



SmokeHaz

Systematic Reviews and Meta-analyses of the Effects of Smoking on Respiratory Health

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BACKGROUND: Smoking tobacco increases the risk of respiratory disease in adults and children, but communicating the magnitude of these effects in a scientific manner that is accessible and usable by the public and policymakers presents a challenge. We have therefore summarized scientific data on the impact of smoking on respiratory diseases to provide the content for a unique resource, SmokeHaz.

METHODS: We conducted systematic reviews and meta-analyses of longitudinal studies (published to 2013) identified from electronic databases, gray literature, and experts. Random effect meta-analyses were used to pool the findings.

RESULTS: We included 216 articles. Among adult smokers, we confirmed substantially increased risks of lung cancer (risk ratio (RR), 10.92; 95% CI, 8.28-14.40; 34 studies), COPD (RR, 4.01; 95% CI, 3.18-5.05; 22 studies), and asthma (RR, 1.61; 95% CI, 1.07-2.42; eight studies). Exposure to passive smoke significantly increased the risk of lung cancer in adult nonsmokers and increased the risks of asthma, wheeze, lower respiratory infections, and reduced lung function in children. Smoking significantly increased the risk of sleep apnea and asthma exacerbations in adult and pregnant populations, and active and passive smoking increased the risk of tuberculosis.

CONCLUSIONS: These findings have been translated into easily digestible content and published on the SmokeHaz website. CHEST 2016; 150(1):164-179

KEY WORDS: health risks; lung diseases; meta-analysis; passive smoking; policymakers; public awareness; respiratory diseases; smoking; systematic review

ABBREVIATIONS: FRC = functional residual capacity; LRTI = lower respiratory tract infection; RR = risk ratio

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Part of this article has been presented as a poster at the Lancet Public Health Science Conference, November 19, 2014, Glasgow, Scotland; as a poster at the 16th World Conference on Tobacco or Health, March 17-21, 2015, Abu Dhabi, UAE; and the website was launched at a press conference, May 8, 2014, Athens, Greece.

FUNDING/SUPPORT: The study was funded by the European Respiratory Society (ERS) and carried out by the UK Centre for Tobacco and Alcohol Studies, with the oversight of the ERS Tobacco Control Committee. The website was developed with the aid of the European Lung Foundation.

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Tobacco smoking is the leading cause of preventable death in the European Union, responsible for nearly 700,000 deaths every year. Approximately 50% of smokers die prematurely, resulting in the loss of an average of 14 years of life.¹ An estimated further 13 million people in the European Union are living in poor health with chronic diseases as a result of smoking. Many forms of cancer and cardiovascular and respiratory diseases are linked to tobacco use, which causes more problems than alcohol, drugs, high blood pressure, excess weight, or high cholesterol. Passive smoking is a significant health hazard to children and nonsmoking adults, being responsible for causing excess cases of sudden infant death syndrome, asthma, middle ear infections, and meningitis.² Therefore, preventing smoking remains a key health priority. Because smoking prevention requires population-level policy measures and individual treatment interventions,³ it is important that accurate data on the effects of tobacco use on health are readily available to policymakers, policy advocates, and the general public.

In this respect, one major difficulty is that the available evidence on smoking and health is extensive, disparate,

and at times conflicting. Therefore, it is particularly important that the evidence base is regularly captured, through systematic review, and synthesized to provide easily understandable and accurate summary estimates of effects.

This article reports on the findings of the SmokeHaz project, which summarizes the harms of smoking on respiratory health in a freely accessible online resource for policymakers, researchers, students, health care professionals, and the public.⁴ SmokeHaz is a collaborative project between the UK Centre for Tobacco and Alcohol Studies, the European Respiratory Society, and the European Lung Foundation. In this project, all of the available worldwide literature up to 2013 has been used to update a series of systematic reviews and meta-analyses on associations between tobacco smoking and a range of respiratory health outcomes. This article presents the detailed scientific data for validation by independent peer review and is designed to promote and strengthen public awareness of tobacco control issues as requested in Article 12 of the World Health Organization's *Framework Convention on Tobacco Control*.³

Methods

Inclusion Criteria

We included longitudinal, cohort, or nested case-control studies that assessed the effect of active or passive tobacco smoking on the risk of developing respiratory diseases. Outcomes of interest included lung cancer, COPD, asthma and wheeze, asthma exacerbations, or sleep apnea or tuberculosis in adults and asthma and wheeze, asthma exacerbations, lung function, sleep apnea, or lower respiratory tract infection (LRTI) in children. Where possible we used biochemically verified measures of smoking, for example exhaled carbon monoxide or saliva cotinine levels, in preference to self-reported smoking status. Active smoking was defined as ever smoker, current smoker, or ex- or former smoker; passive smoking was defined as being in contact with secondhand smoke from any source: domestic, occupational, or other sources. Studies assessing levels of exposure to smoke based on cigarette consumption (pack years defined as number of packs smoked per day multiplied by number of years smoked, duration of smoking, or the number of cigarettes smoked per day) were also included. For passive smoking, we included studies which assessed effects either in non- or never smokers or where the effect of active smoking was adjusted for in the statistical analyses. In addition to adult populations, studies

focusing on in utero, infants, children, and adolescents were also included. Where insufficient studies were identified for particular outcomes, we extended our searches to include studies reporting disease-specific mortality. Studies which only looked at passive smoke exposure relating to cooking fuels and those looking at active or passive smoking from illegal substances were excluded. To ensure the strictest independence of the science as far as possible within the limits of disclosed knowledge, we omitted any primary studies with declared or identifiable involvement of the tobacco industry.

Search Strategy

Comprehensive literature searches in MEDLINE, Embase, and Web of Science were conducted from 1985 to 2013 (precise end dates varied for each health outcome), with no language restrictions imposed. We also searched conference proceedings from major international tobacco control conferences and a range of websites hosted by relevant professional societies. Contact with experts in the field was made to identify further relevant published or unpublished research. References lists of all included studies were screened to identify further potentially eligible studies.

Study Selection and Data Extraction

Titles, abstracts, and full-text articles identified from the searches were screened by one reviewer (L. J.) to select relevant articles. A second reviewer (J. L.-B.) independently screened a minimum of 10% of titles and abstracts and 30% of full-text articles. Two authors (L. J. and J. L.-B.) independently extracted data from included studies using previously piloted data extraction forms and independently assessed the quality of the included studies using the Newcastle-Ottawa Scale⁵ for primary studies and the Assessment of Multiple Systematic Reviews Scale for existing systematic reviews.⁶ A Newcastle-Ottawa Scale score of ≥ 7 indicated high quality in the

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DOI: <http://dx.doi.org/10.1016/j.chest.2016.03.060>

primary studies. Disagreements and discrepancies in study selection and data extraction were resolved through discussion.

Statistical Analyses

We extracted measures of effect for the association between exposure to smoking and the risk of disease using either ORs, risk ratios (RRs), hazard ratios, or incidence rate ratios, with 95% CIs. Estimates adjusted for potential confounders were used in preference to crude estimates. Pooled relative RRs were estimated using random effect meta-analyses. Heterogeneity between the studies was assessed using

the I^2 statistic.⁷ Subgroup analyses were performed to explore reasons for heterogeneity based on sex, age of children, country (Europe compared with the rest of the world), methodologic quality, and level of exposure (eg, pack years of active smoking). Evidence of publication bias was assessed using funnel plots. The P values $< .05$ were considered statistically significant. Statistical analysis was performed using STATA version 11 (StataCorp) and Review Manager 5.3 (Cochrane). The reviews adhered to the Meta-analysis of Observational Studies in Epidemiology⁸ and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.⁹

Results

The main findings from the systematic reviews and meta-analyses are presented. The characteristics of the studies included in the systematic reviews are presented in Table 1. Tables giving more information about the study populations and wider data, including funnel plots, and additional figures containing more detailed data are available on the SmokeHaz website.⁴

Lung Cancer

Active Smoking: Thirty-four studies assessing the effect of active smoking vs nonsmoking on the development of lung cancer were eligible for inclusion in the review.¹⁰⁻⁴³ Nineteen (56%) studies were deemed to be of high quality; 13 were conducted in Europe.

Smokers were 11 times more likely than nonsmokers to develop lung cancer (RR, 10.92; 95% CI, 8.28-14.40; $I^2 = 95%$; 34 studies) (Fig 1).¹⁰⁻⁴³ The results were similar in both the higher- and lower-quality studies. Higher risks of developing lung cancer were seen in women (12-fold increase) than men (nine-fold increase); however, the test for subgroup differences was not statistically significant ($P = .40$). Studies conducted in European countries tended to show higher risks of lung cancer (15-fold increase) among smokers than those conducted elsewhere (nine-fold increase), but not reaching significance (P value for subgroup differences, $P = .06$). All of the included studies reported that the incidence of lung cancer was consistently greater in those with higher cigarette consumption. A pooled analysis in

TABLE 1] Characteristics of Studies Included in the Systematic Reviews

Diseases	Tobacco Smoking	No. of Studies	References	Used a Cohort Design	Conducted in Europe	Assessed as High Quality	Published Since 2000
Adult							
Lung cancer	Active	34	10-43	27 (79)	13 (38)	19 (56)	22 (65)
	Passive	15	44-58	13 (91)	4 (27)	6 (40)	8 (53)
COPD	Active	24	59-82	22 (92)	15 (63)	5 (21)	20 (83)
	Passive	3	72, 84, 85	3 (100)	1 (33)	0 (0)	0 (0)
Asthma	Active	8	88-95	8 (100)	6 (75)	4 (50)	3 (38)
Asthma exacerbations	Active	2	97, 98	1 (50)	1 (50)	2 (100)	2 (100)
	Passive	3	99-101	3 (100)	2 (67) ^a	1 (33)	2 (67)
Tuberculosis	Active	4	102-105	4 (100)	0 (0)	3 (75)	4 (100)
	Passive	2	104, 106	2 (100)	0 (0)	2 (100)	2 (100)
Sleep apnea	Active	3	112, 113, 116	3 (100)	2 (67)	0 (0)	1 (33)
	Passive	2	114, 115	2 (100)	2 (100)	0 (0)	1 (50)
Childhood							
LRTI	Passive	34	118-151	34 (100)	17 (50)	16 (47)	16 (47)
Asthma/wheeze	Passive	71	153	71 (100)	32 (45)	31 (44)	55 (77)
Lung function in infants	Passive	13	154-166	13 (100)	7 (57)	6 (46) ^b	5 (38)
Lung function in school-aged children	Passive	12	167-178	12 (100)	4 (33)	0 (0)	6 (50)

Data are No. (%) or as otherwise indicated. LRTI = lower respiratory tract infection.

^aOne study was conducted in both the United Kingdom and the United States.

^bAssessed based on adjustment for confounders.

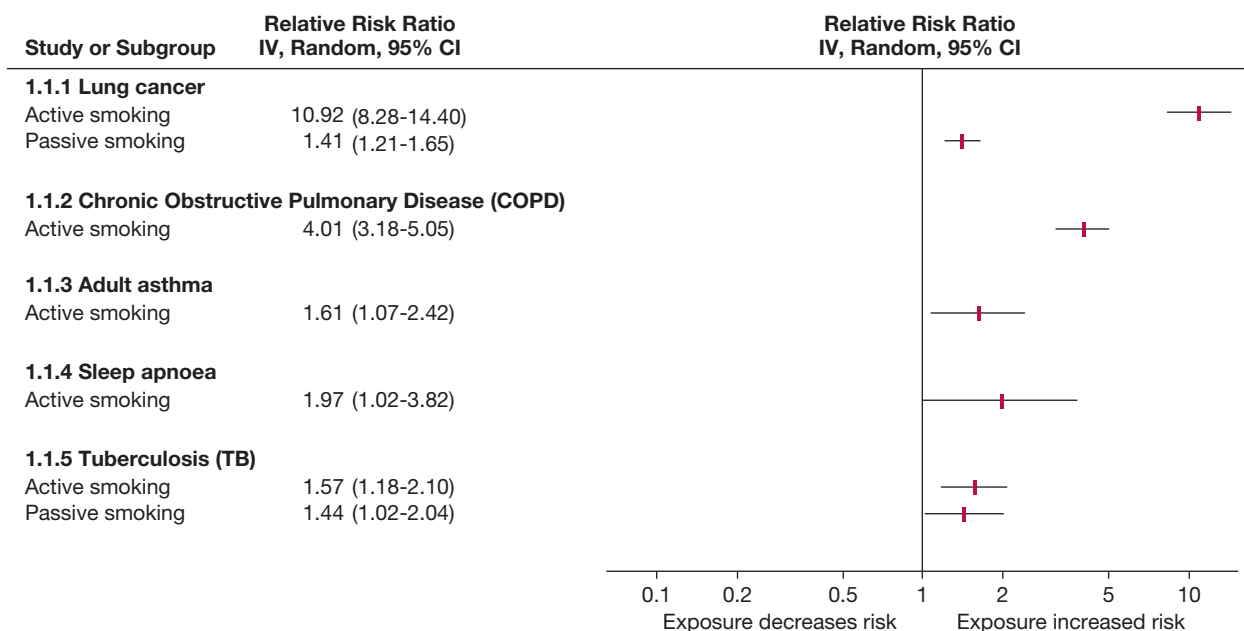


Figure 1 – Summary estimates from meta-analyses assessing the effect of active and passive smoking on the risk of lung cancer, COPD, asthma, sleep apnea, and tuberculosis in adults.

the 13 comparisons from 11 studies^{10-12,16,25,26,31-33,35,37} that reported pack years found a significant dose response relationship between increasing risk (from threefold to 12-fold) of development of lung cancer with increasing exposure (< 20 pack years: RR, 3; 20-40 pack years: RR, 7; 40-60 pack years: RR, 11; > 60 pack years: RR, 12).

Passive Smoking: Fifteen studies⁴⁴⁻⁵⁸ that assessed the effect of passive smoking on the risk of lung cancer were included in the review. Six (40%) were deemed to be of higher quality. The main results are based on data from 13 of the studies (two studies^{45,47} were excluded because of using duplicate data).

Exposure to passive smoke increased the risk of developing lung cancer by 1.41-fold (41%) compared with never smokers unexposed to passive smoke (RR, 1.41; 95% CI, 1.21-1.65; $I^2 = 0\%$; 13 studies) (Fig 1).^{44,46,48-58} Most of this evidence was based on data from nonsmoking women who were exposed to passive smoke from their smoker husbands (11 of the studies). Similar risks of lung cancer were seen in European countries compared with studies conducted elsewhere in the world and in higher-quality studies compared with lower-quality studies. A meta-analysis to investigate the effect of levels of exposure to passive smoke was possible in four studies,^{48,51,52,54} which found women whose husbands smoked > 20 cigarettes per day had a 1.46-fold (46%) increased risk of lung cancer than women with nonsmoker husbands (RR, 1.46; 95% CI, 1.10-1.44; four studies).

COPD

Active Smoking: Twenty-four studies⁵⁹⁻⁸² assessing the effect of smoking on the risk of developing COPD were identified from a previous systematic review⁸³ and an updated search; however, only 22 of the studies provided sufficient data to be included in the meta-analysis.

Most (n = 13) of the included studies used the Global Initiative for Chronic Obstructive Lung Disease criteria to define COPD based on FEV₁/FVC < 70%. Only five of the studies (21%) were deemed to be of high quality.

Smokers were 4.01 times more likely to develop COPD than nonsmokers (RR, 4.01; 95% CI, 3.18-5.05, $I^2 = 87\%$; 22 studies) (Fig 1).^{59-68,70,72-82} Similar risks of COPD were seen between men and women, in higher- and lower-quality studies, and between studies conducted in Europe and the rest of the world.

Passive Smoking: Three studies^{72,84,85} assessing the effect of passive smoking on the risk of COPD were identified from two previous systematic reviews^{86,87} and an updated search. COPD was defined as either FEV₁ < 65%, FEV₁/maximum FVC < 65% or percent predicted FEV₁ < 75%, or as a clinical diagnosis of acute obstructive disease. None of the studies were deemed to be of high quality.

In adults, exposure to passive smoking for at least 1 h/d was associated with a 1.44-fold (44%) increased risk of COPD compared with non-smokers (RR, 1.44; 95% CI, 1.02-2.01)⁸⁵; however, another study found no

consistent effect of passive smoking on the development of COPD in nonsmokers.⁷² Exposure to passive smoking during childhood and adulthood was associated with a 1.72-fold (72%) increased risk of developing COPD in adulthood (RR, 1.72; 95% CI, 1.31-2.23); however, no increased risk was seen in those only exposed during childhood.⁸⁴

Adult Asthma

Eight studies⁸⁸⁻⁹⁵ assessing the effect of active smoking on the risk of asthma in adults were identified from a previous systematic review.⁹⁶ Asthma was ascertained through physician reports in most studies, whereas two studies relied on self-reports. Four of the studies (50%) were deemed to be of high quality. All but two of the included studies^{91,95} were conducted in Europe.

Smokers were 1.61 times (61%) more likely to develop asthma than adults who had never smoked (RR, 1.61; 95% CI, 1.07-2.42; $I^2 = 91%$; eight studies) (Fig 1).⁸⁸⁻⁹⁵ The high level of heterogeneity appeared to be related to a low-quality study,⁹¹ which reported a significantly reduced risk of asthma in smokers. A sensitivity analysis excluding this study⁹¹ found smokers were 1.81 times (81%) more likely to develop asthma than people who never smoked (RR, 1.81; 95% CI, 1.37-2.38; $I^2 = 68%$; seven studies). The risk of developing asthma from active smoking was similar between European and non-European studies and between higher- and lower-quality studies.

Asthma Exacerbations

Five studies⁹⁷⁻¹⁰¹ were identified for inclusion which assessed the effect of active and passive smoking on exacerbations of asthma in adults, pregnant women, or children. Three of the studies (60%) were deemed to be of high quality.

Active Smoking: Two studies assessed the effect of active smoking on asthma exacerbations.^{97,98} Adults with asthma who were current or ex-smokers had a 1.71 times higher risk of subsequent asthma exacerbations than adults with asthma who had never smoked (RR, 1.71; 95% CI, 1.48-1.97; one study).⁹⁷ A study of 80 pregnant women with asthma found that being a current smoker or ex-smoker significantly increased the number of severe asthma exacerbations per year, and being a current smoker also resulted in poorer asthma control compared with those who never smoked.⁹⁸

Passive Smoking: Three studies assessed the effect of passive smoking on asthma exacerbations.⁹⁹⁻¹⁰¹ In nonsmoking adults, exposure to passive smoke

significantly increased the risk of being restricted in daily activities (RR, 1.61; 95% CI, 1.06-2.46; one study),¹⁰⁰ but had no significant effect on increased risk of cough, shortness of breath, or being awakened by asthma⁹¹ or on admission to hospital for asthma.⁹⁹ In a study of 140 children with asthma between 3 and 15 years of age, exposure to passive smoke in the household or by the mother more than doubled the risk of multiple hospital admissions for asthma per year (RR, 2.55; 95% CI, 1.12-5.82; one study), and exposure to maternal smoking more than tripled the risk of multiple hospital admissions for asthma per year (RR, 3.25; 95% CI, 1.13-8.85).¹⁰¹

TB

Five studies¹⁰²⁻¹⁰⁶ assessing the effect of active and passive smoking on the risk of developing TB were identified from four previous systematic reviews¹⁰⁷⁻¹¹⁰ and an updated search. Four of the studies (80%) were deemed to be of high quality. None of the studies were conducted in Europe.

Active Smoking: Four studies assessed the effect of active smoking.¹⁰²⁻¹⁰⁵ People who smoked were 1.57 times (57%) more likely to develop TB than those who had never smoked (RR, 1.57; 95% CI, 1.18-2.10; $I^2 = 93%$; four studies) (Fig 1). Significantly higher risks of TB from smoking were seen from the higher-quality studies (2.2 times) compared with the study with a lower quality (1.1 times) (test for subgroup differences, $P < .00001$); however, similar risks were seen in studies of men and women. All of the studies reported an increased risk of TB with increasing numbers of cigarettes smoked per day.

Passive Smoking: Two studies assessed the effect of passive smoking.^{104,106} Exposure to household tobacco smoke increased the risk of developing TB by 1.44 times (44%) compared with people who were unexposed to household tobacco smoke (RR, 1.44; 95% CI, 1.02 to 2.04; $I^2 = 0%$; two studies). Both of the included studies were deemed to be of high quality, and similar results were seen for men and women. However, no significant trend was seen between the increased frequency of exposure to passive smoke (numbers of days per week exposed) and the risk of TB ($P = .74$).¹⁰⁴

Sleep Apnea

Five studies¹¹¹⁻¹¹⁶ assessing the effect of active and passive smoking on the risk of sleep apnea were identified from a previous review¹¹⁷ and an updated search. None of the included studies were deemed to be of high quality.

Active Smoking: Three studies assessed the effect of active smoking on the development of sleep apnea in adults.^{112,113,116} Two of these studies reported numerical data, which found that people who smoke are twice as likely to have sleep apnea than those that do not smoke (RR, 1.97; 95% CI, 1.02-3.82; two studies).^{113,116} Men and women were found to have similar risks of sleep apnea from smoking (1.5-fold increase) when compared with nonsmokers.¹¹⁶ One study investigated the intensity of exposure and found a dose-dependent relationship where the greatest risk of sleep apnea was associated with smoking at least 40 cigarettes per day (RR, 8.38; 95% CI, 1.68-41.94; one study).¹¹³

Passive Smoking: Two studies assessed the effect of passive smoking on the risk of development of sleep apnea in infants or young children.^{114,115} Maternal smoking during pregnancy approximately doubled the risk of their infant developing sleep apnea (age range, 1 day to 29 weeks) (RR, 1.76; 95% CI, 1.17-2.64; one study).¹¹⁴ Maternal smoking after birth significantly increased the risk of developing sleep apnea in infants between the ages of 6 and 18 months (RR, 1.25; 95% CI, 1.06-1.47; one study).¹¹⁵ One study¹¹⁴ also reported significantly more infants developed sleep apnea where both parents had smoked during pregnancy compared with only mothers smoking during pregnancy ($P = .007$).

LRTI in Childhood

Thirty-four studies¹¹⁸⁻¹⁵¹ assessing the effect of passive smoking on the risk of LRTI in children < 2 years of age were identified from a previous review¹⁵² and an updated search. Eighteen studies considered the effects of any household member smoking: six of both parents smoking, nine of paternal smoking, 16 of maternal smoking, and 11 of prenatal maternal smoking (some studies covered more than one exposure). Sixteen (47%) studies were deemed to be of high quality, and 17 were conducted in Europe.

Infants exposed to smoking by any household member were 1.43 times (43%) more likely to develop LRTI than those not exposed to smoking in the home (RR, 1.43; 95% CI, 1.28-1.59; $I^2 = 45%$; 18 studies) (Fig 2). Similar risks of LRTI were seen in European studies (1.42 times) and non-European studies (1.46 times) and in higher-quality (1.49 times) and lower-quality (1.35 times) studies.

Significant increased risks of developing LRTI were also seen in infants exposed to both parents smoking (RR, 1.82; 95% CI, 1.51-2.19; $I^2 = 45%$; six studies), prenatal maternal smoking (RR, 1.19; 95% CI, 1.10-1.29; $I^2 = 78%$; 11 studies), and maternal smoking in the postnatal period (RR, 1.62; 95% CI, 1.46-1.79; $I^2 = 50%$; 16 studies), but not to paternal smoking (RR, 1.15; 95% CI, 0.97-1.36; $I^2 = 51%$; nine studies).

Childhood Asthma and Wheeze

Seventy-one studies assessing the effect of passive smoking in the risk of developing asthma or wheeze in childhood were identified from a recent systematic review.¹⁵³ Thirty one of the studies (44%) were deemed to be of high quality, and 32 were conducted in Europe.

Wheeze in Childhood: Children ≤ 2 years of age who had been exposed to prenatal maternal smoking had a 1.41 times (41%) increased risk of developing wheeze compared with unexposed children (RR, 1.41; 95% CI, 1.19- 1.67) (Fig 3). Similar effects were observed for the relationship between prenatal maternal smoking and the incidence of wheeze in children between 3 and 4 years of age (1.28 times) and 5 and 18 years (1.52 times) of age. Similar effect sizes were seen in children between 5 and 18 years of age who were exposed to paternal smoking (1.39 times) and in children exposed to household tobacco smoke (1.32 times).

The strongest impact on the incidence of wheeze was seen in children exposed to postnatal maternal smoking, where children < 5 years of age exposed to postnatal

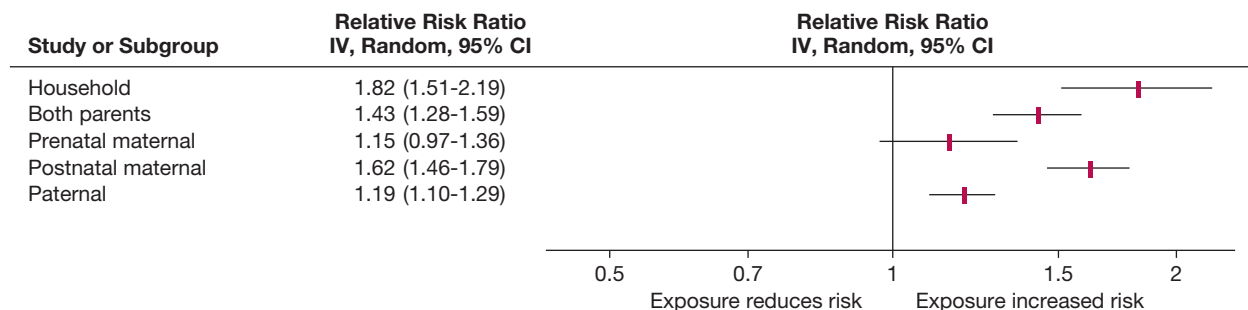


Figure 2 – Summary estimates from meta-analyses assessing the effect of passive smoking on the risk of lower respiratory tract infection in infants.

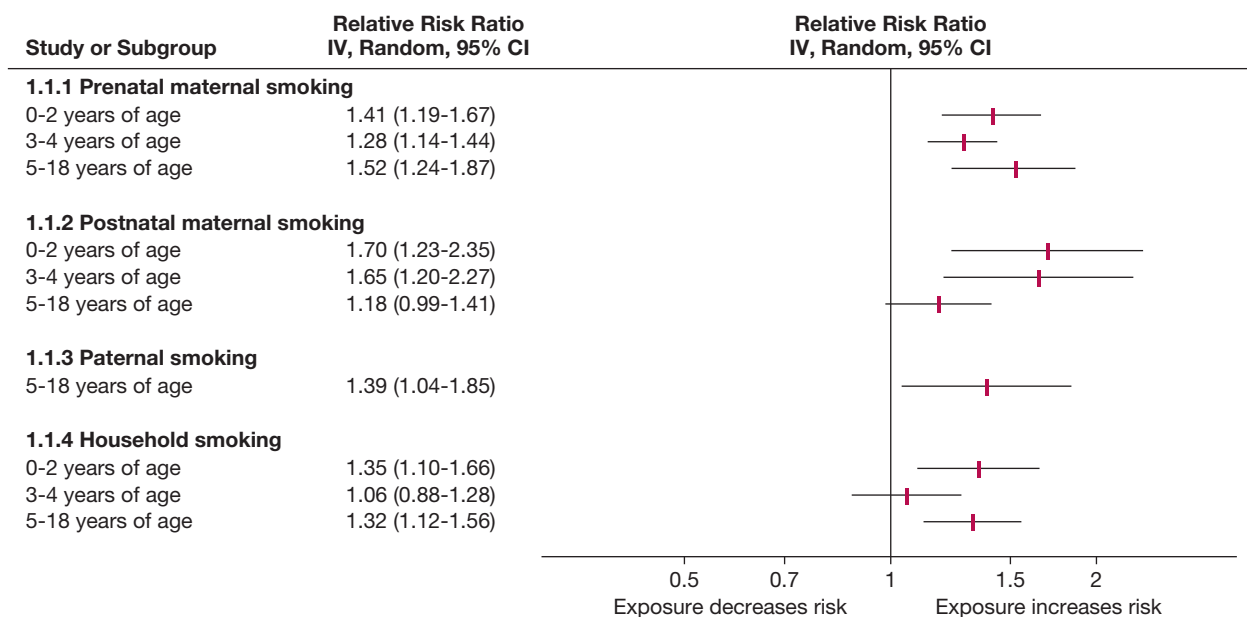


Figure 3 – Summary estimates from meta-analyses assessing the effect of exposure to passive smoking on the risk of developing wheeze in children.

maternal smoking were 1.65 to 1.70 times (65%-70%) more likely than unexposed children to develop wheeze (≤ 2 years: pooled RR, 1.70; 95% CI, 1.23-2.35; 3-4 years: RR, 1.65; 95% CI, 1.20-2.27).

For all sources of exposure to smoking (prenatal, postnatal, paternal, and household), the effect size for the increased risk of wheeze was similar in sensitivity analyses based methodologic quality and geographic location of the studies, except for the following sensitivity analyses: In European studies, the magnitudes of the risks of wheeze from prenatal maternal smoking in children < 2 years of age were larger (2.21 times) than all studies (1.41 times). For children between 3 and 4 years of age, a larger magnitude of risk of household smoking on the risk of wheeze was seen in higher quality studies (1.20 times) than all studies (1.06 times).

Asthma in Childhood: Children ≤ 2 years of age who were exposed to prenatal maternal smoke were 1.85 times (85%) more likely to develop asthma than unexposed children (RR, 1.85; 95% CI, 1.35-2.54) (Fig 4). However, smaller magnitudes of risk were seen in children between 3 and 4 years of age (1.30 times) and those between 5 and 18 years of age (1.23 times). Across the age groups, children exposed to household smoking were 1.14 to 1.30 times (14%-30%) more likely to develop asthma. However, exposure to postnatal maternal or paternal smoke did not appear to consistently increase the risk of developing asthma in any age group.

For all sources of exposure to smoking (prenatal, postnatal, paternal, and household), the effect size for

the increased risk of asthma was similar in sensitivity analyses based methodologic quality and geographic location of the studies, except for the following sensitivity analyses: In European studies, the magnitudes of the risks of asthma from postnatal maternal smoking in children between 5 and 18 years of age were larger (1.48 times) than all studies (1.20 times). In children between 5 and 18 years of age, the magnitude of the risk of asthma from exposure to household smoking was larger (2.02 times) than all studies (1.30 times).

Lung Function in Childhood

Infants: Thirteen studies¹⁵⁴⁻¹⁶⁶ assessing the effect of exposure to passive smoking on lung function in infants were identified from a previous review² and an updated search. Lung function measurements were assessed within 8 weeks of birth in all studies. Seven studies were conducted in Europe.

Prenatal Exposure: Seven of the studies assessed the effect of prenatal exposure of infants to maternal smoking on maximal flow at functional residual capacity (FRC), with most finding no significant reductions.^{155,159,160,162,166} However, the two remaining studies found prenatal maternal smoking significantly reduced maximal flow at FRC.^{158,165} Prenatal maternal smoking had no significant effect on FRC at 8 weeks of age.¹⁵⁶ Prenatal maternal smoking was significantly associated with reduced tidal breathing ratio (tPTEF:tE [time to reach peak tidal expiratory flow as a proportion of total expiratory time]) in the infants within 1 week

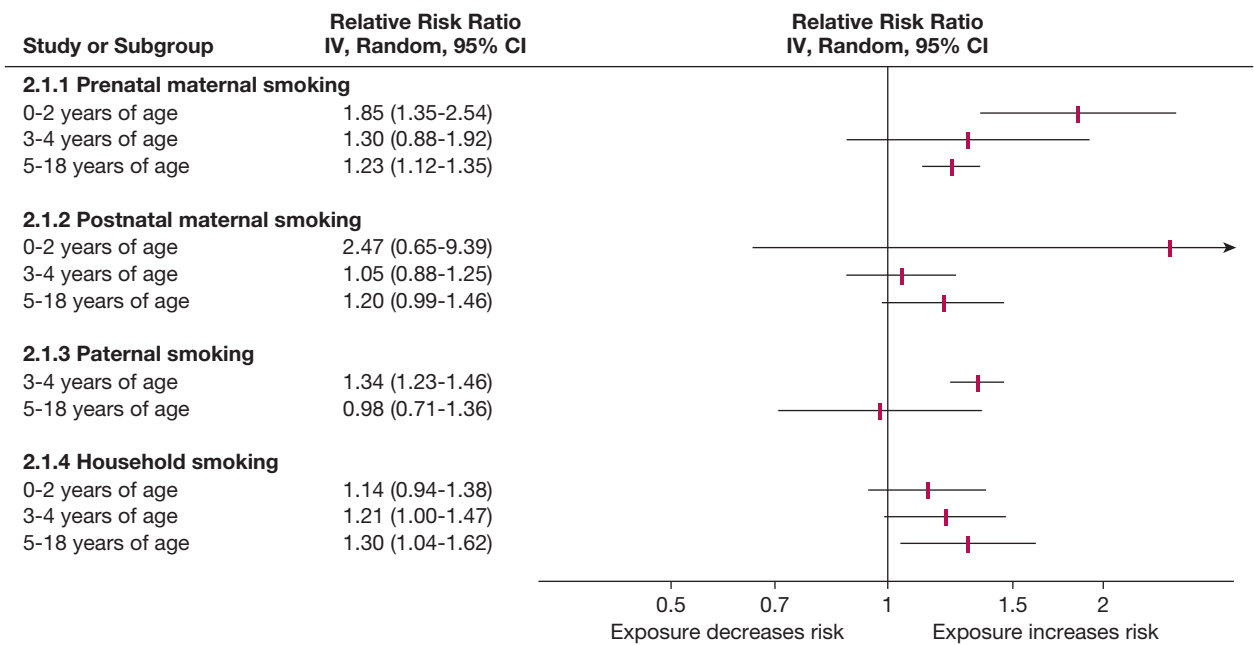


Figure 4 – Summary estimates from meta-analyses assessing the effect of exposure to passive smoking on the risk of developing asthma in children.

after birth¹⁶³ and in those born preterm at 37 weeks' gestation,¹⁵⁹ but no association between tidal breathing ratio in infants and maternal smoking was seen in the other studies.¹⁵⁵⁻¹⁵⁷ No apparent effect of prenatal smoking was seen on infant respiratory system compliance,^{156,157,159,165} except for one study where respiratory system compliance was reduced in boys but not girls.¹⁶¹ Prenatal maternal smoking reduced lung function (FEV_{0.5} [forced expiratory volume in 0.5 seconds]), in infants at 6 weeks of age.¹⁵⁴

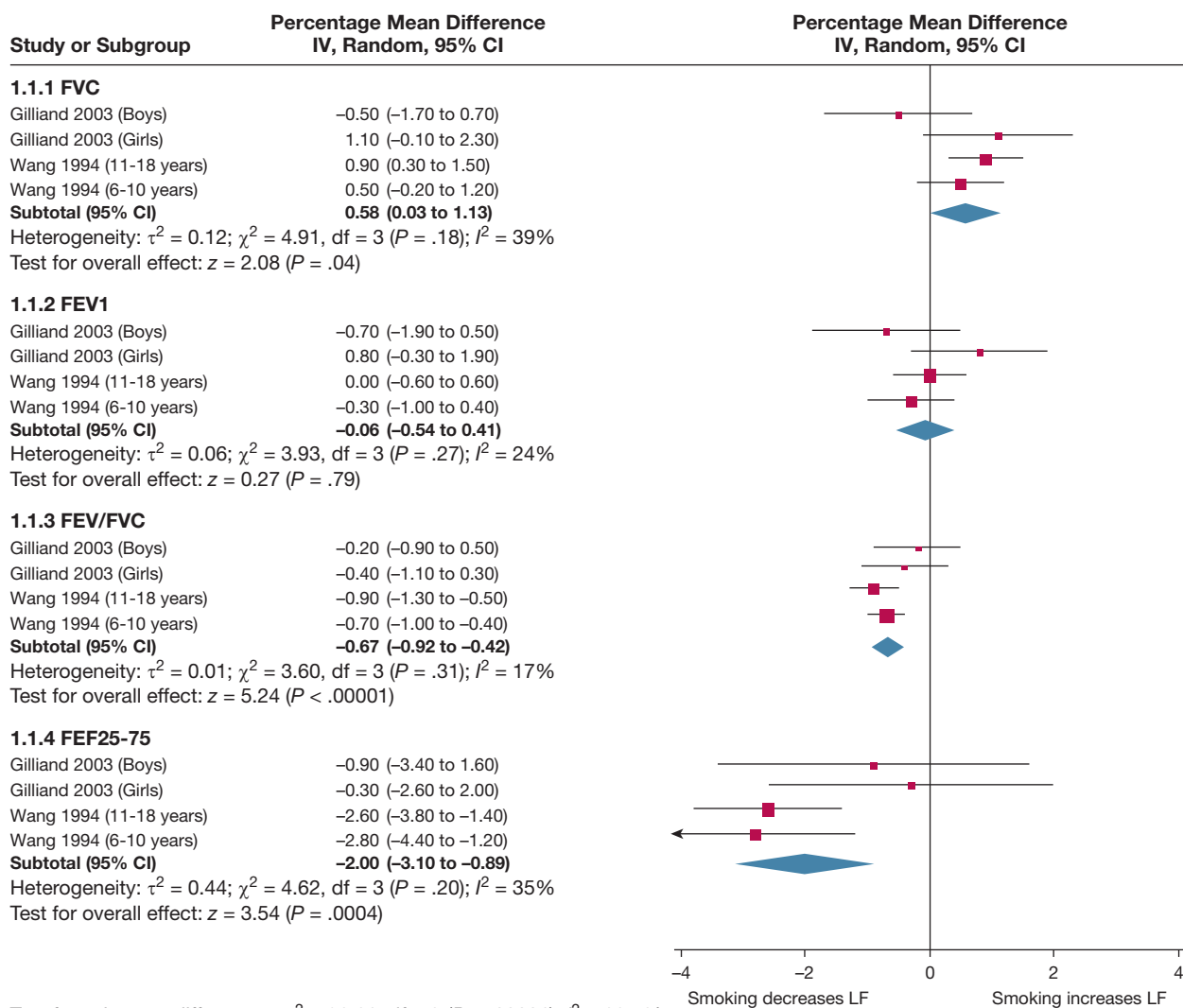
Postnatal Exposure: Postnatal maternal smoking significantly reduced airflow during inspiration and expiration in their infants as measured by specific conductance and hence potentially increased susceptibility to asthma and/or COPD.¹⁵⁷ However, maternal postnatal smoking was not associated with bronchial responsiveness in their infants^{154,155} or a reduction in lung volume.^{156,158,161} Paternal smoking during pregnancy had no significant impact on various measures of lung function (tidal volume, respiratory rate, minute ventilation, and time to peak expiratory flow).¹⁶⁴

School-Aged Children: Twelve studies¹⁶⁷⁻¹⁷⁸ assessing the effect of passive smoking on lung function in school-aged children were identified from a previous review² and an updated search. None of the studies were deemed to be of high quality, and only four studies were conducted in Europe.

Prenatal Exposure: Individual studies found smoking during pregnancy was significantly associated with children having a 62-mL reduction in FEV₁ and 53-mL reduction in FVC at age 5 years of age¹⁷⁴ and significantly lowered peak expiratory flow at 8 years of age¹⁶⁷; however, no significant effect on lung function was seen in other studies.^{168,171}

Postnatal Exposure: Any parental smoking significantly reduced FEV/FVC ratios by 0.67% and forced expiratory flow during the midportion of the FVC by 2% and significantly increase FVC by 0.58%, but had no effect on FEV₁ (two studies) (Fig 5).^{171,178} Data from individual studies showed postnatal maternal smoking had no significant effect on measures of lung function^{167,172,173,176}; however, continual maternal smoking during and after pregnancy significantly reduced some measures of lung function (FEV/FVC and forced expiratory flow during the midportion of the FVC), with similar magnitudes of reductions seen in boys and girls.¹⁷¹ Furthermore, having both parents smoke resulted in significantly lower FEV₁/FVC ratios in boys, but not in girls; but no effect was seen for only exposure to paternal smoking.¹⁷⁶ In another study, exposure to smoke measured using cotinine levels in hair resulted in significant decreases in peak expiratory flow, but not FEV₁.¹⁷⁵

Three of the included studies assessed the effect of exposure to smoking on lung growth^{169,170,177}; however,



Test for subgroup differences: $\chi^2 = 26.61$, df = 3 ($P < .00001$), $I^2 = 88.7\%$

Figure 5 – Meta-analysis for the effect of passive smoke exposure on lung function in school-aged children. FEF25-75 = forced expiratory flow during the midportion of the FVC; LF = lung function.

no consistent effect of parental or household smoking on lung function assessment of lung growth was demonstrated. Exposure to household smoking resulted in a significant increase in lung growth by 7 mL in girls, but significantly reduced growth by 12 mL in boys.¹⁶⁹ Having both parents smoke resulted in a significant reduction in lung growth in children between 8 and 9 years of age, but no effect was seen at older ages or in those with one parental smoker.¹⁷⁰ However in another study, maternal smoking significantly reduced the expected annual lung growth.¹⁷⁷

Discussion

After decades of public skepticism among tobacco smokers, this millennium has seen major advances in public awareness that tobacco smoking poses a risk to

health as a result of highly successful tobacco control policies and public information campaigns.^{3,179-181} However, the battle to ensure the public fully understands the health risks of tobacco smoking is far from won. The public and policymakers are well aware that lung cancer is one of the greatest risks of tobacco smoking. However, there is little awareness of the risk of other diseases from active and passive smoking, and few parents understand the damage their smoking can do to their children.¹⁸⁰ This lack of knowledge remains a major challenge for policymakers. Without full understanding of the risks, smokers are less likely to have the motivation to quit, even when effective smoking cessation measures are readily available.^{182,183}

The data presented in this article provide policymakers, the public, and health professionals with an easy one-stop

shop where they can find evidence-based meta-analyses of pooled data from studies published to 2013, on the relationship between tobacco smoking and increased risks of respiratory diseases in adults and in children. The main findings from our updated systematic reviews and meta-analyses are subsequently discussed.

As previously mentioned, it is recognized that the public knows smoking increases the risk of lung cancer¹; however, they have little knowledge of the level of the risk, where smokers are 11 times more likely to develop lung cancer, and there is no safe minimum number of cigarettes per day. More education and publicity is needed to increase public awareness of these very high risks. Exposure to passive smoke increased the risk of lung cancer in nonsmokers by 1.41 times. Raising public awareness about lung cancer is also important because motivation to quit may be improved through better awareness and knowledge about the symptoms of lung cancer; the lack of a curative treatment; the catastrophic effect on life expectancy, with only 12.6% of patients being alive 5 years after diagnosis; and lung cancer now being the leading cause of cancer deaths worldwide in both men and women.¹⁸¹

It is estimated that 40% to 50% of lifelong smokers will develop COPD¹⁸¹; however, the exact mechanism by which tobacco smoking causes or promotes COPD is not known. Furthermore, the general public have little knowledge of this disease and its increased risk as a result of smoking. We found smokers are 4.01 times more likely to develop COPD, and nonsmokers exposed to passive smoking had 1.44 to 1.72 fold increased risk of developing COPD. However, the latter finding is only based on data from three studies; therefore, more research is needed to better define the relationship between passive smoking and the risk of development of COPD and to establish whether there are differential effects based on whether passive smoke exposure occurs in childhood or adulthood.

Tobacco smoking is not generally thought of as a risk factor for asthma; therefore, the public should be made aware that adult smokers are 1.61 times more likely to develop asthma, and adult smokers are 1.71 times more likely to have asthma exacerbations. We found pregnant women with asthma who smoke have more asthma exacerbations per year and poorer asthma control, and children exposed to passive smoke are more than twice as likely to have multiple hospital admissions.

Although there has been a major reduction in the prevalence and incidence of TB in past decades, the

threat of TB is now growing once again because of the emergence of new strains that are resistant to anti-TB drugs. With the inevitable threat of multidrug-resistant TB increasing across Europe, it is important for policymakers to learn of any preventative measures, large or small, that might contribute to reducing this emerging new threat. Therefore, it is important that we highlight the need to raise public awareness in relation to our findings that (1) adults smokers are 1.57 times more likely to develop TB, (2) the risk of TB increases with increasing consumption of cigarettes per day for a longer period of time, and (3) nonsmokers who are exposed to passive smoke have a 1.44 times increased risk of developing TB. This evidence provides a motivator to ensure effective smoking-cessation programs are provided for in populations who live in regions identified as at especially high risk of TB.

The role of smoking on the risk of sleep apnea is currently unclear. We found adult smokers were 1.97 times as likely to develop sleep apnea, and the risk could be as great as 8.38 times when at least 40 cigarettes are smoked per day. We also found maternal smoking during pregnancy increased the risk of sleep apnea in infants by 1.76 times; postnatal maternal smoking increased the risk of sleep apnea in childhood by 1.25 times. Our review indicates that smoking is a significant contributory factor to sleep apnea, but the evidence base is limited and needs strengthening. Therefore, efforts should be made to increase public awareness of the link between smoking and sleep apnea.

LRTIs are an especial problem in childhood.¹⁸¹ We found the risk of infants developing LRTI was significantly increased from their exposure to passive smoking within the household, where the largest increase in risk (1.82-fold) was from both parents smoking. We also found prenatal exposure to maternal smoking increased the risk of LRTI by 1.19-fold. Policymakers are already aware of the harm passive smoking can do to children, and they should be informed that smoke-free legislation has already led to a decrease in passive smoke exposure, with a corresponding reduction in hospital admissions of children with respiratory tract infections.¹⁸⁴

Regarding childhood asthma and wheeze, exposure to passive smoking in the home environment significantly increased the risk of developing asthma and/or wheeze, where the largest increases in risk seemed to be from maternal prenatal smoking on asthma in infants < 2 years of age (1.85-fold) and maternal postnatal smoking

on wheeze in children < 5 years of age (up to 1.70-fold). The findings indicate that passive smoking has a greater effect on the risk of wheeze in children across all age groups than on the risk of asthma, where infants < 2 years of age are at greater risk. More research is needed to understand the mechanisms underlying these effects and the components of tobacco smoke involved. It is encouraging that adoption of comprehensive smoke-free legislation has led to a significant reduction in the rate of hospital admissions for childhood asthma.¹⁸⁵

Regarding lung function, we found exposure to passive smoking can decrease lung function in infants within 8 weeks of birth and in school-aged children. The findings of these studies were variable, and most lung function measurements were normal. The only findings of note were that exposure of infants to maternal smoking after birth is associated with reduced airflow, which may reflect the reported increased susceptibility of children to the various airways diseases previously discussed, and that maternal smoking during pregnancy and parental smoking after birth may have a detrimental effect on lung function in school-aged children. However, there is currently insufficient evidence to reach firm conclusions on the effect of prenatal and postnatal parental smoking on lung function of their children.

The strength of our systematic reviews is that methodologic quality of the evidence within the systematic reviews was generally good, with most of the more recent studies providing adjusted effect estimates, thereby reducing the potential for confounding within our pooled estimates. We are confident that our search strategies were comprehensive, and we were able to identify further eligible studies through contact with experts with an interest in tobacco control within the respiratory medicine field. A limitation of the systematic reviews relates to the high levels of heterogeneity found within some comparisons; however, we performed

exploration analyses using subgroup and sensitivity analyses to assess whether the association varied by participant-level characteristics (age and sex) and study-level characteristics (geographic location and methodologic quality) and found relatively consistent findings across these subgroups.

Conclusions

SmokeHaz provides a useful resource enabling policymakers and others to rapidly view the available evidence-based scientific data on the increased risk of development of respiratory diseases in adults and children caused by active and passive tobacco smoking. The high levels of risk reported support smoke-free legislation and justify its continuance and expansion, not only in public places, but also in the home and other confined spaces (eg, cars), to protect children. All governmental efforts against smoking should be strengthened, with the ultimate aim of phasing out tobacco use. Because of the now indisputable health hazards, measures to help all current smokers to quit should be widely available to the general public and to patients suffering from smoking-related diseases, ensuring cost is not a barrier. Education to disseminate information to increase public awareness of the many health risks of smoking should be improved, and education and training on the health risks and in smoking cessation methods should be included in the curricula of all health professionals and medical students. The SmokeHaz systematic review of respiratory health risks of smoking and its companion free public website⁴ are ideal as educational resources because they aim to promote and strengthen public awareness of tobacco control issues, therefore complying with Article 12 (education, communication, training, and public awareness) of the World Health Organization's *Framework Convention on Tobacco Control*.³

Acknowledgments

Author contributions: J. L.-B. takes responsibility for (is the guarantor of) the content of the manuscript, including the data and analysis. J. L.-B. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, including and especially any adverse effects. L. J., P. L. H., C. G. G., and J. L.-B. made substantial contributions to conception and design, acquisition of data, analysis and interpretation of data, and drafted the submitted article. P. P., J. B., C. V., and C. J.-R. contributed substantially to the study design, data analysis and interpretation, and revised the manuscript critically for important intellectual content. All authors have provided final approval of the version of the manuscript to be published and have agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Financial/nonfinancial disclosures: None declared.

Role of sponsors: The sponsor had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript.

Other contributions: We thank Rachel Murray, PhD (UK Centre for Tobacco and Alcohol Studies, University of Nottingham) for her help with screening titles and abstracts to identify systematic reviews assessing the effect of active smoking on asthma in adults; and Tricia McKeever, PhD (Division of Epidemiology and Public Health, University of Nottingham) for her help with the identification of eligible studies of the effect of active and passive smoking on asthma exacerbations and for sharing the summary data from passive smoking on the risk of asthma and wheeze in childhood review. We also thank the other European Respiratory Society Tobacco Control Committee Members who served during the period 2012 to 2015 (Bertrand Dautzenberg, MD, PhD, Bo Lundbäck, MD, PhD, Monica Fletcher, OBE, MSc Archie Turnbull, Paraskevi Katsounou, MD, PhD, Dick Heederik, MD, PhD, Dan Smyth, PhD, Sofia Ravara, MD, Jean-Paul Sculier, MD, PhD, Fernando Martin, PhD, and Jose Ignacio De Grada Orive, MD, PhD) and the European Respiratory Society Officers for their assistance.

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