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

Judith C.S. Holtjer[1], Lizan D. Bloemsma[2,3,4], Rosanne J.H.C.G. Beijers[5], Merel E.B. Cornelissen[2,3,4], Bart Hilvering[2], Laura Houweling[1,2], Roel C.H. Vermeulen[1,6], George S. Downward[1,6] and Anke-Hilse Maitland-Van der Zee[2,3,4] on behalf of the P4O2 consortium

[1]Department of Environmental Epidemiology, Institute for Risk Assessment Sciences (IRAS), Utrecht University, Utrecht, The Netherlands. [2]Department of Pulmonary Medicine, Amsterdam UMC, Amsterdam, The Netherlands. [3]Amsterdam Institute for Infection and Immunity, Amsterdam, The Netherlands. [4]Amsterdam Public Health, Amsterdam, The Netherlands. [5]Department of Respiratory Medicine, NUTRIM School of Nutrition and Translational Research in Metabolism, Maastricht University Medical Centre, Maastricht, The Netherlands. [6]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands.

Corresponding author: Anke-Hilse Maitland-Van der Zee (a.h.maitland@amsterdamumc.nl)

Shareable abstract (@ERSpublications)
This umbrella review provided an overview of nongenetic risk factors for both COPD and adult-onset asthma. Commonly found factors included smoking, BMI, air pollution, early life exposures and occupational exposures. https://bit.ly/3kyeWZL

Cite this article as: Holtjer JCS, Bloemsma LD, Beijers RJHCG, *et al*. Identifying risk factors for COPD and adult-onset asthma: an umbrella review. *Eur Respir Rev* 2023; 32: 230009 [DOI: 10.1183/16000617.0009-2023].

Received: 9 Jan 2023
Accepted: 27 Feb 2023

Abstract

Background COPD and adult-onset asthma (AOA) are the most common noncommunicable respiratory diseases. To improve early identification and prevention, an overview of risk factors is needed. We therefore aimed to systematically summarise the nongenetic (exposome) risk factors for AOA and COPD. Additionally, we aimed to compare the risk factors for COPD and AOA.

Methods In this umbrella review, we searched PubMed for articles from inception until 1 February 2023 and screened the references of relevant articles. We included systematic reviews and meta-analyses of observational epidemiological studies in humans that assessed a minimum of one lifestyle or environmental risk factor for AOA or COPD.

Results In total, 75 reviews were included, of which 45 focused on risk factors for COPD, 28 on AOA and two examined both. For asthma, 43 different risk factors were identified while 45 were identified for COPD. For AOA, smoking, a high body mass index (BMI), wood dust exposure and residential chemical exposures, such as formaldehyde exposure or exposure to volatile organic compounds, were amongst the risk factors found. For COPD, smoking, ambient air pollution including nitrogen dioxide, a low BMI, indoor biomass burning, childhood asthma, occupational dust exposure and diet were amongst the risk factors found.

Conclusions Many different factors for COPD and asthma have been found, highlighting the differences and similarities. The results of this systematic review can be used to target and identify people at high risk for COPD or AOA.

Background

COPD is one of the most common chronic respiratory disorders, with a prevalence ranging from 3.6 to 10.1% [1, 2] Currently, COPD is the third leading cause of death worldwide [3], with 2–6% of global disability-adjusted life years attributed to COPD in 2015 [4]. Additionally, COPD patients are at an increased risk of developing extrapulmonary manifestations or comorbidities that highly affect disease burden, such as cardiovascular diseases and lung cancer [5, 6, 7]. Besides COPD, another 300 million children and adults globally are estimated to be suffering from asthma [8]. Even though adult-onset asthma (AOA) is less studied than childhood asthma, previous research shows that incidence has been rising over the past two decades [9]. For example, de Marco *et al*. [10] showed asthma prevalence in Italy to have increased by 38% between 1991 and 2010, irrespective of age. Distinguishing between COPD and asthma

can be difficult, especially in older adults, as the predicted forced expiratory volume in 1 s falls to 50% in both asthma and COPD patients over 60 years old [11]. Some patients with asthma develop COPD later in life and some patients with COPD show clinical features commonly observed in asthma [12]. For patients who show characteristics of both COPD and asthma, the label asthma–COPD overlap syndrome (ACOS) is being considered [13]. It has been widely reported that patients suffering from ACOS have worse disease outcomes, such as more exacerbations and a more rapid decline in lung function, than patients suffering from only asthma or COPD [13, 14, 15]. As there is considerable overlap between the two conditions, this could mean overlapping risk factors as well.

As both COPD and AOA have a high disease burden, and there is no curative treatment for COPD [16], early identification and prevention are key. To optimise prevention strategies, a better understanding of especially nongenetic risk factors for developing either condition is needed. Additionally, risk factors for childhood asthma are well established, but it is unclear how those risk factors translate to AOA. Furthermore, previous research has shown similarities in nongenetic risk factors for developing either COPD or AOA, such as smoking and high exposure to air pollution [17]. However, to our knowledge, there is currently no overview comparing risk factors for COPD and asthma. The aim of this systematic umbrella review is to provide an overview and comparison of all nongenetic risk factors for COPD and AOA, identifying similarities as well as differences.

Methods

Search strategy

We conducted an umbrella review, a systematic collection and assessment of multiple systematic reviews and meta-analyses [18]. The review was conducted according to the study protocol, registered in the International Prospective Register of Systematic Reviews (PROSPERO-CRD42021284614) and according to PRISMA guidelines. The full PRISMA checklist can be found in the supplemental material.

PubMed was systematically searched from inception to 1 February 2023 to identify systematic reviews and meta-analyses of studies examining one or multiple nongenetic risk factors for either COPD or AOA. The search strategy consisted of terms on COPD, asthma, epidemiology, aetiology, risk factors and study design (full search strategy in the supplemental material). In addition, reference lists of included papers were screened for additional relevant reviews that might have been missed during the initial search. A first screening was independently done by two researchers (J.C.S.H. and L.D.B.) based on title and abstract. Subsequently, the full text of all relevant articles was assessed for eligibility by one researcher (J.C.S.H.), with an additional researcher (M.E.B.C.) assessing a random 10% of the articles. Initial discrepancies were first discussed amongst the reviewers with a third reviewer (R.J.H.C.G.B.) being available for final decision making in case of disagreement. However, this did not occur.

Inclusion and exclusion criteria

Systematic reviews with or without meta-analyses of observational epidemiological studies, including systematic reviews of Mendelian randomisation studies, in humans that assessed nongenetic risk factors for incidence asthma or COPD were included. Regarding AOA, reviews were included regardless of specifying age of onset. Only studies available in English were included. Studies examining risk factors for either mortality, exacerbations or management of either disease were excluded. Additionally, studies examining the impact of another disease on development of either COPD or AOA were considered noneligible. When multiple analyses or reviews included the same original studies, the most recent one was included.

Data extraction

Data extraction was performed by one reviewer (J.C.S.H.), with a second reviewer (M.E.B.C.) extracting data from a random 10% for quality control purposes. From each eligible article, the authors, year of publication, examined nongenetic risk factor(s), examined outcome, number of epidemiological studies included, the total number of participants per review and the main conclusions were recorded. Additionally, for AOA it was recorded whether age of onset was specified. Study quality and risk of bias of the included reviews was checked by applying the Joanna Briggs Institute (JBI) checklist for systematic reviews and research synthesis [19]. Scores were given for every included aspect, resulting in a score ranging from 1 (poorly conducted) to 11 (well conducted). For studies without a meta-analysis, the maximum score is 10.

Results

Literature review

Our literature search identified 2040 publications. Of those, 1867 were excluded following title and abstract review (figure 1), mainly because they focused on genetic risk factors or on exacerbations or

management of disease. Additionally, one review was identified through snowballing. Of those, 99 were excluded after reviewing the full texts, resulting in 75 eligible articles included in this umbrella review. Of these, 45 focused on risk factors for COPD, 28 on asthma and two reviews included both COPD and asthma. Out of the 75 included reviews, 45 included a meta-analysis and narrative review, 12 conducted only a meta-analysis but no narrative review and 18 only included a narrative review.

Regarding AOA, 47 of the included studies mentioned COPD, addressing 45 different risk factors. A selection of characteristics of the included articles are described in tables 1 and 2 for AOA and COPD, respectively. Full characteristics are shown in tables S1 and S2. A summary of the found risk factors and their corresponding effect sizes is shown in tables 3 and 4, respectively. For both AOA and COPD, the JBI scores ranged between 5 and 11. For AOA, age of onset was not clear for all papers, with only seven specifying AOA. An additional four compared exposed *versus* nonexposed individuals within occupational settings, implying adult-onset. All were included, but this uncertainty was noted. When a meta-analysis was conducted, the meta-results are given as opposed to single-study results.

Asthma

Air pollution and chemical exposures

Eight reviews identified either chemical exposures or air pollution as risk factors for asthma [21, 27, 31, 38, 43, 46, 47, 49]. Sio and Chew [31] identified exposure to several types of air pollution, including nitrogen dioxide (NO_2), particulate matter and ozone as risk factors for AOA, with included pooled odds ratios (ORs) ranging between 1.03 and 1.22. Yu *et al*. [21] reported that high indoor residential formaldehyde exposure (>22.5 $\mu g \cdot m^{-3}$) was associated with an increased risk of asthma as compared to low exposure ($\leqslant$22.5 $\mu g \cdot m^{-3}$), with a meta OR (mOR) of 1.81 (95% CI 1.18–2.78). Moreover, Nurmatov *et al*. [27] reported that domestic exposure to volatile organic compounds (VOCs), *i.e.* aromatic VOCs, chlorinated hydrocarbons, propylene glycol and glycol ethers, alkanes, alcohols, aldehydes, ketones, and terpenes, increased asthma risk. Doust *et al*. [46] reported both occupational and nonoccupational pesticide exposure to increase asthma risk. However, there was variation in pooled estimates for pesticide exposure, ranging from 0.41 (95% CI 0.15–1.11) to 3.67 (95% CI 1.19–11.30) for exposed *versus* nonexposed, with inconsistent reporting on the type of pesticide examined. Jaakkola and Knight [47] found a high exposure

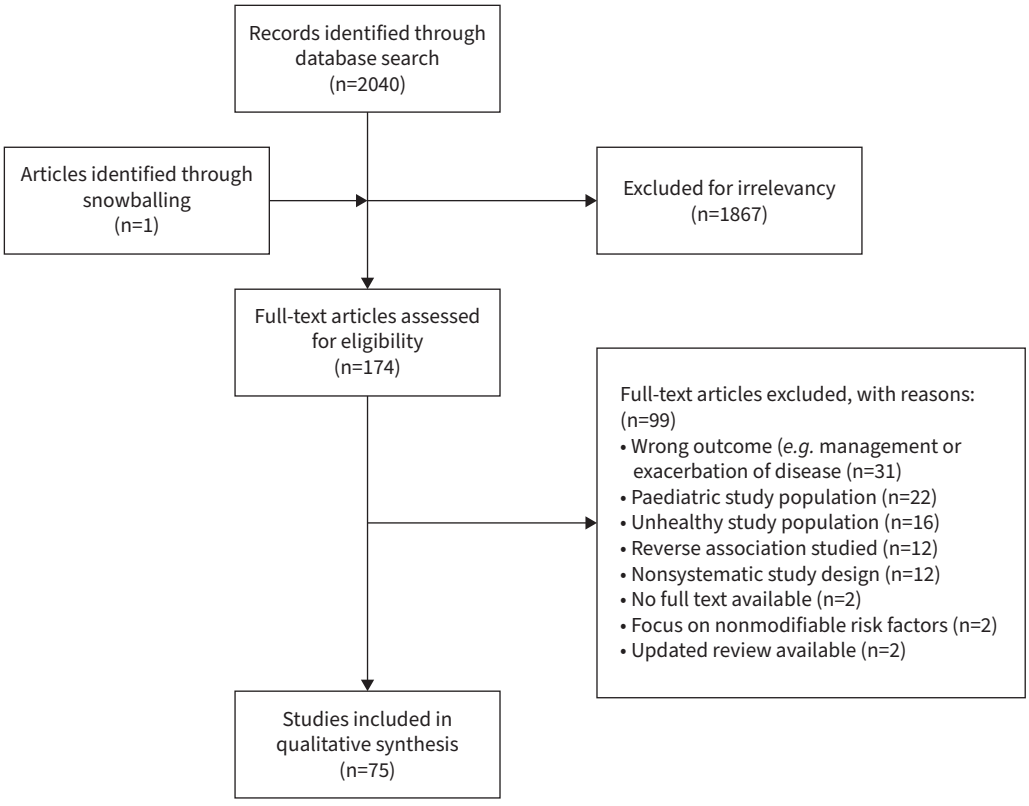

FIGURE 1 Results of the searches, screening and data extraction.

TABLE 1 Characteristics of 30 included systematic reviews for adult-onset asthma, ranked by Joanna Briggs Institute (JBI) score

Authors	Risk factor(s)	Main findings	Adult-onset asthma[#]	JBI score
Romero Starke *et al.* [20]	Occupational exposure to cleaning and disinfection agents	Nurses exposed to cleaning products to have an increased risk of asthma.	Yes	11
Yu *et al.* [21]	Formaldehyde exposure	A significantly increased risk of asthma in adults with high concentrations of formaldehyde exposure was found.	Unclear	11
Wang *et al.* [22]	Exposure to greenness	The results are contradictory, with all three included studies showing different associations.	Unclear	10
Chen *et al.* [23]	Zinc and selenium levels	The meta-analysis provides evidence that lower circulating Zn and Se levels are associated with an increased risk of asthma.	Unclear	10
Etminan *et al.* [24]	Acetaminophen use	The results are consistent with an increase in the risk of asthma in adults exposed to acetaminophen.	Unclear	10
Zhang *et al.* [25]	Organic dust exposure	The meta-analysis found organic dust exposure to be a risk factor for asthma.	No	9
Shen *et al.* [26]	Early life vitamin D deficiency	No statistically significant association between early life vitamin D deficiency and asthma development later in life was found.	Unclear	9
Nurmatov *et al.* [27]	Volatile organic compounds	The results of the effect on volatile organic compounds on the development of asthma are inconsistent.	Unclear	9
Sharpe *et al.* [28]	Exposure to indoor fungi	Exposure to certain species of fungi might increase the risk of developing asthma.	Unclear	9
Mu *et al.* [29]	Birth weight	The results suggest that low birth weight (<2500 g) is associated with increased risk of asthma both in children in adults, but high birth weight (>4000 g) was not associated with increased risk of asthma.	Unclear	9
Macan *et al.* [30]	Persulphates	Persulphates were associated with asthma in hairdressers, in particular bleaching products.	Yes	8
Sio *et al.* [31]	Wide range	The study showed housing related factors such as mould, male sex, smoke exposure and BMI-related factors to be associated with asthma.	Mixed	8
Rodriguez *et al.* [32]	Urban–rural differences	The findings provide evidence that urban residence and urbanisation are important determinants of asthma.	Unclear	8
Cong *et al.* [33]	Temperature changes	There was no increased risk for asthma development in adults when temperature dropped.	No	8
Wiggans *et al.* [34]	Wood dust	Work in this sector was associated with a significantly increased risk of respiratory symptoms and asthma.	Unclear	8
Uphoff *et al.* [35]	Socioeconomic position	Low socioeconomic position was found to be associated with asthma risk.	Unclear	8
Tan *et al.* [36]	Risk factors associated with age of onset	Adults with late-onset current asthma are more likely to be female (58–75%), smokers (56%).	Yes	8
Lieberoth *et al.* [37]	Age at menarche	Early menarche (<12 years) appears to be associated with increased risk of asthma.	Unclear	8
Kakutani *et al.* [38]	Arachidonic acid intake	The results suggest that arachidonic acid exposure is not consistently associated with asthma risk.	Mixed	8
Takkouche *et al.* [39]	Exposure to furry pets	In adults, the evidence regarding either an increased or decreased risk of asthma when exposed to furry pets is inconclusive.	Unclear	8
Beuther *et al.* [40]	BMI	Higher BMI is associated with developing asthma.	Yes	8
Jaakkola *et al.* [41]	Pre-term delivery	Premature babies seem to have an increased risk of developing asthma later in life, but the results in adults are inconclusive.	Unclear	8
Mikkelsen *et al.* [42]	Wide range	A higher BMI and early puberty increase asthma risk. Lifetime smoking, alcohol consumption, late puberty and linoleic acid seem to be protective factors. Vitamin B12, iron and folate intake are not significant.	Yes	7
Canova *et al.* [43]	Domestic paints	The variable quality of the exposure assignment makes it difficult to draw firm conclusions on whether there is an association.	Unclear	7
Baur *et al.* [44]	Workplace irritants	There is evidence that long-term exposure to workplace irritants could increase asthma development.	Unclear	7
Flaherman *et al.* [45]	High childhood BMI	High body weight in childhood seems to increase the risk of asthma later in life. However, in adults, results are not conclusive.	Yes	7
Doust *et al.* [46]	Pesticide exposure	The results were suggestive of potentially adverse associations between pesticide exposure and an increased likelihood of asthma.	Mixed	7

Continued

TABLE 1 Continued

Authors	Risk factor(s)	Main findings	Adult-onset asthma[#]	JBI score
Jaakkola *et al.* [47]	Exposure to phthalates	Heated PVC fumes possibly contribute to development of asthma in adults.	Unclear	6
Folletti *et al.* [48]	Cleaning work/products	Increased risk of asthma has been shown when exposed to cleaning products.	Unclear	6
Vincent *et al.* [49]	Cleaning products	The evidence linking exposure to cleaning agents as a risk factor for causing new onset asthma is limited.	No	6

[#]Adult-onset asthma indicates whether the study specifies if the target group had adult-onset asthma or whether it is asthma in adults. BMI: body mass index; PVC: polyvinyl chloride.

to phthalates, such as heated polyvinyl chloride fumes, increased asthma risk, with an mOR of 1.55 (95% CI 1.18–2.05). Canova *et al.* [43] found that domestic paint use was associated with asthma, with one study providing an OR of 1.60 (95% CI 1.00–2.50). The final two reviews did not find either consistent or significant results. Vincent *et al.* [49] did not find significant associations between exposure to cleaning products and an increased risk of asthma. The review by Kakutani *et al.* [38] did not show arachidonic acid intake to be consistently associated with asthma.

Early life exposures

Four reviews identified early life factors as risk factors for asthma later in life [26, 29, 41, 45]. First, a review by Flaherman and Rutherford [45] identified that both a high weight during middle childhood (body mass index (BMI) ⩾85th percentile for age and gender) (mOR 1.32, 95% CI 0.82–2.40) and high birth weight (⩾3.8 kg) (mOR 1.26, 95% CI 0.88–1.82) could increase the risk of asthma. Jaakkola *et al.* [41] identified pre-term delivery as a possible risk factor, with ORs of included studies ranging between 1.86 (95% CI 0.23–12.00) and 1.14 (95% CI 0.92–1.40). However, these results were not statistically significant. Mu *et al.* [29] reported low birth weight to be a risk factor, with a birth weight of <2500 g to be associated with a higher risk of asthma (mOR 1.25, 95% CI 1.12–1.40) as compared to babies with a birth weight between 2500 and 4000 g. Lastly, Shen *et al.* [26] studied early life vitamin D deficiency and risk of asthma later in life, but found no statistically significant association (mOR 0.57, 95% CI 0.35–0.93).

Nutrition and weight status

Four reviews focused on nutritional or weight-related risk factors [23, 31, 40, 42]. Beuther and Sutherland [40] found that compared to a healthy BMI, overweight and obese participants had mORs of 1.38 (95% CI 1.17–1.62) and 1.92 (95% CI 1.43–2.59) for developing asthma, respectively. This is in accordance with Sio and Chew [31], who found an mOR of 2.02 (95% CI 1.63–2.50) for participants with a BMI of ⩾30 $kg \cdot m^{-2}$. Additionally, Mikkelsen *et al.* [42] found a meta risk ratio (mRR) of 1.05 (95% CI 1.03–1.07) per $kg \cdot m^{-2}$ increase in BMI. Chen *et al.* [23] identified lower zinc and selenium plasma levels as possible risk factors for asthma, with a standardised mean difference (SMD) between asthma patients and healthy controls of −0.26 (95% CI −0.40–−0.13) for zinc and −0.06 (95% CI −0.13–0.02) for selenium. However, they did not provide which unit they standardised to.

Occupational exposures

Six reviews examined occupational risk factors for asthma [20, 25, 30, 34, 44, 48]. Romero Starke *et al.* [20] focused on healthcare workers exposed to cleaning products with an mRR of 1.67 (95% CI 1.11–2.50) among nurses exposed to different types of cleaning products compared to unexposed nurses. Folletti *et al.* [48] also reported cleaning workers to be at an increased risk, with ORs of the included studies ranging between 1.50 and 3.00. Baur *et al.* [44] reported exposure to workplace irritants, such as chloride, led to an increased asthma risk. Wiggans *et al.* [34] reported wood dust exposure in wood workers to increase asthma risk, with only one study providing a risk ratio of 1.53 (95% CI 1.25–1.87) as compared to the general population. Furthermore, Zhang *et al.* [25] identified exposure to organic dust when compared to healthy individuals to increase asthma risk in different occupations. They found associations with paper/wood dust (mOR 1.62, 95% CI 1.38–1.90), flour/grain (mOR 1.48, 95% CI 1.11–1.97) and textile dust (mOR 1.50, 95% CI 1.08–2.09). Lastly, Macan *et al.* [30] found that exposure to persulphates, such as hair bleach, was associated with asthma in hairdressers.

TABLE 2 Characteristics of 47 included systematic reviews for COPD, ranked by Joanna Briggs Institute (JBI) score

Authors	Risk factor(s)	Main findings	JBI score
Duan *et al.* [50]	Early life exposures	Childhood respiratory disease, maltreatment, maternal smoking and low birth weight increase the risk of COPD development.	11
Parvizian *et al.* [51]	Unhealthy dietary patterns	Unhealthy dietary patterns seemed to be associated with a higher risk of COPD; however, the meta-analysis was not statistically significant. Healthy dietary patterns were associated with a reduced risk.	11
Asamoah-Boaheng *et al.* [52]	History of asthma	Individuals with a previous history of asthma were found to have an increasing likelihood of developing COPD in later life.	11
Su *et al.* [53]	Inflammatory markers	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
Awokola *et al.* [54]	Age, biomass exposure, smoking	An increased prevalence of COPD was associated with increasing age, smoking and biomass smoke exposure.	10
Kamal *et al.* [55]	Smoking	The results suggest a positive association between current smokers and the prevalence of COPD compared with former and nonsmokers.	10
Sadhra *et al.* [56]	Occupational dust exposure	Overall occupational exposure to airborne pollutants as assessed by JEMs reported an increased risk of COPD.	10
Yang *et al.* [57]	Wide range investigating risk factors	12 risk factors were found to be associated with the occurrence of COPD on the 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
Peng *et al.* [58]	Occupational dust exposure	Being exposed to occupational dust was found to increase COPD risk.	10
Xiong *et al.* [59]	High altitude	The meta-analysis found a higher prevalence of COPD at high altitudes.	10
Park *et al.* [60]	$PM_{2.5}$, PM_{10}, NO_2	Both higher $PM_{2.5}$ and NO_2 levels were shown to increase risk of COPD. No association was found for PM_{10}.	10
Njoku *et al.* [61]	Wide range	Smoking, previous tuberculosis, use of biomass fuels, older age, wheeze and asthma were associated with increased COPD risk.	9
Gershon *et al.* [62]	Low SES	The study found consistent inverse associations between SES and COPD prevalence.	9
Zheng *et al.* [63]	Dietary patterns	An increase in the risk of COPD development was shown for the highest compared with the lowest categories of “unhealthy/ Western-style” dietary patterns.	9
Ryu *et al.* [64]	Exposure to VGDFs	The study suggests that exposure to VGDFs is associated with a higher risk of COPD development.	9
Li *et al.* [65]	Parental COPD	The prevalence of COPD in adult offspring of people with COPD is greater than population-based estimates, showing that parental COPD is associated with COPD development in offspring.	9
Borup *et al.* [66]	Construction dust	The review suggests that COPD occurs more often among construction workers than among workers who are not exposed to construction dust.	9
Guillien *et al.* [67]	Agricultural work	The meta-analysis reported that cattle farming, swine farming and poultry farming are strongly associated with airflow limitation and chronic bronchitis. However, the results were inconsistent	9
Ma *et al.* [68]	Childhood wheezing	The results suggest an association between childhood wheezing and an increased risk of COPD.	9
Kamal *et al.* [69]	Indoor biomass burning	The meta-data analysis has shown that household air pollutants may be a factor associated with increased risk of COPD in women.	9
Sutradhar *et al.* [70]	All risk factors	Tobacco consumption, exposure to biomass fuel, old age and history of asthma were identified as major risk factors for COPD development.	9
Vinnikov *et al.* [71]	Occupational exposure to VGDFs	The study reported occupational exposure to VGDFs increased the risk of COPD.	9
Chen *et al.* [72]	Wide range	PM exposure, smoking history, passive smoking history, sex, exposure to biomass burning, childhood respiratory infections and family history were found to be risk factors for COPD in the Chinese population	8

Continued

TABLE 2 Continued

Authors	Risk factor(s)	Main findings	JBI score
van Iersel *et al.* [73]	Nutrition	A high dietary intake of red and/or processed meats, refined grains, sweets, desserts and French fries are associated with an increased risk of COPD.	8
Zhang *et al.* [74]	BMI	The study reported underweight might increase the risk of COPD development, where being overweight might reduce the risk.	8
Gan *et al.* [75]	Age in female adult smokers	As female smokers age, they appear to be at higher risk of developing COPD when compared to male smokers.	8
Finney *et al.* [76]	Exploration of risk factors	The current study identified biomass burning and smoking as risk factors for COPD development.	8
Zhu *et al.* [77]	Tobacco exposure, biomass fuel/solid fuel usage, gender, age, low BMI, family history, history of respiratory disease, occupational dust exposure, low education level	The study found all aforementioned risk factors to be important risk factors for COPD development.	8
Salari-Moghaddam *et al.* [78]	Processed red meat intake	The meta-analysis found a positive association between processed red meat intake and risk of COPD development.	8
Bellou *et al.* [79]	Environmental risk factors	The review showed that active and passive smoking, exposure to biomass fuels, history of tuberculosis and history of rheumatoid arthritis were associated with COPD.	7
Ali [80]	Childhood asthma	Children with asthma were found to be at risk of developing COPD later in life.	7
Pathak *et al.* [81]	Indoor air pollution from biomass cooking fuel	Exposure to indoor air pollution due to solid biomass fuels was associated with an increased risk of COPD.	7
Zhang *et al.* [82]	Exposure to nitrogen dioxide	The study found consistent evidence of the positive association between NO_2 exposure and COPD risk.	7
Kurmi *et al.* [83]	Indoor air pollution from solid fuel	Exposure to solid fuel smoke was found to be consistently associated with COPD development.	7
Doust *et al.* [46]	Pesticide exposure	There was weak evidence for an association between pesticide exposure and increased likelihood of COPD.	7
Brüske *et al.* [84]	Bio persistent granular dust	Exposure to impersistent granular dust was associated with COPD development.	7
Baur *et al.* [44]	Workplace irritants	There is evidence that long-term exposure to workplace irritants could increase COPD development.	7
Adeloye *et al.* [85]	Wide range	Male sex, age, smoking status, second-hand tobacco smoke, biomass exposure, occupational exposure to dust or smoke, BMI, previous respiratory illness, SES, education level and area of living were associated with COPD.	6
Budhathoki *et al.* [86]	Smoking and traditional firewood cooking	Smoking and traditional firewood cooking were identified as major risk factors for COPD	6
Lee *et al.* [87]	Cigarette smoking	An increased risk of COPD development with current smoking and a lesser increase with ex-smoking was found.	6
Fontana *et al.* [88]	Agricultural work	The review found farming work to be associated with a greater risk of developing COPD.	6
Wang *et al.* [89]	Smoking	Risk of COPD for ever-smokers is higher than the risk of COPD development in never-smokers.	6
Forey *et al.* [90]	Smoking	The risk of male smokers seems to be higher than female smokers, as well as the risk of cigarette smoking as compared to smoking other products.	6
Chaudhary *et al.* [91]	Elevated serum homocysteine	Elevated serum homocysteine was found to contribute to risk of COPD development.	6
Lee *et al.* [92]	ETS	The evidence suggests that exposure to ETS is a risk factor for COPD development.	6
Cunalata-Paredes *et al.* [93]	Wide range	The study found associations with second-hand smoking, male sex, older age, biomass exposure, asthma, respiratory problems in childhood and tuberculosis and COPD development.	5
Pando-Sandoval *et al.* [94]	Wide range in never-smokers	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

BMI: body mass index; CRP: c-reactive protein; ETS: environmental tobacco smoke; IL: interleukin; PM: particulate matter; JEM: job exposure matrix; SES: socioeconomic status; TNF-α: tumour necrosis factor-α; VGDFs: vapours, gases, dusts or fumes.

Physiological, personal and socioeconomic characteristics

Of the included reviews, 11 studied either physiological, personal, or socioeconomic risk factors [22, 24, 28, 31–33, 35–37, 39, 42]. Wang *et al*. [22] examined exposure to greenness as a risk factor for asthma, but found contradicting results, with one of their included studies finding an increased asthma risk, one finding exposure to greenness to be a protective factor and one not showing an association. Etminan *et al*. [24] found acetaminophen use was associated with an increased risk of asthma when compared to nonexposed individuals (mOR 1.63, 95% CI 1.46–1.77). Four studies focused on aspects of the home environment [28, 31, 32, 39]. The first, by Rodriguez *et al*. [32], compared participants living in urban environments to participants in rural environments and found people living in urban areas to have an increased asthma risk (mOR 1.89, 95% CI 1.47–2.41). The second, by Sharpe *et al*. [28], reported that exposure to indoor fungi from the *Penicillium*, *Aspergillus* and *Cladosporium* species, could increase asthma risk when compared to individuals with lower exposure. However, an OR was only given for one of the included studies (1.25, 95% CI 0.99–1.58). The third, by Takkouche *et al*. [39], examined having furry pets indoors as a risk factor for asthma and found an mOR for exposure to any pet of 1.58 (95% CI 0.99–2.54). The fourth, by Sio and Chew [31], found household factors such as mould to be associated with asthma, with ORs of the included studies ranging between 1.43 and 1.73. Cong *et al*. [33] investigated the effect of ambient temperature drops on asthma risk, per 1°C decrease, but found no significant results (mOR 1.00, 95% CI 0.93–1.08). Furthermore, Uphoff *et al*. [35] found a lower socioeconomic status (SES) to be associated with increased asthma risk (mOR 1.38, 95% CI 1.37–1.39). Tan *et al*. [36] reported that participants with late-onset asthma were more likely to be female (58–75%) and smokers (56%), while Sio and Chew [31] found males to be at an increased risk (mOR 1.30, 95% CI 1.23–1.38). Both Mikkelsen *et al*. [42] and Sio and Chew [31] examined smoking as a risk factor, with the former finding it a protective factor (risk ratio 0.97, 95% CI 0.96–0.99) and the latter finding an association with an increased asthma risk (mOR 1.66, 95% CI 1.44–1.90). However, Mikkelsen *et al*. [42] only included two papers on smoking, with the other included paper finding smoking to be associated with an increased asthma risk. Additionally, Sio and Chew [31] found an association with second-hand smoke exposure (mOR 1.44, 95% CI 1.30–1.60) [31]. Mikkelsen *et al*. [42] found early as compared to average age at puberty to be a risk factor (mRR 1.37, 95% CI 1.15–1.64), where late *versus* average age at puberty was found to be a protective factor (mRR 0.93, 95% CI 0.90–0.96) [42]. Lastly, Lieberoth *et al*. [37] found a younger age at menarche to be associated with asthma risk (mOR 1.37, 95% CI 1.15–1.64).

COPD

Air pollution and chemical exposures

We identified 19 reviews, studying six different risk factors [46, 54, 57, 60, 61, 64, 69, 70, 72, 76, 77, 79, 81–83, 85, 86, 93, 94]. Park *et al*. [60] found an association between exposure to ambient fine particulate matter ($PM_{2.5}$) and COPD (meta hazard ratio (mHR) 1.18, 95% CI 1.13–1.23) per 10 $\mu g \cdot m^{-3}$ increase, which was also found by Chen *et al*. [72] (mOR 1.73, 95% CI 1.16–2.58). Additionally, they found significant associations between NO_2 and COPD, which was also found by Zhang *et al*. [82], with a 10 $\mu g \cdot m^{-3}$ increase in NO_2 being associated with an mHR of 1.07 (95% CI 1.00–1.16) [60] and an mRR of 1.02, respectively. Indoor air pollution caused by indoor biomass burning was found to be a risk factor for COPD in several reviews [54, 57, 61, 69, 70, 72, 76, 77, 79, 81, 83, 85, 86, 93, 94]. Found mORs ranged between 1.52 (95% CI 1.39–1.67), found by Njoku *et al*. [61] and 3.16 (95% CI 1.82–5.49), found by Kamal *et al*. [69], when compared to unexposed controls. Doust *et al*. [46] identified both occupational and nonoccupational pesticide exposure as a possible risk factor, with ORs of the included studies ranging from 1.05 (95% CI 0.74–1.51) to 4.10 (95% CI 2.20–6.30) for exposed *versus* nonexposed individuals, with inconsistent reporting on the type of pesticide examined. Yang *et al*. [57] reported living in polluted areas, defined as areas with high levels of outdoor air pollution, as a risk factor for COPD, with an mOR of 1.63 (95% CI 1.20–2.21). Lastly, Ryu *et al*. [64] reported being exposed to vapours, gases, dusts and fumes to increase COPD risk (mOR 1.43, 95% CI 1.19–1.73).

Early life exposures

12 reviews identified risk factors in early life [50, 52, 57, 68, 70, 72, 80, 85, 92, 93, 94]. Six of these focused on respiratory problems in early life and COPD risk [50, 57, 72, 85, 93, 94], with found mORs ranging between 2.23 (95% CI 1.63–3.07) [50] and 3.44 (95% CI 1.33–8.90) [72]. Additionally, Duan *et al*. [50] identified childhood asthma (mOR 3.45, 95% CI 2.37–5.02), maternal smoking during both pregnancy and childhood (mOR 1.42, 95% CI 1.17–1.72), child maltreatment, *e.g.* physical abuse (mOR 1.30, 95% CI 1.18–1.42), and low birth weight (mOR 1.58, 95% CI 1.08–2.32) as risk factors for COPD. They did not find statistical significant associations for childhood environmental tobacco smoke exposure (mOR 1.30, 95% CI 0.83–1.61), which is in accordance with results found by Lee *et al*. [92] (mRR 0.88, 95% CI 0.72–1.07), or premature birth (mOR 1.17, 95% CI 0.87–1.58) [50]. Childhood asthma was found to be a risk factor by Sutradhar *et al*. [70], Ali [80] and Asamoah-Boaheng *et al*. [52], with, respectively,

TABLE 3 Overview of the identified risk factors for adult-onset asthma, and their corresponding effect sizes

Category	Risk factor	Number of reviews	Effect measure	Effect size (95% CI), reference
Air pollution and chemical exposures	Indoor formaldehyde exposure	1	OR	1.81 (1.18–2.78) [21]
	VOC exposure	1	NA	NA [27]
	Air pollution (NO_2, PM_{10}, O_3)	1	OR	Range: 1.03–1.22 [31]
	Pesticide exposure	1	OR	Range: 0.41 (0.15–1.11)–3.67 (1.19–11.30) [46]
	Phthalate exposure	1	OR	1.55 (1.18–2.05) [47]
	Domestic paint exposure	1	OR	1.60 (1.00–2.50) [43]
	Arachidonic acid intake	1	NA	NA [38]
	Domestic cleaning products	1	NA	NA [49]
Early life exposures	Low birth weight	1	OR	1.25 (1.12–1.40) [29]
	Early life vitamin D deficiency	1	OR	0.57 (0.35–0.93) [26]
	High birth weight	1	OR	1.26 (0.88–1.82) [45]
	High weight during childhood	1	OR	1.32 (0.82–2.40) [45]
	Pre-term delivery	1	OR	Range: 1.86 (0.23–12.00)–1.14 (0.92–1.40) [41]
Nutrition and weight status	BMI between 25 and 29.9 $kg \cdot m^{-2}$	1	OR	1.38 (1.17–1.62) [40]
	BMI $\geqslant$30 $kg \cdot m^{-2}$	2	OR	1.92 (1.43–2.59) [40]; 2.02 (1.63–2.50) [31]
	BMI per $kg \cdot m^{-2}$ increase	1	Risk ratio	1.05 (1.03–1.07) [42]
	Vitamin B12	1	Risk ratio	0.99 (0.95–1.04) [42]
	Iron	1	Risk ratio	0.92 (0.67–1.25) [42]
	Folate	1	Risk ratio	0.80 (0.43–1.21) [42]
	Linoleic acid	1	Risk ratio	0.89 (0.85–0.93) [42]
	Alcohol intake	1	Risk ratio	0.95 (0.91–0.99) [42]
	Zinc plasma levels	1	SMD	−0.26 (−0.40– −0.13) [23]
	Selenium plasma levels	1	SMD	−0.06 (−0.13–0.02) [23]
Occupational exposures	Cleaning products	2	Risk ratio/OR	Risk ratio: 1.67 (1.11–2.50) [20]; OR range: 1.50–3.00 [48]
	Workplace irritants	1	NA	NA [44]
	Wood dust exposure	1	Risk ratio	1.53 (1.25–1.87) [34]
	Organic dust (wood, textile, *etc.*)	1	OR	Paper/wood: 1.62 (1.38–1.90); flour/grain: 1.48 (1.11–1.97); textile: 1.50 (1.08–2.09) [25]
	Persulphates (*e.g.* hair bleach)	1	NA	NA [30]
Physiological, personal and socioeconomic characteristics	Younger age at menarche	1	OR	1.37 (1.15–1.64) [37]
	Age at puberty: early *versus* average	1	Risk ratio	1.10 (1.04–1.15) [42]
	Age at puberty: late *versus* average	1	Risk ratio	0.93 (0.90–0.96) [42]
	Smoking	3	Percentage/risk ratio/OR	56% [36]; 0.97 (0.96–0.99) (risk ratio) [42]; 1.66 (1.44–1.90) (OR) [31]
	Second-hand smoke	1	OR	1.44 (1.30–1.60) [31]
	Housing-related factors, *e.g.* mould	1	OR	Range: 1.43–1.73 [31]
	Acetaminophen use	1	OR	1.63 (1.46–1.77) [24]
	Living in urban areas	1	OR	1.89 (1.47–2.41) [32]
	Low SES	1	OR	1.38 (1.37–1.39) [35]
	Female sex	1	Percentage	58–75% [36]
	Male sex	1	OR	1.30 (1.23–1.38) [31]
	Indoor fungi exposure	1	OR	1.25 (0.99–1.58) [28]
	Temperature drops	1	OR	1.00 (0.93–1.08) [33]
	Indoor furry pets	1	OR	1.58 (0.99–2.54) [39]
	Exposure to greenness	1	NA	NA [22]

95% confidence intervals are given when available. BMI: body mass index; NA: not assigned, indicates studies without a meta-analysis and without effect sizes; PM: particulate matter; SES: socioeconomic status; SMD: standardised mean difference; VOC: volatile organic compound.

an OR of 6.90 (95% CI 4.90–9.50), an mOR of 3.00 (95% CI 2.25–4.00) and an mOR of 7.87 (95% CI 5.40–11.45). Lastly, Ma *et al*. [68] found childhood wheeze to increase the risk of COPD later in life (mRR 5.31, 95% CI 1.03–27.27).

Nutrition and weight status

10 reviews identified nutritional factors or weight-related aspects as risk factors for COPD [51, 57, 63, 72–74, 76, 78, 79, 85], of which five studies identified having a low BMI as a risk factor for COPD [57, 72, 74, 76, 85]. The found mORs ranged from 1.96 (95% CI 1.78–2.17), found by Zhang *et al*. [74],

TABLE 4 Overview of the identified risk factors for COPD and their corresponding effect sizes

Category	Risk factor	Number of reviews	Effect measure	Effect size (95% CI)
Air pollution and chemical exposures	NO_2 exposure	2	HR/risk ratio	HR: 1.07 (1.00–1.16) [60]; risk ratio: 1.02 [82]
	Ambient $PM_{2.5}$ exposure	2	HR/OR	HR: 1.18 (1.13–1.23) [60]; OR: 1.73 (1.16–2.58) [72]
	Indoor biomass burning	15	OR	Range from 1.52 (1.39–1.67) [61] to 3.16 (1.82–5.49) [69]
	Pesticide exposure	1	OR	Range from 1.05 (0.74–1.51) to 4.10 (2.20–6.30) [46]
	Living in polluted areas	1	OR	1.63 (1.20–2.21) [57]
	VGDF exposure	1	OR	1.43 (1.19–1.73) [64]
Early life exposures	Low birth weight	1	OR	1.58 (1.08–2.32) [50]
	Childhood wheeze	1	Risk ratio	5.31 (1.03–27.27) [68]
	Early life respiratory problems	6	OR	Range from 2.23 (1.63–3.07) [50] to 3.44 (1.33–8.90) [72]
	Childhood asthma	4	OR	Range from 3.00 (2.25–4.0) [80] to 7.87 (5.40–11.45) [52]
	Child maltreatment	1	OR	1.30 (1.18–1.42) [50]
	Childhood environmental tobacco smoke exposure	2	OR/risk ratio	OR: 1.30 (0.83–1.61) [50]; risk ratio: 0.88 (0.72–1.07) [92]
	Maternal smoking	1	OR	1.42 (1.17–1.72) [50]
	Pre-term birth	1	OR	1.17 (0.087–1.58) [50]
Nutrition and weight status	BMI between 25.0 and 29.9 $kg \cdot m^{-2}$	3	OR	Range from 0.80 (0.73–0.87) [74] to 0.96 (0.76–1.22) [72]
	BMI $\geqslant$30 $kg \cdot m^{-2}$	1	OR	0.86 (0.73–1.02) [74]
	Low BMI	5	OR	Range from 3.83 (2.22–6.60) [57] to 1.96 (1.78–2.17) [74]
	Consumption of red meat	2	HR	1.08 (1.03–1.13) [78]
	Western style/unhealthy diet	3	OR	2.12 (1.64–2.74) [63], 1.22 (0.84–1.76) [51]
	Vitamin D deficiency	1	OR	1.77 (1.18–2.64) [79]
	Drinking history	1	OR	0.82 (0.54–1.23) [72]
	Healthy diet	1	OR	0.88 (0.82–0.94) [51]
Occupational exposures	Dust exposure (wood, mineral)	11	OR	Range from 0.97 (0.68–1.39) [79] to 1.79 (1.15–2.79) [57]
	Workplace irritants	1	NA	NA [44]
	Agricultural work	2	OR	1.77 (1.50–2.08) [67]
Physiological, personal, and socioeconomic characteristics	Smoking	12	OR	Range from 2.89 (2.63–3.17) [90] to 5.50 (4.20–7.20) [70]
	Second-hand smoke	6	Risk ratio/OR	Range from 1.20 (1.08–1.34) [92] to 1.56 (1.40–1.74) [79]
	Chewing tobacco	1	OR	12.90 (3.40–49.40) [70]
	Parental COPD	4	OR	1.57 (1.29–1.93) [65], 2.07 (1.47–2.92) [57]
	Recurrent respiratory infections	1	OR	15.02 (4.54–49.68) [57]
	History of rheumatoid arthritis	1	OR	1.99 (1.61–2.45) [79]
	History of psoriasis	1	OR	1.45 (1.21–1.73) [79]
	History of tuberculosis	4	OR	2.80 (1.90–4.00) [85], 5.98 (4.18–8.56) [61]
	Waterpipe smoking	1	OR	3.18 (1.25–8.09) [79]
	Poor housing ventilation	1	OR	3.99 (1.24–12.82) [57]
	Low SES	5	OR	Range from 0.80 (0.50–1.30) [62] to 1.61 (1.21–2.15) [57]
	Age	4	OR	Range from 1.50 (1.30–1.50) [85] to 4.70 (3.50–6.40) [70]
	Male sex	3	OR	Range from 1.47 (1.10–1.96) [57] to 2.10 (1.90–2.30) [85]
	Serum homocysteine	1	MD	3.05 [91]
	Inflammatory markers in serum	1	SMD	Range from 0.87 (0.44–1.31) [53] to 2.34 (0.69–4.00) [53]
	Traffic intensity	1	OR	1.26 (0.95–1.70) [79], 1.30 (0.92–1.82) [79]
	Living at high altitudes	1	OR	1.18 (0.85–1.62) [59]
	Living in urban areas	1	OR	1.20 (1.00–1.50) [85]
	Living in rural areas	1	OR	1.40 (1.30–1.60) [85]

95% confidence intervals are given when available. BMI: body mass index; HR: hazard ratio; PM: particulate matter; (S)MD: (standardised) mean difference; NA: not assigned, indicates studies without a meta-analysis and without effect sizes; SES: socioeconomic status; VGDF: vapours, gases, dusts and fumes.

to 3.83 (95% CI 2.22–6.60), found by YANG *et al.* [57]. Additionally, ZHANG *et al.* [74] found an association between COPD and overweight (mOR 0.80, 95% CI 0.73–0.87) and obese (mOR 0.86, 95% CI 0.73–1.02) participants, but found it to be a protective factor, which was also found by ADELOYE *et al.* [85] (mOR 0.90, 95% CI 0.80–0.90). CHEN *et al.* [72] found an mOR of 0.96 (95% CI 0.76–1.22) for participants with a BMI >28 $kg \cdot m^{-2}$.

Both VAN IERSEL *et al.* [73] and ZHENG *et al.* [63] identified a Western-style diet, characterised by a high intake of refined grains, red and processed meat, saturated fats, sweets, and desserts, as a risk factor for COPD, with the latter providing an mOR of 2.12 (95% CI 1.64–2.74) [63]. PARVIZIAN *et al.* [51] studied unhealthy dietary patterns, *i.e.* Western diets and diets high in carbohydrates, but the results were not statistically significant (mOR 1.22, 95% CI 0.84–1.76). Additionally, they found a healthy dietary pattern, *i.e.* high in fruit and vegetables, to reduce COPD risk (mOR 0.88, 95% CI 0.82–0.94)) [51]. BELLOU *et al.* [79] found vitamin D deficiency to be a risk factor for COPD (mOR 1.77, 95% CI 1.18–2.64). CHEN *et al.* [72] identified drinking history as a risk factor and found an mOR of 0.82 (95% CI 0.54–1.23). Drinking history was not further defined. Lastly, both VAN IERSEL *et al.* [73] and SALARI-MOGHADDAM *et al.* [78] identified high consumption of red and processed meat as a risk factor for COPD, with the latter finding an mHR of 1.08 (95% CI 1.03–1.13) for every 50 g increase per week in intake.

Occupational exposures

11 reviews identified occupational exposures associated with an increased risk of COPD [44, 56–58, 66, 67, 71, 79, 84, 88, 93]. Eight of those studies found that workers exposed to dust as compared to nonexposed had an increased risk of COPD [56–58, 66, 71, 79, 84, 93], with found mORs ranging from 0.97 (95% CI 0.68–1.39) by BELLOU *et al.* [79] to 1.79 (95% CI 1.15–2.79), found by YANG *et al.* [57]. Both GUILLIEN *et al.* [67] and FONTANA *et al.* [88] found an association between COPD and agricultural work, with only the former providing an mOR of 1.77 (95% CI 1.50–2.08) [67]. Lastly, BAUR *et al.* [44] found an association between workplace irritants, such as chloride or welding fumes, and COPD.

Physiological, personal and socioeconomic characteristics

Physiological, personal and socioeconomic risk factors for COPD were examined by 20 reviews [53–55, 57, 59, 61, 62, 65, 70, 72, 75, 76, 79, 85–87, 89–91, 93]. 12 reviews identified active smoking as the main risk factor for COPD [54, 55, 57, 61, 70, 72, 79, 85–87, 89, 90] and six identified second-hand smoking to be a risk factor [72, 79, 85, 92–94]. Regarding active smoking, found mORs ranged from 2.89 (95% CI 2.63–3.17), found by FOREY *et al.* [90], to 5.50 (95% CI 4.20–7.20), found by SUTRADHAR *et al.* [70]. Regarding second-hand smoke exposure, found risk estimates range from an mRR of 1.20 (95% CI 1.08–1.34) found by LEE *et al.* [92], to an mOR of 1.56 (95% CI 1.40–1.74) [79]. SUTRADHAR *et al.* [70] found women who chewed tobacco to be at an increased risk for COPD (OR 12.90, 95% CI 3.40–49.40) [70]. BELLOU *et al.* [79] identified waterpipe smoking as a risk factor (mOR 3.18, 95% CI 1.25–8.09).

Five studies identified having a low SES as a risk factor [57, 62, 76, 85, 93], with an mOR of 1.61 (95% CI 1.21–2.15) found by YANG *et al.* [57], using an education level of ⩽9 years as a proxy for low SES, and ORs ranging from 0.80 (95% CI 0.50–1.30) to 3.70 (95% CI 1.90–7.00) in included studies in the review by GERSHON *et al.* [62], using measures such as education, occupation and income as proxies for SES.

Additionally, four reviews identified older age as a risk factor [54, 70, 75, 85]. The first, by SUTRADHAR *et al.* [70], found that compared to 40–49-year-old participants, participants aged 50–59 and 60–69 years have an OR of 2.20 (95% CI 1.60–3.00) and 4.70 (95% CI 3.50–6.40), respectively. The second, by GAN *et al.* [75] found that with age, female smokers have a greater incline in lung function. The third, by ADELOYE *et al.* [85] found that under the age of 50 years, COPD risk increased with an mOR of 1.50 (1.30–1.50) per 10-year increase, as well as an increased risk in participants aged 50–59 (mOR 2.10, 95% CI 1.80–2.60) and older than 60 (mOR 4.2, 95% CI 3.10–5.60).

Two reviews identified biomarkers as risk factors [53, 91]. CHAUDHARY *et al.* [91] found an association between elevated serum homocysteine and COPD risk (mean difference 3.05) as compared to healthy controls, with elevated serum homocysteine being associated with cigarette smoking. SU *et al.* [53] found several inflammatory markers to be associated with COPD risk. Elevated C-reactive protein compared to regular levels had an SMD of 1.21 (95% CI 0.92–1.50), leukocytes SMD 1.07 (95% CI 0.25–1.88), interleukin (IL)-6 SMD 0.90 (95% CI 0.48–1.31), IL-8 SMD 2.34 (95% CI 0.69–4.00) and fibrinogen SMD 0.87 (95% CI 0.44–1.31). They did not find a significant relationship between COPD and tumour necrosis factor-α levels.

Xiong *et al.* [59] identified living at high altitudes (>1500 m) as a possible risk factor for COPD, but it was noted it was not an independent risk factor (mOR 1.18, 95% CI 0.85–1.62). Bellou *et al.* [79] identified traffic intensity as a possible risk factor and found an mOR of 1.30 (95% CI 0.92–1.82) per 5000 vehicles per day increase on the nearest road and an mOR of 1.26 (95% CI 0.95–1.70) for traffic load on major roads within 100 m per 500 000 vehicles per day increase. However, results were not significant. Adeloye *et al.* [85] identified living in both rural (mOR 1.40, 95% CI 1.30–1.60) and urban (mOR 1.20, 95% CI 1.00–1.50) areas as a risk factor; however, only the results for living in rural areas were significant.

Yang *et al.* [57] reported males to be at an increased risk for COPD (mOR 1.47, 95% CI 1.10–1.96), which is in accordance with results from Adeloye *et al.* [85] (mOR 2.10, 95% CI 1.90–2.30) and Chen *et al.* [72] (mOR 1.70, 95% CI 1.31–2.22)). They also reported poor housing ventilation, *e.g.* poor kitchen ventilation (mOR 3.99, 95% CI 1.24–12.82), to increase COPD risk [57]. Yang *et al.* [57] also found recurrent respiratory infections to increase the risk of COPD (mOR 15.02, 95% CI 4.54–49.68). Bellou *et al.* [79] identified a history of rheumatoid arthritis (mOR 1.99, 95% CI 1.61–2.45) or psoriasis (mOR 1.45, 95% CI 1.21–1.73) as risk factors for COPD. Four studies identified previous tuberculosis as a risk factor for COPD [61, 85, 93, 94], with mORs of 2.80 (95% CI 1.90–4.00) [85] and 5.98 (95% CI 4.18–8.56) [61].

Lastly, four reviews identified an increased risk of COPD when one of the parents has the condition as well [57, 65, 72, 85], with found mORs ranging from 1.57 (95% CI 1.29–1.93) [65] to 2.07 (95% CI 1.47–2.92) [57], respectively.

Discussion

To the best of our knowledge, this is the first umbrella review that provides an overview and comparison of nongenetic risk factors for COPD and asthma. We identified 43 risk factors for AOA and 45 for COPD. Risk factors were grouped into different categories.

AOA

Two reviews reported wood dust workers to be at an increased risk for asthma [25, 34], which was also one of the workplace irritants included by Baur *et al.* [44]. This indicates the importance of occupational factors in asthma development, which is supported by the asthma-specific job exposure matrix developed by Kennedy *et al.* [95]. Additionally, the lowest JBI score was six out of 10, indicating no major issues. Second, a strong association was found between a higher BMI and increased asthma risk [31, 40, 42]. The association was found for both overweight and obese participants, compared to participants with a healthy BMI. Female sex was also associated with late-onset asthma [36] in a review specifically examining AOA. They stated the underlying mechanism was unclear, but that it could be related to lifetime changes in female sex hormones and gender-specific differences in allergic sensitivities [36]. However, male sex was also identified as a risk factor in one review [31]. Lastly, several chemical exposures were associated with asthma, such as formaldehyde [21], VOCs [27], pesticides [46] and phthalates [47]. Three reviews [31, 36, 42] focused on smoking as a risk factor, of which two specified age of onset [36, 42]. Two showed an association with AOA [31, 36]. The third, not showing an association with an increased risk, only included two papers on smoking in total with contradicting results. One found a protective effect and one showed an increased risk [42]. We did not differentiate between allergic and nonallergic asthma as this was not clearly stated in each review, but since we are focusing on adult asthma, most are likely nonallergic cases.

COPD

12 reviews [54, 55, 57, 61, 70, 72, 79, 85–87, 89, 90] stated active smoking, as compared to nonsmokers, to be the main risk factor for COPD. 15 reviews [54, 57, 61, 69, 70, 72, 76, 77, 79, 81, 83, 85, 86, 93, 94] identified indoor biomass burning as a risk factor for COPD. Even though most of those studies were performed in lower income countries, it highlights the importance of particulate matter exposure, and the need for proper ventilation and the use of less damaging fuels indoors (*e.g.* natural gas, electric instead of solid fuels). Four reviews [57, 60, 72, 82] found ambient $PM_{2.5}$ and NO_2 concentrations to increase COPD risk. According to the World Health Organization (WHO), 99% of the global population lives in places where air pollution levels exceed the WHO requirements [96]. This highlights the need for concrete policies to reduce emissions. Several studies identified early life exposures [50, 52, 57, 68, 70, 72, 80, 85, 92, 93, 94], such as childhood asthma and respiratory problems, as risk factors for COPD. This shows the importance of prioritising children's respiratory health, as the consequences might linger into adulthood.

Three reviews reported a western, unhealthy diet to increase COPD risk [51, 63, 73] and five studies identified low BMI as a risk factor [57, 74, 76]. A proposed biological pathway has been oxidative stress,

which is associated with COPD development, and certain foods could have a protective role [97]. This shows how efforts of prevention could take advantage of this protective effect by including lifestyle measures, beyond smoking cessation, and include nutritional counselling. Eight reviews [56–58, 66, 71, 79, 84, 93] identified occupational dust as a risk factor, indicating efforts should be made to reduce dust exposure in the workplace and/or provide workers with protective equipment to mitigate the risk. Lastly, four reviews identified parental COPD as a risk factor independent of having specific genetic variations [57, 65, 72, 85], possibly making it easier to identify people at risk early on.

Differences and similarities

A second aim of this review was to identify both differences and similarities between risk factors for COPD and asthma. One of the main differences is BMI, with a high BMI being a risk factor for asthma, as opposed to a low BMI being a risk factor for COPD, and a high BMI being a protective factor. Second, both male and female sex were found to be risk factors for AOA, while males had a higher risk of COPD. However, YANG *et al*. [57] mention that currently COPD prevalence in males and females is close to equal, due to changes in smoking behaviour. Furthermore, even though most found risk factors differed, they were not contradicting.

We also found several similarities. First, for both diseases a low birth weight and pre-term delivery were implied as risk factors, even though pre-term delivery was not statistically significant for either. Second, occupational dust exposure was found in multiple reviews for both conditions, indicating an area for prevention. Third, active and passive smoking are important risk factors for both COPD and AOA. Even though the number of included reviews specifically focusing on smoking is limited, most studies adjusted for smoking. Fourth, ambient air pollution, in the form of NO_2 and particulate matter, was found to be a risk factor for both COPD and AOA. Finally, both pesticide exposure and exposure to workplace irritants such as chloride, were identified as risk factors for both AOA and COPD.

Strengths and limitations

There were several strengths. First, we conducted a comprehensive search on two highly prevalent diseases and provided an overview of nongenetic risk factors. This could help further develop prevention strategies and aid in the correct classification of both. Second, multiple authors did a partial screening and extraction of data, to limit errors in inclusion and data extraction. Last, because of the design, we were able to include most nongenetic risk factors for both asthma and COPD, which could have been unfeasible otherwise.

The review also has several limitations, which need to be considered. First, only seven out of the 30 studies that examined risk factors for asthma specified AOA, as opposed to asthma in adults. Four more only imply adult onset, as they investigate asthma development since starting work in certain occupational groups, but it is not explicitly specified that this is the case. As we were specifically interested in AOA and not asthma developed early in life, this might have impacted our results. This could be because risk factors for childhood asthma, lingering on into adulthood, are not the same as risk factors for developing asthma at a later age. Additionally, only a few studies confirmed asthma diagnosis by means of specific symptoms in combination with airway reversibility, the other studies did not specify the diagnosis which may result in the inclusion of patients with airway symptoms due to other diseases. Second, asthma studies including only adults were scarce. For most studies, the main focus was on asthma in children, leading to small sample sizes when excluding the population younger than 18 years of age. This lack of studies makes it difficult to draw firm conclusions. Third, for both asthma and COPD, not every review included a meta-analysis and/or provided a quantitative outcome measure or pooled estimates. This made comparing the results more difficult and could have led to some findings being over- or under-represented. However, as we did a risk of bias assessment, with JBI scores ranging between five and 11, this risk might be limited, as none indicated a high risk of bias. Fourth, we included every review regardless of quality and did not distinguish between the different JBI scores when interpreting results. Last, since we focused on incidence, we might have missed risk factors that become more apparent when taking mortality and exacerbations into account, such as ozone.

Implications

As our review provides an overview of risk factors of asthma and COPD, this provides possible targets for early identification and prevention. Since the costs of chronic diseases, both for healthcare and for individual health are high, this might result in significant financial savings and reduce the loss of quality of life [98]. Further, the Global Burden of Disease Study currently calculates risk based on six risk factors for COPD (smoking, second-hand smoke, household air pollution, ambient particulate matter, ozone and occupational particulates) and two for asthma (smoking and occupational asthmagens, *e.g.* occupational wood dust and cleaning materials) [4]. As this review identified many more risk factors, the burden of

disease might currently be underestimated. Additionally, our review has highlighted the differences in risk factors for COPD and AOA, meaning interventions need to be targeted to the specific population at risk.

Our review has also highlighted areas in which more research is needed. Few reviews focus on asthma in adults and even fewer focus on AOA. As research has shown AOA is less atopic and has a worse prognosis than childhood asthma [9], more research into this specific population is needed.

Conclusions

In this umbrella review, we provided an overview of nongenetic risk factors for COPD and AOA. Importantly, both diseases share several known lung-damaging and nongenetic factors such as smoking and occupational exposures. There are also some notable differences, such as BMI and air pollution. More research specifically on AOA should be performed to better understand these risk factors. Overall, the results of this review could help in differentiating between these diseases when diagnosing, as well as more targeted and earlier identification of cases, by identifying people at risk.

Provenance: Submitted article, peer reviewed.

Conflict of interest: A.H. Maitland-Van der Zee is the PI of P4O2 (Precision Medicine for more Oxygen) public–private partnership sponsored by Health Holland involving many private partners who contribute in cash and/or in kind. Partners in the Precision Medicine for more Oxygen (P4O2) consortium are the Amsterdam UMC, Leiden University Medical Center, Maastricht UMC+, Maastricht University, UMC Groningen, UMC Utrecht, Utrecht University, TNO, Aparito, Boehringer Ingelheim, Breathomix, Clear, Danone Nutricia Research, Fluidda, MonitAir, Ncardia, Ortec Logiqcare, Philips, Proefdiervrij, Quantib-U, RespiQ, Roche, Smartfish, SODAQ, Thirona, TopMD, Lung Alliance Netherlands (LAN) and the Lung Foundation Netherlands (Longfonds). The consortium is additionally funded by the PPP Allowance made available by Health Holland, Top Sector Life Sciences & Health (LSHM20104; LSHM20068), to stimulate public-private partnerships and by Novartis. A.H. Maitland-Van der Zee has received grants from Boehringer Ingelheim, Vertex Innovation Award, Dutch Lung Foundation, Stichting Asthma Bestrijding, and Innovative Medicine Initiative (IMI). A.H. Maitland-Van der Zee has received consulting fees from AstraZeneca and Boehringer Ingelheim. A.H. Maitland-Van der Zee has received GSK honarium for a lecture. A.H. Maitland-Van der Zee is the chair of DSMB SOS BPD study and advisory board member of the CHAMP study. A.H. Maitland-Van der Zee is the president of the federation of innovative drug research in the Netherlands (FIGON) and president of the European Association of systems medicine (EASYM). The remaining authors have no conflicts to declare.

Support statement: Partners in the Precision Medicine for more Oxygen (P4O2) consortium are the Amsterdam UMC, Leiden University Medical Center, Maastricht UMC+, Maastricht University, UMC Groningen, UMC Utrecht, Utrecht University, TNO, Aparito, Boehringer Ingelheim, Breathomix, Clear, Danone Nutricia Research, Fluidda, MonitAir, Ncardia, Ortec Logiqcare, Philips, Proefdiervrij, Quantib-U, RespiQ, Roche, Smartfish, SODAQ, Thirona, TopMD, Lung Alliance Netherlands (LAN) and the Lung Foundation Netherlands (Longfonds). The consortium is additionally funded by the PPP Allowance made available by Health Holland, Top Sector Life Sciences & Health (LSHM20104; LSHM20068), to stimulate public-private partnerships and by Novartis. Funding information for this article has been deposited with the Crossref Funder Registry.

References

1 Hajat C, Stein E. The global burden of multiple chronic conditions: a narrative review. *Prev Med Rep* 2018; 12: 284–293.
2 Rycroft CE, Heyes A, Lanza L, *et al.* Epidemiology of chronic obstructive pulmonary disease: a literature review. *Int J Chron Obstruct Pulmon Dis* 2012; 7: 457–494.
3 World Health Organization. Chronic obstructive pulmonary disease (COPD). www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd) Date last updated: 16 March 2023. Date last accessed: 28 September 2022.
4 GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet Respir Med* 2017; 5: 691–706.
5 Sarkar M, Srinivasa Madabhavi I, *et al.* Tuberculosis associated chronic obstructive pulmonary disease. *Clin Respir J* 2017; 11: 285–295.
6 Lee CH, Lee MC, Shu CC, *et al.* Risk factors for pulmonary tuberculosis in patients with chronic obstructive airway disease in Taiwan: a nationwide cohort study. *BMC Infect Dis* 2013; 13: 194.
7 Schneider C, Jick SS, Bothner U, *et al.* COPD and the risk of depression. *Chest* 2010; 137: 341–347.

8 Masoli M, Fabian D, Holt S, *et al.* The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy* 2004; 59: 469–478.
9 de Nijs SB, Venekamp LN, Bel EH. Adult-onset asthma: is it really different? *Eur Respir Rev* 2013; 22: 44–52.
10 de Marco R, Cappa V, Accordini S, *et al.* Trends in the prevalence of asthma and allergic rhinitis in Italy between 1991 and 2010. *Eur Respir J* 2012; 39: 883–892.
11 Postma DS, Rabe KF. The asthma-COPD overlap syndrome. *N Engl J Med* 2015; 373: 1241–1249.
12 Marcon A, Locatelli F, Dharmage SC, *et al.* The coexistence of asthma and COPD: risk factors, clinical history and lung function trajectories. *Eur Respir J* 2021; 58: 2004656.
13 Papaiwannou A, Zarogoulidis P, Porpodis K, *et al.* Asthma–chronic obstructive pulmonary disease overlap syndrome (ACOS): current literature review. *J Thorac Dis* 2014; 6: Suppl. 1, S146–SS51.
14 Menezes AMB, Montes de Oca M, Pérez-Padilla R, *et al.* Increased risk of exacerbation and hospitalization in subjects with an overlap phenotype: COPD–asthma. *Chest* 2014; 145: 297–304.
15 Miravitlles M, Soriano JB, Ancochea J, *et al.* Characterisation of the overlap COPD–asthma phenotype. Focus on physical activity and health status. *Respir Med* 2013; 107: 1053–1060.
16 Martinez FD. Early-life origins of chronic obstructive pulmonary disease. *N Engl J Med* 2016; 375: 871–878.
17 To T, Zhu J, Larsen K, *et al.* Progression from asthma to chronic obstructive pulmonary disease. Is air pollution a risk factor? *Am J Respir Crit Care Med* 2016; 194: 429–438.
18 Ioannidis JP. Integration of evidence from multiple meta-analyses: a primer on umbrella reviews, treatment networks and multiple treatments meta-analyses. *CMAJ* 2009; 181: 488–493.
19 Aromataris E, Fernandez R, Godfrey CM, *et al.* Summarizing systematic reviews: methodological development, conduct and reporting of an umbrella review approach. *Int J Evid Based Healthc* 2015; 13: 132–140.
20 Romero Starke K, Friedrich S, Schubert M, *et al.* Are healthcare workers at an increased risk for obstructive respiratory diseases due to cleaning and disinfection agents? A systematic review and meta-analysis. *Int J Environ Res Public Health* 2021; 18: 5159.
21 Yu L, Wang B, Cheng M, *et al.* Association between indoor formaldehyde exposure and asthma: a systematic review and meta-analysis of observational studies. *Indoor Air* 2020; 30: 682–690.
22 Wang X, Zhou N, Zhi Y. Association between exposure to greenness and atopic march in children and adults–a systematic review and meta-analysis. *Front Public Health* 2022; 10: 1097486.
23 Chen M, Sun Y, Wu Y. Lower circulating zinc and selenium levels are associated with an increased risk of asthma: evidence from a meta-analysis. *Public Health Nutr* 2020; 23: 1555–1562.
24 Etminan M, Sadatsafavi M, Jafari S, *et al.* Acetaminophen use and the risk of asthma in children and adults: a systematic review and metaanalysis. *Chest* 2009; 136: 1316–1323.
25 Zhang Y, Ye B, Zheng H, *et al.* Association between organic dust exposure and adult-asthma: a systematic review and meta-analysis of case-control studies. *Allergy Asthma Immunol Res* 2019; 11: 818–829.
26 Shen SY, Xiao WQ, Lu JH, *et al.* Early life vitamin D status and asthma and wheeze: a systematic review and meta-analysis. *BMC Pulm Med* 2018; 18: 120.
27 Nurmatov U, Tagieva N, Semple S, *et al.* Volatile organic compounds and risk of asthma and allergy: a systematic review and meta-analysis of observational and interventional studies. *Primary Care Respir J* 2013; 22: PS9–PS15.
28 Sharpe RA, Bearman N, Thornton CR, *et al.* Indoor fungal diversity and asthma: a meta-analysis and systematic review of risk factors. *J Allergy Clin Immunol* 2015; 135: 110–122.
29 Mu M, Ye S, Bai MJ, *et al.* Birth weight and subsequent risk of asthma: a systematic review and meta-analysis. *Heart Lung Circ* 2014; 23: 511–519.
30 Macan J, Babić Ž, Hallmann S, *et al.* Respiratory toxicity of persulphate salts and their adverse effects on airways in hairdressers: a systematic review. *Int Arch Occup Environ Health* 2022; 95: 1679–1702.
31 Sio YY, Chew FT. Risk factors of asthma in the Asian population: a systematic review and meta-analysis. *J Physiol Anthropol* 2021; 40: 22.
32 Rodriguez A, Brickley E, Rodrigues L, *et al.* Urbanisation and asthma in low-income and middle-income countries: a systematic review of the urban-rural differences in asthma prevalence. *Thorax* 2019; 11: 1020–1030.
33 Cong X, Xu X, Zhang Y, *et al.* Temperature drop and the risk of asthma: a systematic review and meta-analysis. *Environ Sci Pollut Res Int* 2017; 24: 22535–22546.
34 Wiggans RE, Evans G, Fishwick D, *et al.* Asthma in furniture and wood processing workers: a systematic review. *Occup Med* 2016; 66: 193–201.
35 Uphoff E, Cabieses B, Pinart M, *et al.* A systematic review of socioeconomic position in relation to asthma and allergic diseases. *Eur Respir J* 2015; 46: 364–374.
36 Tan DJ, Walters EH, Perret JL, *et al.* Age-of-asthma onset as a determinant of different asthma phenotypes in adults: a systematic review and meta-analysis of the literature. *Expert Rev Respir Med* 2015; 9: 109–123.
37 Lieberoth S, Gade EJ, Brok J, *et al.* Age at menarche and risk of asthma: systematic review and meta-analysis. *J Asthma* 2014; 51: 559–565.

38 Kakutani S, Egawa K, Saito K, *et al.* Arachidonic acid intake and asthma risk in children and adults: a systematic review of observational studies. *J Nutr Sci* 2014; 3: e12.
39 Takkouche B, González-Barcala FJ, Etminan M, *et al.* Exposure to furry pets and the risk of asthma and allergic rhinitis: a meta-analysis. *Allergy* 2008; 63: 857–864.
40 Beuther DA, Sutherland ER. Overweight, obesity, and incident asthma: a meta-analysis of prospective epidemiologic studies. *Am J Respir Crit Care Med* 2007; 175: 661–666.
41 Jaakkola JJ, Ahmed P, Ieromnimon A, *et al.* Preterm delivery and asthma: a systematic review and meta-analysis. *J Allergy Clin Immunol* 2006; 118: 823–830.
42 Mikkelsen H, Landt EM, Benn M, *et al.* Causal risk factors for asthma in Mendelian randomization studies: a systematic review and meta-analysis. *Clin Transl Allergy* 2022; 12: e12207.
43 Canova C, Jarvis D, Walker S, *et al.* Systematic review of the effects of domestic paints on asthma related symptoms in people with or without asthma. *J Asthma* 2013; 50: 1020–1030.
44 Baur X, Bakehe P, Vellguth H. Bronchial asthma and COPD due to irritants in the workplace – an evidence-based approach. *J Occup Med Toxicol* 2012; 7: 19.
45 Flaherman V, Rutherford GW. A meta-analysis of the effect of high weight on asthma. *Arch Dis Child* 2006; 91: 334–339.
46 Doust E, Ayres JG, Devereux G, *et al.* Is pesticide exposure a cause of obstructive airways disease? *Eur Respir Rev* 2014; 23: 180–192.
47 Jaakkola JJ, Knight TL. The role of exposure to phthalates from polyvinyl chloride products in the development of asthma and allergies: a systematic review and meta-analysis. *Environ Health Perspect* 2008; 116: 845–853.
48 Folletti I, Zock JP, Moscato G, *et al.* Asthma and rhinitis in cleaning workers: a systematic review of epidemiological studies. *J Asthma* 2014; 51: 18–28.
49 Vincent MJ, Parker A, Maier A. Cleaning and asthma: a systematic review and approach for effective safety assessment. *Regul Toxicol Pharmacol* 2017; 90: 231–243.
50 Duan P, Wang Y, Lin R, *et al.* Impact of early life exposures on COPD in adulthood: a systematic review and meta-analysis. *Respirology* 2021; 26: 1131–1151.
51 Parvizian MK, Dhaliwal M, Li J, *et al.* Relationship between dietary patterns and COPD: a systematic review and meta-analysis. *ERJ Open Res* 2020; 6: 00168-2019.
52 Asamoah-Boaheng M, Acheampong L, Tenkorang EY, *et al.* Association between early history of asthma and COPD diagnosis in later life: a systematic review and meta-analysis. *Int J Epidemiol* 2018; 47: 1865–1876.
53 Su B, Liu T, Fan H, *et al.* Inflammatory markers and the risk of chronic obstructive pulmonary disease: a systematic review and meta-analysis. *PLoS One* 2016; 11: e0150586.
54 Awokola BI, Amusa GA, Jewell CP, *et al.* Chronic obstructive pulmonary disease in sub-Saharan Africa. *Int J Tuberc Lung Dis* 2022; 26: 232–242.
55 Kamal R, Srivastava AK, Kesavachandran CN. Meta-analysis approach to study the prevalence of chronic obstructive pulmonary disease among current, former and non-smokers. *Toxicol Rep* 2015; 2: 1064–1074.
56 Sadhra S, Kurmi OP, Sadhra SS, *et al.* Occupational COPD and job exposure matrices: a systematic review and meta-analysis. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 725–734.
57 Yang Y, Mao J, Ye Z, *et al.* Risk factors of chronic obstructive pulmonary disease among adults in Chinese mainland: a systematic review and meta-analysis. *Respir Med* 2017; 131: 158–165.
58 Peng C, Yan Y, Li Z, *et al.* Chronic obstructive pulmonary disease caused by inhalation of dust: a meta-analysis. *Medicine* 2020; 99: e21908.
59 Xiong H, Huang Q, He C, *et al.* Prevalence of chronic obstructive pulmonary disease at high altitude: a systematic review and meta-analysis. *PeerJ* 2020; 8: e8586.
60 Park J, Kim HJ, Lee CH, *et al.* Impact of long-term exposure to ambient air pollution on the incidence of chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Environ Res* 2021; 194: 110703.
61 Njoku CM, Hurst JR, Kinsman L, *et al.* COPD in Africa: risk factors, hospitalisation, readmission and associated outcomes-a systematic review and meta-analysis. *Thorax* 2023; in press [https://doi.org/10.1136/thorax-2022-218675]
62 Gershon AS, Dolmage TE, Stephenson A, *et al.* Chronic obstructive pulmonary disease and socioeconomic status: a systematic review. *COPD* 2012; 9: 216–226.
63 Zheng PF, Shu L, Si CJ, *et al.* Dietary patterns and chronic obstructive pulmonary disease: a meta-analysis. *COPD* 2016; 13: 515–522.
64 Ryu JY, Sunwoo YE, Lee SY, *et al.* Chronic obstructive pulmonary disease (COPD) and vapors, gases, dusts, or fumes (VGDF): a meta-analysis. *COPD* 2015; 12: 374–380.
65 Li LS, Paquet C, Johnston K, *et al.* '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. *Int J Chron Obstruct Pulmon Dis* 2017; 12: 403–415.
66 Borup H, Kirkeskov L, Hanskov DJA, *et al.* Systematic review: chronic obstructive pulmonary disease and construction workers. *Occup Med* 2017; 67: 199–204.

67 Guillien A, Soumagne T, Dalphin JC, *et al.* COPD, airflow limitation and chronic bronchitis in farmers: a systematic review and meta-analysis. *Occup Environ Med* 2019; 76: 58–68.
68 Ma H, Li Y, Tang L, *et al.* Impact of childhood wheezing on lung function in adulthood: a meta-analysis. *PLoS One* 2018; 13: e0192390.
69 Kamal R, Srivastava AK, Kesavachandran CN, *et al.* Chronic obstructive pulmonary disease (COPD) in women due to indoor biomass burning: a meta analysis. *Int J Environ Health Res* 2022; 32: 1403–1417.
70 Sutradhar I, Das Gupta R, Hasan M, *et al.* Prevalence and risk factors of chronic obstructive pulmonary disease in Bangladesh: a systematic review. *Cureus* 2019; 11: e3970.
71 Vinnikov D, Rybina T, Strizhakov L, *et al.* Occupational burden of chronic obstructive pulmonary disease in the commonwealth of independent states: systematic review and meta-analysis. *Front Med* 2020; 7: 614827.
72 Chen H, Liu X, Gao X, *et al.* Epidemiological evidence relating risk factors to chronic obstructive pulmonary disease in China: a systematic review and meta-analysis. *PLoS One* 2021; 16: e0261692.
73 van Iersel LEJ, Beijers R, Gosker HR, *et al.* Nutrition as a modifiable factor in the onset and progression of pulmonary function impairment in COPD: a systematic review. *Nutr Rev* 2021; 80: 1434–1444.
74 Zhang X, Chen H, Gu K, *et al.* Association of body mass index with risk of chronic obstructive pulmonary disease: a systematic review and meta-analysis. *COPD* 2021; 18: 101–113.
75 Gan WQ, Man SF, Postma DS, *et al.* Female smokers beyond the perimenopausal period are at increased risk of chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Respir Res* 2006; 1: 52.
76 Finney LJ, Feary JR, Leonardi-Bee J, *et al.* Chronic obstructive pulmonary disease in sub-Saharan Africa: a systematic review. *Int J Tuberc Lung Dis* 2013; 17: 583–589.
77 Zhu B, Wang Y, Ming J, *et al.* Disease burden of COPD in China: a systematic review. *Int J Chron Obstruct Pulmon Dis* 2018; 13: 1353–13.
78 Salari-Moghaddam A, Milajerdi A, Larijani B, *et al.* Processed red meat intake and risk of COPD: a systematic review and dose-response meta-analysis of prospective cohort studies. *Clin Nutr* 2019; 38: 1109–1116.
79 Bellou V, Belbasis L, Konstantinidis AK, *et al.* Elucidating the risk factors for chronic obstructive pulmonary disease: an umbrella review of meta-analyses. *Int J Tuberc Lung Dis* 2019; 23: 58–66.
80 Ali KM. Childhood asthma as a risk factor for adult chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Expert Rev Respir Med* 2022; 16: 461–467.
81 Pathak U, Gupta NC, Suri JC. Risk of COPD due to indoor air pollution from biomass cooking fuel: a systematic review and meta-analysis. *Int J Environ Health Res* 2020; 30: 75–88.
82 Zhang Z, Wang J, Lu W. Exposure to nitrogen dioxide and chronic obstructive pulmonary disease (COPD) in adults: a systematic review and meta-analysis. *Environ Sci Pollut Res Int* 2018; 25: 15133–15145.
83 Kurmi OP, Semple S, Simkhada P, *et al.* COPD and chronic bronchitis risk of indoor air pollution from solid fuel: a systematic review and meta-analysis. *Thorax* 2010; 65: 221–228.
84 Brüske I, Thiering E, Heinrich J, *et al.* Biopersistent granular dust and chronic obstructive pulmonary disease: a systematic review and meta-analysis. *PLoS One* 2013; 8: e80977.
85 Adeloye D, Song P, Zhu Y, *et al.* Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis. *Lancet Respir Med* 2022; 10: 447–458.
86 Budhathoki P, Shrestha DB, Sedhai YR, *et al.* Prevalence and risk factors of COPD in Nepal: a systematic review and meta-analysis. *J Nepal Health Res Counc* 2022; 19: 652–660.
87 Lee PN, Forey BA, Thornton AJ, *et al.* The relationship of cigarette smoking in Japan to lung cancer, COPD, ischemic heart disease and stroke: a systematic review. *F1000Res* 2018; 7: 204.
88 Fontana L, Lee SJ, Capitanelli I, *et al.* Chronic obstructive pulmonary disease in farmers: a systematic review. *J Occup Environ Med* 2017; 59: 775–788.
89 Wang B, Xiao D, Wang C. Smoking and chronic obstructive pulmonary disease in Chinese population: a meta-analysis. *Clin Respir J* 2015; 9: 165–175.
90 Forey BA, Thornton AJ, Lee PN. Systematic review with meta-analysis of the epidemiological evidence relating smoking to COPD, chronic bronchitis and emphysema. *BMC Pulm Med* 2011; 11: 36.
91 Chaudhary D, Sharma N, Senapati S. Serum homocysteine could be used as a predictive marker for chronic obstructive pulmonary disease: a meta-analysis. *Front Public Health* 2019; 7: 69.
92 Lee PN, Forey BA, Coombs KJ, *et al.* Epidemiological evidence relating environmental smoke to COPD in lifelong non-smokers: a systematic review. *F1000Res* 2018; 7: 146.
93 Cunalata-Paredes AV, Gea-Izquierdo E. COPD in the major nonsmoking adult: a systematic review and meta-analysis. *Arch Environ Occup Health* 2021; 76: 319–329.
94 Pando-Sandoval A, Ruano-Ravina A, Candal-Pedreira C, *et al.* Risk factors for chronic obstructive pulmonary disease in never-smokers: a systematic review. *Clin Respir J* 2022; 16: 261–275.
95 Kennedy SM, Le Moual N, Choudat D, *et al.* Development of an asthma specific job exposure matrix and its application in the epidemiological study of genetics and environment in asthma (EGEA). *Occup Environ Med* 2000; 57: 635–641.

96 World Health Organization. Air pollution data portal. www.who.int/data/gho/data/themes/air-pollution Date last updated: 2023. Date last accessed: 4 November 2022.
97 Romieu I. Nutrition and lung health. *Int J Tuberc Lung Dis* 2005; 9: 362–374.
98 May SM, Li JT. Burden of chronic obstructive pulmonary disease: healthcare costs and beyond. *Allergy Asthma Proc* 2015; 36: 4–10.