD	10	OR for high altitudes compared to lowlands: 1.18 (0.85, 1.62)
Cunalata-Paredes & Gea-Izquierdo, 2020	7	1,492	2012-2017	2 studies from India, 2 in Sweden, 1 in Canda, 1 in Egypt,	Multiple risk factors; smoking, passive smoking,	No	Secondhand smoking important risk factor among non-smokers, males more likely to develop COPD, older age risk factor. Nevertheless, it is followed by the presence of	6	Secondhand smoke OR 52.97 (44.65, 62.83). Low economic status 32.67 (27.94, 38.22). Biomass exposure 29.28 (25.09, 34.17). Asthma 22.01

				1 in Latin America All participants older than 65	age, low SES, biomass exposure, asthma, respiratory problems in childhood, tuberculosis,		biomass exposure, asthma, as well as respiratory problems in childhood and tuberculosis. Likewise, there was another essential association found with biomass exposure and low economic status.		(18.95, 25.57). Occupational exposure 18.68 (16.11, 21.66). Respiratory problems 16.09 (13.89, 18.63). Tuberculosis 7.91 (6.82, 9.17).
Ali, 2020	11	48,657	2007-2018	4 from Australia, 3 from USA, 2 from Japan, 1 from New Zealand, 1 from Scotland, 25-75	Childhood asthma	Yes	Overall, the odds of developing adulthood COPD in children with asthma were 3.0 times higher than that in non-asthmatic children	7	OR 3.00 (2.25, 4.00).
Peng et al., 2020	9	10,906	2009-2019	2 from Africa, 2 from Europe, 1 from Pakistan, 1 from Malaysia, 1 from the Wismut Cohort, 2 from Asia. Age range 18-84m	Occupational dust exposure	Yes, only meta-analysis	The risk of developing COPD for workers exposed to dust was 1.51 times higher than for controls (I2 = 40%, 95% confidence interval: 1.27-1.79).	10	1.51 (1.27, 1.79)
Bellou, Belbasis, Konstantinidis & Evangelou, 2019	19	518,966	2010-2016	Not specified	Occupational dust exposure, history of tuberculosis, biomass fuel smoke, tobacco smoking, traffic intensity, history of psoriasis, history of rheumatoid arthritis, waterpipe smoking, vitamin D deficiency	No	The review has shown shown that active and passive smoking, exposure to biomass fuels, history of TB and history of RA were associated with an increased risk for developing COPD	7	Biological dust OR 0.99 (0.75, 1.31). Mineral dust 0.97 (0.68, 1.39). Gases/fumes 1.03 (0.73, 1.45), TB history 3.10 (95%CI 2.24,4.31), Second hand smoking 1.56(95%CI 1.40,1.74) & 1.43(95%CI 1.24,1.65), tobacco smoking 3.90 (95%CI 3.08,4.94) & 4.28(95%CI 3.09,5.92), biomass fuel smoke 2.37(95%CI 1.72,3.26), traffic intensity on nearest road per 5000 vehicles/day increase 1.30(95%CI 0.92,1.82), traffic load on major roads within 100m per 500.000 vehicles/day increase 1.26(95%CI 0.95,1.70), history of psoriasis 1.45(95%CI 1.21,1.73), history of rheumatoid arthritis 1.99(95%CI 1.61,2.45), waterpipe smoking 3.18(95%CI 1.25,8.09), vitamin D deficiency 1.77(95%CI 1.18,2.64)
Sutradhar et al., 2019	9	9,172	2013-2017	All in Bangladesh, 1 aged 15 or older, rest aged 35 or older	All risk factors	No	Tobacco consumption, exposure to biomass fuel, old age, and history of asthma were identified as major risk factors of COPD	9	Current smokers OR 5.5 (4.2, 7.2), former smokers 4.5 (3.3, 6.0), chewing tobacco in rural women (12.9 (3.4, 49.4), biomass fuel use 5.9 (1.0, 34.5). Old age, compared to 40-49 year olds, 50 to 59 year old have an OR of 2.2 (1.6, 3.0) to develop COPD, en 60 to 69 have 4.7 (3.5, 6.4). History of asthma 6.9 (4.9, 9.5)
Pathak, Gupta & Suri, 2019	35	73,122	1991-2015	20 from Asia, 5 from Africa, 4 from South America, 3 from North America, 1 from Europe. All aged 18 or older	Indoor air pollution from biomass cooking fuel	Yes	The pooled analysis showed that exposure to indoor air pollution due to solid biomass fuels increased risk of COPD by 2.65. The results of our meta-analysis indicated that exposure to indoor air pollution due to biomass smoke is strongly associated with COPD	7	2.65 (2.13, 3.31)
Salari-Moghaddam, Milajerdi, Larijani & Esmaillzadeh, 2019	5	289,952	2007-2018	3 from the USA, 2 from Sweden. Age range 27-83	Processed red meat intake	Yes	In this systematic review and meta-analysis, they found a significant positive association between processed red meat intake and risk of COPD.	8	HR 1.08 (1.03, 1.13) with every 50 gram/week increase in processed reat meat intake
Chaudhary, Sharma & Senapati, 2019	4	252	2006-2016	Regions unknown, age range 44-79	Elevated serum homocysteine	Yes, only meta-analysis	Present meta-analysis suggested considerable risk attributed by elevated serum homocysteine in pathogenesis of COPD, however, the results were not significant	6	Mean difference with elevated serum homocysteine: 3.05
Asamoah-Boaheng et al., 2018	9 in review, 7 in meta-analysis	41,502	2007-2017	Studies from unknown countries, Age range 20 till >65,	History of Asthma	Yes	Sufficient evidence was found to suggest that individuals with previous history of asthma have an increasing likelihood of developing COPD in later life	11	OR 7.87 (5.40, 11.45)

Lee et al., 2018	28	6,768	1976-2015	9 in Asia, 8 in Europe, 7 in North America, 1 in the Middle East, 3 in multiple ecountries. Age range 16-87	Environmental tobacco smoke	Yes	Although the evidence strongly suggests that ETS is a risk factor for COPD, study weaknesses and absence of well-designed large studies preclude reliable effect estimation. More definitive evidence is required.	6	RR 1.20 (1.08, 1.34)
Zhang, Wang & Lu, 2018	28	Stated nowhere	1997-2016	12 in Europe, 9 in Asia, 3 in North America, 2 in Iran, 2 in Australia,18-89 (all ages studies too)	Exposure to nitrogen dioxide	Yes	Overall, our study reported consistent evidence of the potential positive association between NO2 and COPD risk	7	RR with a 10 µg/m3 increase in NO2: 2.0%
Guillien, Soumagne, Dalphin & Degano, 2018	22	63,572	1986-2017	Age range 24-90	Agricultural work	Yes	10 studies showed positive association, 12 showed no association.The meta-analysis demonstrates that cattle farming, swine farming and poultry farming are strongly associated with airflow limitation and chronic bronchitis. Our analysis also demonstrates for the first time that crop/grain farmers have a higher prevalence of airflow limitation and of chronic bronchitis compared with unexposed controls. However, the results concerning farmers breeding undefined livestock depend on the chosen respiratory outcome and, perhaps, on the real exposure of the different groups of farmers studied. The current meta-analysis highlights the fact that at this stage, it is not possible to draw firm conclusions regarding the relationships between farming and COPD, as there are very few studies in which COPD has been defined according to appropriate criteria.	9	OR 1.77 (1.50, 2.08)
Ma et al., 2018	6	2,146	2003-2016	3 in Europe,2 in Australia, 1 in North America. Age range 18-55	Childhood wheezing	Yes, only meta-analysis	The meta-analysis suggests an increased risk of COPD when accompanied with atopy	9	COPD prevalence: RR 5.31 (1.03, 27.27)
Zhu et al., 2018	47, 14 on risk factors	486,382	2002-2015	All in China, ages 15-99	Tobacco exposure, biomass fuel/solid fuel usage, gender, age, low BMI, family history, history of respiratory disease, occupational dust exposure, low education level,	No	All aforementioned risk factors have been shown to be important risk factors for COPD	8	Not given
Lee, Forey, Thornton & Coombs, 2018	40 in total, 7 on COPD	2,482	2004-2013	All in Japan, aged 30+	Cigarette smoking	Yes	There is an increased risk of COPD with smoking and a lesser increase with ex-smoking. However, evidence based on cross-sectional studies and doesn't provide information on amount smoked or time quit.	6	RR 3.57 (2.72, 4.70)
Yang et al., 2017	19	18,893	2008-2016	All in China, no info on age range	Wide range investigating risk factors	Yes	Twelve risk factors are associated with the occurrence of COPD in Chinese Mainland (male sex, smoking, low education level, low BMI, family history of respiratory disease, allergy history, respiratory infection during childhood, recurrent respiratory infection, occupational dust exposure, biomass burning, poor housing ventilation, and living around polluted areas)	10	Male sex OR 1.47 (1.10, 1.96), Smoking OR 2.09 (1.71, 2.57), Low education level OR 1.61 (1.21, 2.15), low BMI OR 3.83 (2.22, 6.60), family history of respiratory disease OR 2.07 (1.47, 2.92), allergy history OR 2.38 (1.39, 4.09), respiratory infection during childhood OR 2.70 (1.50, 4.83), recurrent respiratory infection OR 15.02 (4.54, 49.68), occupational dust exposure OR 1.79 (1.15, 2.79), biomass burning OR 2.22 (1.31, 3.76), poor housing ventilation OR 3.99

									(1.24, 12.82), living around polluted area OR 1.63 (1.20, 2.21)
Li, Paquet, Johnston & Williams, 2017	8	89,173	1975-2015	4 in North America, 3 in Europe, 1 in Middle East. Age range 16-72	Parental COPD	Yes	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.	9	OR 1.57 (1.29, 1.93)
Borup, Kirkesov, Hanskov & Brauer, 2017	12	627,294	1993-2016	7 in Europe, 5 in North America. Age range 20-84	Construction dust	No	The review suggests that COPD occurs more often among construction workers than among workers who are not exposed to construction dust.	9	Not given
Fontana et al., 2017	14	34,538	Up untill dec 2016	10 in Europe, 3 in Asia, 1 in USA. Age range unknown	Agricultural work	No	Farming work was associated with greater risk of developing COPD. However, considering the several variables that may influence the disease prevalence in farmers, the adoption of a standardized research strategy was suggested.	6	No overall OR or RR given
Sadhra et al., 2017	42, 29 in meta analysis	1,092,475	1989-2015	30 in Europe 7 in USA, 4 in Oceania, 1 in South Africa, 20-84 yrs	Occupational dust exposure	Yes	Overall occupational exposure to airborne pollutants as assessed by JEMs showed a 22% increased risk of COPD (diagnosed by physician or based on spirometry), which was lower compared to the risk estimate obtained by self-reported exposures. Although there was no significant difference in COPD risk estimates for individual forms of pollutants such as vapors, gases, dusts, and fumes, exposure to biological dusts appeared to confer a higher risk than that to mineral dusts.	10	Overall pooled OR: 1.22 (1.18, 1.27). Biological dust OR 1.33 (1.17, 1.51)
Su et al., 2016	24	39,327	Up untill april 2015	12 in Europe, 5 in North America, 5 in Asia, 1 in Africa, and 1 in multiple coutnries. Mean age was between 52-73.	Inflammatory markers	Yes	The findings suggested that COPD was associated with elevated serum CRP, leukocytes, IL-6, IL-8, and fibrinogen, without any significant relationship with TNF-α.	11	Elevated serum CRP standard mean difference (SMD); 1.21 (0.92, 1,50), leukocytes SMD 1.07 (0.25, 1.88), IL-6 SMD 0.90 (0.48, 1.31), IL-8 SMD 2.34 (0.69, 4.00) amd fibrinogen SMD 0.87 (0.44, 1.31).
Zheng et al., 2016	13	550,614	2002-2015	7 in USA, 3 in Asia, 3 in Europe. Age range 15-75. 15 in 1 study, rest 20+.	Dietary patterns	Yes, only meta-analysis	The highest category of healthy/prudent dietary patterns when compared with the lowest category was apparently associated with a decreased risk. An increase in the risk of chronic obstructive pulmonary disease was shown for the highest compared with the lowest categories of "unhealthy/western-style" dietary patterns.	9	OR 2.12 (1.64, 2.74)
Kamal, Srivastava & Kesavachandran, 2015	42	547,391	1991-2012	22 in Europe, 10 in Asia, 9 in North America, 1 in Oceania. Age range 15-80	Smoking	Yes, only meta-analysis	The results from this meta-analysis suggest a positive association between current smokers and the prevalence of COPD compared with former and non-smokers. The findings of the study shows evidence of smoking as a major risk factor for COPD prevalence.	10	Current vs non smokers: OR 3.26 (2.67, 3.98). Current vs former smokers OR 1.29 (1.01, 1.64)
Ryu et al., 2015	11	26,959	1991-2012	4 in USA, 3 in Europe, 1 in Africa, 1 in Asia, 1 in Australia, 1 in various countries. Age range 20-75	Exposure to vapors, gases, dusts or fumes (VGDF)	Yes, only meta-analysis	The study suggests that exposure to VGDF is associated with a higher risk of COPD.	9	Pooled OR 1.43 (1.19, 1.73)
Wang, Xiao & Wang, 2015	24	93,045	1998-2012	All in Chinese population, age range unknown	Smoking	Yes, only meta-analysis	Risk of COPD for ever smokers is higher than never smokers (OR 2.90, 95%CI 2.22 ~ 3.80). The risks of COPD are higher for male and female ever smokers than male and female never smokers, and the risk of COPD is higher for female smokersthan male smokers. The risk of COPD is higher withgreater smoking index.	6	OR ever smokers vs never smokers: 2.90 (2.22, 3.80). Stratified for gender: female ever vs never: 2.67 (2.01, 3.56), male ever vs never: 1.93 (1.35, 2.77)
Doust et al., 2014	6 out of 23	25,367	2003-2009	Countries of origin + age range not mentioned in review	Pesticide exposure	No	There was weak evidence for an association between pesticide exposure and increased likelihood op COPD.	7	OR ranging from 1.05 (0.74, 1.51) to 4.1 (2.2, 6.3). 3 contain 1 in CI.
Finney et al., 2013	17	3,673	1975-2011	All in Africa. Age range 20-90	Explorative of risk factors	No	Besides smoking, many aetiological risk factors associated with poverty, such as pre- and post-natal exposures, nutritional deficiencies, low BMI and low education levels,	8	Not given

							may put adults at risk of developing COPD at an early age. Indoor air pollution due to indoor biomass fuel burning is also an important risk factor. This review identified biomass and smoking.		
Brüske et al., 2013	27	27,261	1976-2011	Mainly USA & Europe, some in Asia, Africa, Middle-east. Age range unknown.	Biopersistent granular dust	Yes	Occupational inhalative exposure to bg-dust was associated with a statistically significant decreased FEV1 and FEV1/FVC revealing airway obstruction consistent with COPD.	7	No pooled results given
Baur, Bakehe & Vellguth, 2012	474 in total, 20 COPD	Not given	Up untill June 2012	No information	Workplace irritants	No	There is evidence that long-term exposure to workplace irritant could increase COPD development	7	Not given
Gershon, Dolmage, Stephenson & Jackson, 2012	15 total, 8 on risk for development	67,664	1996-2011	6 in Europe, 1 in North America, 1 in multiple countries. Age range 15-70	Low socioeconomic status	No	Consistent inverse associations between SES and COPD were found.	9	OR education ranging from 1.0 (0.9, 1.2) to 2.5 (1.0, 5.8). For occupation, OR ranging from 1.2 (0.6, 2.8) to 1.4 (1.1, 1.7). Income ranging from 0.8 (0.5, 1.3) to 3.7 (1.9, 7.0)
Forey, Thornton & Lee, 2011	133 for COPD	Not given	Up until 2006	60 in Europe, 36 in North America, 23 in Asia, 7 in South America, 4 in multiple countries, 3 in Oceania. Age range 15-98	Smoking	Yes	For COPD, RRs are higher for males, for studies conducted in North America, for cigarette smoking rather than any product smoking, and where the unexposed base is never smoking any product, and are markedly lower when asthma is included in the COPD definition. Risk increases with amount smoked and pack-years. Limited data show risk decreases with increasing starting age for COPD and with increasing quitting duration. No clear relationship is seen with duration of smoking.	6	OR ever smoking 2.89 (2.63, 3.17), current smoking 3.51 (3.08, 3.99), ex smoking 2.35 (2.11, 2.63). Higher for males. Compared to never smokers
Kurmi et al., 2010	23, 12 on COPD	57,220	1994-2008	4 in Europe, 4 in Asia, 3 in South America, 1 in Middle east. Age range probable older than 35, but age range not mentioned for all included studies	Indoor air pollution from solid fuel	Yes	Exposure to solid fuel smoke is consistently associated with COPD	7	OR 2.80 (1.85, 4.0)
Gan et al., 2006	11	55,709	1984-2005	5 in North America, 4 in Europe, 1 in Oceania, 1 in multiple countries. Age range 32-73	Age in female adult smokers	Yes	As female smokers age, they appear to experience an accelerated decline in FEV1% predicted compared with male smokers.	8	Not given