

REVIEW

Meta-Analysis of the Association Between Secondhand Smoke Exposure and Physician-Diagnosed Childhood Asthma

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ABSTRACT

Introduction: Studies suggest an association between secondhand smoke exposure and the development of childhood asthma. Several countries are considering legislation to protect children from exposure.

Methods: A systematic review was conducted using MEDLINE, Embase, PubMed, and Web of Knowledge databases and a random effects meta-analysis was undertaken. Heterogeneity was assessed using the I^2 test. Publication and small study biases were examined visually using a funnel plot and tested formally using Egger test. Univariate and multivariate meta-regression analyses were undertaken, including a subgroup analysis of cohort studies to examine the effect of duration of follow-up.

Results: Twenty relevant studies were identified (14 cross-sectional, 4 cohort, and 2 case-control) and provided 31 estimates of effect size. The pooled odds ratio was 1.32 (95% CI: 1.23, 1.42, $p < .001$). There was moderate heterogeneity ($I^2 = 74.2\%$, $p < .001$). On multivariate meta-regression analysis, effect size estimates were significantly higher for case-control studies ($p = .042$) and those using self-reported exposure to secondhand smoke ($p = .050$). There was no evidence of significant publication or small study bias (Egger test, $p = .121$).

Conclusions: There is now consistent evidence of a modest association between secondhand smoke and physician-diagnosed childhood asthma. These results lend support to continued efforts to reduce childhood exposure to secondhand smoke.

INTRODUCTION

Asthma often commences in childhood (Larsen, 1992) and is associated with significant morbidity (Gerald, Sun, Grad, & Gerald, 2009). There has been an increase in the prevalence of asthma globally, especially among those aged 13–14 years (Pearce et al., 2007). The United Kingdom has the highest prevalence of childhood asthma in the western world (Kaur et al., 1998), with over 1 million children currently living with asthma (Asthma UK Impact Report 2009–2011).

The increased risk of asthma in children following migration from developing to industrialized countries suggests that environmental and lifestyle risk factors play an important role (Waite, Eyles, Tonkin, & O'Donnell, 1980). Active smoking is widely accepted as a risk factor for asthma (Thomson, Chaudhuri, & Livingston, 2004), and some investigators believe that there is also now sufficient evidence to support a causal link with secondhand smoke (SHS) exposure (Mitchell et al., 2012; Tager, 2008). In the United Kingdom, children account for the largest proportion of nonsmokers exposed to SHS (Ashley and Ferrence, 1998). Based on salivary cotinine measurements, 58% of Scottish children are exposed to SHS

(Simms et al., 2010). Parental or caregiver smoking is the main source; predominantly due to maternal smoking (Ashley and Ferrence, 1998). More than 40% of school children live with at least one parent who smokes (Akhtar, Currie, Currie, & Haw, 2007). Children have very little control over their home environment. The majority of SHS exposure in children occurs in private dwellings (Oberg, Jaakkola, Woodward, Peruga, & Pruss-Ustun, 2011). The prevalence of SHS exposure declines by 3.2% for every 1 year increase in age (Simms et al. 2010), due to decreasing time spent in the home. The aim of this study was to collate the existing evidence on the association between SHS exposure and physician-diagnosed childhood asthma.

METHODS

Systematic Review

The systematic review was conducted in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) guidelines. An electronic search was undertaken using the MEDLINE, Embase, Web of Science, and PubMed databases. The search terms comprised (secondhand

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smok* OR passive smok* OR environmental tobacco) AND (child* OR adolescent OR preschool OR toddler) AND asthma*) and were applied to both titles and abstracts. The search was limited to original studies conducted on humans and written in, or translated into, English. No date restrictions were applied. The search was last updated on January 31, 2011. Studies identified by the electronic search were reviewed manually and inclusion was restricted to studies that produced a quantified estimate of effect size and in which participants were younger than 18 years of age and asthma was diagnosed by a physician. The information extracted from each study included year of publication, country, study design, size and population, age and sex of participants, case definition, measurement of SHS, numbers of exposed, unexposed, cases and controls, effect size estimate, and its 95% confidence interval. Where subgroup analyses were undertaken, the results of these were included in favor of the overall result.

Meta-Analysis

Meta-analysis was performed using Stata v11.2 software. Odds ratio (*OR*) was the most commonly reported measure of effect size. In the two studies that reported relative risk (Kattan, Gergen, Eggleston, Visness, & Mitchell, 2007; Teach, Crain, Quint, Hylan, & Joseph, 2006), these were treated as equivalent to *OR*. The individual studies included in the meta-analysis were conducted in different countries and settings. Therefore, we used random effects meta-analysis to take account of possible nonrandom variability in effect estimates. A forest plot was produced to graphically represent the contributions of individual studies, and the I^2 test was used to measure heterogeneity. We also undertook a series of meta-analyses stratified by study design (cross-sectional, cohort, and cases-control), age group (preschool, school-age, and mixed), and continent (America, Asia, and Europe) to produce a pooled effect size for each stratum. Stratification based on study size and measure of exposure was not done because some of the subgroups contained too few studies. A meta-influence analysis was conducted to investigate the influence of individual studies on the overall effect size, and a cumulative meta-analysis to determine how the pooled estimate has changed over time. Possible publication and small study bias were assessed visually using a funnel plot of the log *ORs* against the inverse of the *SE*, and then tested formally using Egger regression test. Meta-regression was used to determine whether any of the following study characteristics had contributed to between-study heterogeneity: study design, size and location, age of participants, and measure of SHS exposure. To reduce the likelihood of false-positive results due to multiple testing, 20,000 random permutations were run for each regression analysis. The meta-regression was rerun for the subgroup of cohort studies, including length of follow-up as a covariate.

RESULTS

Systematic Review

Of the 1,269 studies identified from the electronic search and an additional 19 identified from other sources, 521 remained after exclusion of duplicates and review articles (Appendix). On manual review, a further 482 were excluded as irrelevant.

The full texts were obtained for the remaining 39 studies. Eight related to prenatal exposure, seven used ineligible case definitions including self-diagnoses and diagnostic labels such as “wheeze,” and four did not quantify the effect size. No additional studies were identified from the reference lists. Therefore, 20 studies were eligible for inclusion (Chilmonczyk et al., 1993; Dekker, Dales, Bartlet, Brunekreef, & Zwanenburg, 1991; Dong et al., 2007; Ehrlich et al., 1992; Freeman, Schneider, & McGarvey, 2003; Gilliland, Li, and Peters, 2001; Gupta, Aggarwal, Kumar, & Jindal, 2001; Han, Lee, & Guo, 2009; Horak, Morassa, Ulmerb, 2007; Hugg, Jaakkola, Ruotsalainen, Pushkarev, & Jaakkola, 2008; Jaakkola, Nafstad, & Magnus, 2001; Kattan et al., 2007; Lindfors et al., 1995; Mannino, Homa, & Redd, 2002; Ribeiro, Furuyama, Schenkman, & Jardim, 2002; Sturm, Yeatts, & Loamis, 2004; Tanaka, Miyake, Arakawa, Sasaki, & Ohya, 2007; Teach et al., 2006; Tsai, Huang, Hwang, & Lee, 2010; Barraza Villarreal, Sanfín Aguirre, Téllez Rojo, Lacasaña Navarro, & Romieu, 2003).

Of the 20 studies, 4 were conducted in Europe (Horak et al., 2007; Hugg et al., 2008; Jaakkola et al., 2001; Lindfors et al., 1995), 9 in North America (Chilmonczyk et al., 1993; Dekker et al., 1991; Ehrlich et al., 1992; Freeman et al., 2003; Gilliland et al., 2001; Kattan et al., 2007; Mannino et al., 2002; Sturm et al., 2004; Teach et al., 2006), 2 in Central/South America (Barraza Villarreal et al., 2003; Ribeiro et al., 2002), and 5 in Asia (Dong et al., 2007; Gupta et al., 2001; Han et al., 2009; Tsai et al., 2010; Tanaka et al., 2007) (Table 1). Thirteen of the studies involved more than 1,000 participants each (Barraza Villarreal et al., 2003; Dekker et al., 1991; Dong et al., 2007; Freeman et al., 2003; Gilliland et al., 2001; Gupta et al., 2001; Han et al., 2009; Horak et al., 2007; Hugg et al., 2008; Jaakkola et al., 2001; Sturm et al., 2004; Tanaka et al., 2007; Tsai et al., 2010), and all 20 studies included both male and female participants.

Fourteen were cross-sectional studies (Barraza Villarreal et al., 2003; Dekker et al., 1991; Dong et al., 2007; Freeman et al., 2003; Gilliland et al., 2001; Gupta et al., 2001; Han et al., 2009; Horak et al., 2007; Hugg et al., 2008; Mannino et al., 2002; Ribeiro et al., 2002; Sturm et al., 2004; Tanaka et al., 2007; Tsai et al., 2010), two were case-control studies (Ehrlich et al., 1992; Lindfors et al., 1995), and four were cohort studies (Chilmonczyk et al., 1993; Jaakkola et al., 2001; Kattan et al., 2007; Teach et al., 2006). Three of the cohort studies were hospital-based, disease cohorts (Chilmonczyk et al., 1993; Kattan et al., 2007; Teach et al., 2006), and one was a general population cohort (Jaakkola et al., 2001). Their follow-up period ranged from 9 months (Kattan et al., 2007) to 4 years (Jaakkola et al., 2001). In the three disease cohorts, the outcomes ascertained included exacerbations (Chilmonczyk et al., 1993), unplanned hospital attendances (Teach et al., 2006), symptom frequency and duration (Kattan et al., 2007; Teach et al., 2006), and pulmonary function tests (Chilmonczyk et al., 1993). One case-control study recruited children presenting to hospital with asthma as emergencies, and used children presenting with other conditions as controls (Ehrlich et al., 1992). The second recruited cases from a hospital allergy clinic and controls from the general population (Lindfors et al., 1995). One of the cross-sectional studies recruited children directly from the general population (Mannino et al., 2002), and the remainder recruited them via schools or kindergartens (Barraza Villarreal et al., 2003; Dekker et al., 1991; Dong et al., 2007; Freeman et al., 2003; Gilliland et al., 2001; Gupta et al., 2001;

Table 1. Study Characteristics

Author	Year	Country	Study design	N	Age criteria	Exposure measurement
Barraza Villarreal et al.	2003	Mexico	Cross-sectional	6,174	6–14 years	Parental report
Chlmonczyk et al.	1993	United States	Asthma cohort	199	8 mo to 13 years	Cotinine
Dekker et al.	1991	Canada	Cross-sectional	9,841	5–8 years	Parental report
Dong et al.	2007	China	Cross-sectional	6,053	Preschool	Parental report
Ehrlich et al.	1992	United States	Case-control	223	3–14 years	Cotinine
Freeman et al.	2003	United States	Cross-sectional	4,000	Preschool to grade 5	Child and parental report
Gilliland et al.	2001	United States	Cross-sectional	5,767	School grades 4, 7, and 10	Parental report
Gupta et al.	2001	India	Cross-sectional	9,090	School grades 6 to 12	Child report
Han et al.	2009	Taiwan	Cross-sectional	19,646	6–15 years	Parental report
Horak et al.	2007	Austria	Cross-sectional	1,683	Preschool	Parental report
Hugg et al.	2007	Finland and Russia	Cross-sectional	1,093	7–16 years	Child and parental report
Jaakkola et al.	2001	Norway	General population cohort	2,531	Born 1992–1993	Parental report
Kattan et al.	2007	United States	Asthma cohort	663	4–9 years	Cotinine
Lindfors et al.	1995	Sweden	Case-control	511	1–4 years	Parental report
Mannino et al.	2002	United States	Cross-sectional	523	4–16 years	Cotinine
Ribeiro et al.	2002	Brazil	Cross-sectional	183	4–9 years	Parental report
Sturm et al.	2004	United States	Cross-sectional	128,568	School grades 7 and 8	Child report
Tanaka et al.	2007	Japan	Cross-sectional	23,044	6–15 years	Parental report
Teach et al.	2006	United States	Asthma cohort	488	1–17 years	Parental report
Tsai et al.	2010	Taiwan	Cross-sectional	4,965	School grades 7 and 8	Parental report

Han et al., 2009; Horak et al., 2007; Hugg et al., 2008; Ribeiro et al., 2002; Sturm et al., 2004; Tanaka et al., 2007; Tsai et al., 2010).

Of the 20 studies, only 4 measured cotinine concentrations (Chilmonczyk et al., 1993; Ehrlich et al., 1992; Kattan et al., 2007; Mannino et al., 2002). The remaining 16 studies relied on questionnaire information on SHS exposure provided by either parents (Barraza Villarreal et al., 2003; Dekker et al., 1991; Dong et al., 2007; Gilliland et al., 2001; Han et al., 2009; Horak et al., 2007; Jaakkola et al., 2001; Lindfors et al., 1995; Ribeiro et al., 2002; Tanaka et al., 2007; Teach et al., 2006; Tsai et al., 2010), children (Gupta et al., 2001; Sturm et al., 2004), or both (Freeman et al., 2003; Hugg et al., 2008). Only five of the studies attempted to test for evidence of a dose relationship using either number of household smokers (Chilmonczyk et al., 1993; Sturm et al., 2004; Tsai et al., 2010), number of cigarettes smoked (Dong et al., 2007; Sturm et al., 2004; Tanaka et al., 2007), or pack-years (Tanaka et al., 2007). Two studies reported only unadjusted effect sizes (Lindfors et al., 1995; Ribeiro et al., 2002), 11 reported only adjusted results (Chilmonczyk et al., 1993; Dong et al., 2007; Gilliland et al., 2001; Han et al., 2009; Horak et al., 2007; Hugg et al., 2008; Kattan et al., 2007; Sturm et al., 2004; Tanaka et al., 2007; Teach et al., 2006; Tsai et al., 2010), and 7 reported both (Barraza Villarreal et al., 2003; Dekker et al., 1991; Ehrlich et al., 1992; Freeman et al., 2003; Gupta et al., 2001; Jaakkola et al., 2001; Mannino et al., 2002). Most of the studies that provided adjusted effect sizes adjusted for both the age and the sex of the subjects; 10 also adjusted for parental level of education (Barraza Villarreal et al., 2003; Chilmonczyk et al., 1993; Dekker et al., 1991; Dong et al., 2007; Han et al., 2009; Horak et al., 2007; Jaakkola et al., 2001; Kattan et al., 2007; Tanaka et al., 2007; Tsai et al., 2010), 10 for family history of atopy or asthma (Barraza Villarreal et al., 2003; Gilliland et al., 2001; Han et al., 2009; Hugg et al., 2008; Jaakkola et al., 2001; Kattan et al., 2007; Mannino et al., 2002; Sturm et al., 2004; Tanaka et al., 2007; Tsai et al., 2010), and 10 for household pets, dampness or mould (Barraza Villarreal et al., 2003; Dekker et al., 1991; Ehrlich et al., 1992; Han et al., 2009; Horak et al., 2007; Hugg et al., 2008; Teach et al., 2006). Less commonly, ethnicity or race (Barraza Villarreal et al., 2003; Dekker et al., 1991; Ehrlich et al., 1992; Gilliland et al., 2001; Mannino et al., 2002; Sturm et al., 2004; Teach et al., 2006), breast feeding (Dong et al., 2007; Han et al., 2009; Horak et al., 2007; Jaakkola et al., 2001), and attendance at a day care centre (Chilmonczyk et al., 1993; Jaakkola et al., 2001) were included as potential confounders.

Meta-Analysis

The 20 studies provided 31 effect estimates. Twenty-eight studies suggested a positive association and, of these, 13 studies reached statistical significance. Meta-analysis produced a pooled *OR* of 1.32 (95% *CI*: 1.23–1.42) and suggested a moderate degree of heterogeneity ($I^2 = 74.2\%$, $p < .001$; Figure 1). There were relatively few case-control and cohort studies leading to imprecise pooled estimates of effect size in these subgroups. Case-control studies provided the highest pooled estimate. There was a high level of heterogeneity between cohort studies ($I^2 = 91.6\%$) and the pooled estimate did not reach statistical significance. On stratified analysis, a positive and significant pooled estimate was obtained in all continent

subgroups: Europe (pooled *OR*: 1.57, 95% *CI*: 1.35, 1.83), America (pooled *OR*: 1.33, 95% *CI*: 1.20, 1.46), and Asia (pooled *OR*: 1.23, 95% *CI*: 1.08–1.39). Heterogeneity was greatest among studies conducted in America ($I^2 = 82.6\%$, $p < .001$). There was no statistically significant heterogeneity between studies conducted in Europe. The pooled estimates were significant and positive in all age groups: preschool children (pooled *OR*: 1.32, 95% *CI*: 1.01–1.72), school-aged children (pooled *OR*: 1.28, 95% *CI*: 1.20, 1.38), and studies that included both age groups (pooled *OR*: 1.44, 95% *CI*: 1.11–1.88). Heterogeneity was highest between studies that included both preschool and school-aged children ($I^2 = 86.3\%$, $p < .001$). When the meta-analysis was rerun including only the 10 studies that adjusted for socioeconomic status, the pooled estimate changed little (*OR*: 1.27, 95% *CI*: 1.15–1.41, $p < .001$).

The cumulative meta-analysis suggested that earlier studies tended to report larger effect sizes. In the meta-influence analysis, the study done by Freeman et al. (2003) had the largest influence on the overall pooled estimate. The overall funnel plot was slightly asymmetrical, and indicated a relative absence of smaller studies with no statistically significant effect (Figure 2). However, when formally tested using Egger regression test, the bias was not statistically significant ($p = .121$). On univariate meta-regression analysis, there were no significant associations between study characteristics and effect size estimates even before adjustment for multiple testing (Table 2). However, once all the covariates were entered into the same model, estimates of effect size were significantly larger in case-control studies (multiplicity adjusted $p = .042$) and in studies that included both preschool and school-aged children (multiplicity adjusted $p = .010$). The association with large studies was of borderline statistical significance (multiplicity adjusted $p = .050$), as was the association with studies that used self-reported exposure to SHS (multiplicity adjusted $p = .050$). The adjusted R^2 for the meta-regression was 47.1%. After adjusting for other study characteristics, the residual variation due to between-study heterogeneity was 63.1%. There was relatively few cohort studies and relatively little variation in follow-up. In the subgroup analysis of cohort studies, the association between effect size and length of follow-up was not statistically significant (regression coefficient = 0.123, 95% *CI*: –0.01, –0.262, multiplicity adjusted $p = .10$).

DISCUSSION

Main Findings of Study

To date, 20 studies have examined the association between childhood exposure to SHS and risk of physician-diagnosed asthma. They have provided consistent evidence of a modest, positive association. The subgroup analysis of cohort studies suggested that the association may persist over time, but more cohort studies are required to confirm this. The relationship with dose of exposure has been examined in relatively few studies that used varying definitions. Therefore, further studies are required to determine whether a dose relationship exists.

What Is Already Known

Family history of asthma and allergies, non-Caucasian ethnicity, and lack of prolonged breast feeding are recognized

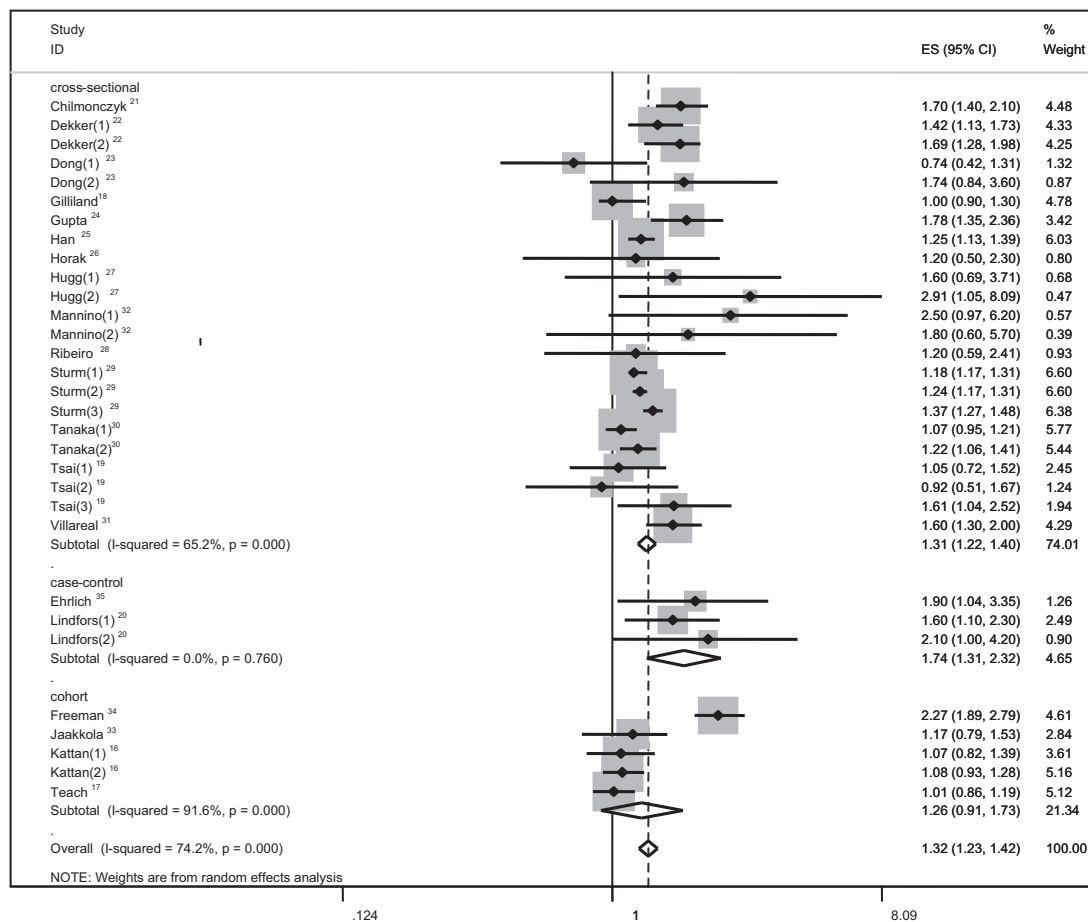


Figure 1. Forest plot of the effect estimates obtained by individual studies stratified by study design.

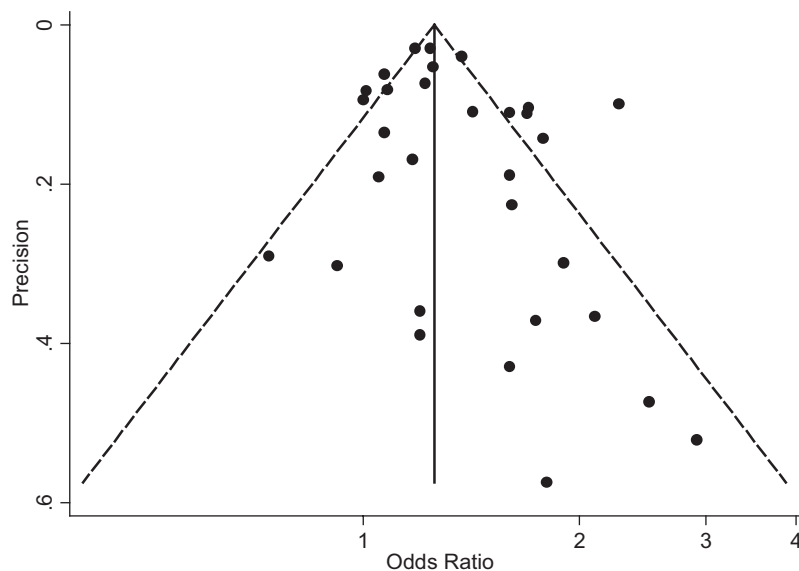


Figure 2. Funnel plot with pseudo 95% confidence limits.

risk factors for asthma (Dietert, 2011). However, the large global geographic variations in asthma incidence are probably best explained by variations in the levels of environmental

pollutants associated with urbanization and industrialization (Strachan, Golding, & Anderson, 1990; Waite et al., 1980). Much of the pathogenesis of asthma has its roots in early life

Table 2. Univariate and Multivariate Meta-Regression Analyses of the Associations Between Study Characteristics and Estimated Effect Size

	Univariate				Multivariate			
	Coefficient	95% CI	<i>p</i> value	Multiplicity adjusted <i>p</i> value	Coefficient	95% CI	<i>p</i> value	Multiplicity adjusted <i>p</i> value
Study design								
Cohort	—	—	—	—	—	—	—	—
Case-control	0.35	0.08, 0.79	.110	.250	0.76	0.26, 1.26	.003	.042
Cross-sectional	0.05	0.18, 0.28	.650	.880	0.41	0.04, 0.78	.030	.181
Age group								
Preschool	—	—	—	—	—	—	—	—
School	−0.004	−0.31, 0.30	.980	.100	0.22	0.21, 0.65	.310	.91
Both	0.67	−0.26, 0.40	.680	.920	0.96	0.39, 1.53	.001	.010
Study size								
<1,000	—	—	—	—	—	—	—	—
≥1,000	−0.11	−0.36, 0.14	.370	.460	0.47	0.11, 0.84	.012	.050
Continent								
America	—	—	—	—	—	—	—	—
Asia	−0.09	−0.30, 0.12	.420	.700	0.05	0.42, 0.13	.530	.980
Europe	0.16	−0.11, 0.43	.250	.410	0.52	0.14, 0.91	.008	.060
Exposure measure								
Cotinine	—	—	—	—	—	—	—	—
Self-reported	−0.04	−0.30, 0.22	.760	.870	0.50	0.12, 0.87	.009	.050

Note. CI = confidence interval.

when the developing immune and respiratory systems can be altered by environmental exposures especially in the presence of underlying genetic predisposition (Martinez, 2004). There is no established safe level for SHS exposure (U.S. Environmental Protection Agency, 1992; U.S. Department of Health and Human Services, 1986). Sidestream smoke contains fine particulate matter and toxins, many of which are present at higher levels than in mainstream smoke (Mohtashamipur et al. 1990), that are easily inhaled and absorbed (Stark et al., 2007).

The adverse effect of active smoking on asthma is well established (Thomson et al., 2004), but the conclusions drawn from previous studies on SHS exposure and childhood asthma have been inconsistent (Alati, Al Mamun, O' Callaghan, Najman, & Williams, 2006; Moyes, Waldon, Ramadas, Crane, & Pearce, 1995; Skorge, Eagen, Eide, Gulsvik, & Bakke, 2005). One source of disparity has been inconsistencies in defining asthma (Skorge et al., 2005; Tsai et al., 2010). In 2006, the Surgeon General stated that the available evidence was suggestive of a causal relationship between SHS exposure and the onset of childhood asthma, but insufficient to be conclusive (Tager, 2008). Since then, an additional seven eligible studies have been published (Dong et al., 2007; Horak et al., 2007; Hugg et al., 2008; Kattan et al., 2007; Tanaka et al., 2007; Teach et al., 2006; Tsai et al., 2010) justifying the need for an updated synthesis of the evidence.

What This Study Adds

This meta-analysis provides an up-to-date review of the available evidence. Systematic quantitative reviews have been conducted in the past to assess the effect of SHS exposure on childhood asthma (Burk et al. 2012; Cook and Strachan, 1997; Strachan and Cook, 1998; Vork, Broadwin, & Blaisdell, 2007). None of the previous reviews restricted inclusion to physician-confirmed diagnosis of asthma, and they used wider definitions

of asthma including wheeze (Burke et al., 2012; Cook and Strachan, 1997; Strachan and Cook, 1998) and wheezy bronchitis (Strachan and Cook, 1998; Vork et al., 2007). Asthma is more difficult to diagnose in preschool children. Nonetheless, our results demonstrated an association between preschool and school-aged children. One of the reviews was restricted to studies that examined exposure to parental smoking, and did not consider other potential sources of SHS exposure such as care-givers (Strachan and Cook, 1998). Three of the reviews produced pooled ORs between 1.2 and 1.4 (Cook and Strachan, 1997; Skorge et al., 2005; Vork et al., 2007), commensurate with our result, and one a slightly higher OR of 1.7 (Burke et al., 2012). We included SHS exposure from all potential sources rather than restricting inclusion to parental smoking. In contrast to previous reviews, we included only studies of physician diagnosed asthma, as wheeze can be reported in the absence of asthma (Cook and Strachan, 1997; Strachan and Cook, 1998). In spite of using a tighter definition of asthma than previous reviews, we obtained a similar pooled OR, suggesting that the associations previously reported cannot be attributed to the inclusion of weaker studies. The meta-analysis was conducted in accordance with PRISMA guidelines. The use of a random effects model allowed for heterogeneity arising from systematic differences between studies and the meta-regression analysis controlled for multiple testing. Most of the individual studies had a study population greater than 1,000 and there was no evidence of statistically significant small study or publication bias.

Study Limitations

Four studies on the association between SHS exposure and childhood asthma had to be excluded because they did not provide the relevant numerical results nor the data to derive them (Clark, Warner, & Dean, 1994; Gerald et al., 2009; Halterman

et al., 2008; Karadag et al., 2003). The majority of individual studies were cross-sectional in design. Unlike cohort studies, these are unable to establish a temporal relationship between exposure to SHS and the development of asthma, one of the criteria for establishing causality. The larger effect sizes obtained from the case-control studies is unsurprising, considering the potential for selection and recall bias. Similarly, the larger effect sizes obtained by studies that used self-reported measures of SHS exposure are likely to reflect recall bias. We included all types of exposure to SHS. However, most of the individual studies only considered household exposure to SHS and not record exposure in other locations. This is not a major weakness in studies of preschool children but may underestimate overall exposure among older children. One study suggested stronger associations among preschool children (Mannino, Moorman, Kingsley, Rose, & Pepace, 2001), which is plausible, given the greater proportion of time spent in the home where the majority of childhood SHS exposure occurs (Oberge et al., 2011). This finding was not corroborated in the meta-analysis, but this may simply reflect the relatively small numbers of studies that reported results specific to preschool children. Active smoking may also occur in older children and introduce confounding. Although only studies that analyzed physician diagnosed asthma as an outcome were included, there were nonetheless variations in the diagnostic criteria used. The aim of this review was to examine the effect of secondhand exposure but the majority of individual studies did not measure or take account of prenatal exposure. Only two of the studies (Gilliland et al., 2001; Tsai et al., 2010) recorded prenatal exposure and then took account of it by either statistical adjustment or reporting results for the subgroup without prenatal exposure.

The majority of eligible studies reported their results in the form of *ORs*. The *SE* of log *ORs* is correlated with the size of the *OR* (Irwig, Macaskill, Berry, & Glasziou, 1998). This can cause funnel plots based on *ORs* to appear asymmetrical and lead to false-positive results when testing for publication bias (Irwig et al., 1998). In spite of this, Egger test was not statistically significant. Because the majority of studies reported *ORs*, the relative risk reported in two studies had to be treated as equivalent to *ORs* in order to be included. In relatively common conditions, such as asthma, relative risk and *OR* may not be equivalent, thereby introducing a systematic error. Establishment of a dose-response relationship is one of the criteria for causality (Höfler, 2005). Some individual studies have provided evidence of a dose relationship between SHS exposure and childhood asthma (Dong et al., 2007; Hugg et al., 2008; Sturm et al., 2004; Tanaka et al., 2007; Tsai et al., 2010). However, these results could not be included in the meta-analysis because of differences in the measurement of dose.

Policy Implications

Children with two smoking parents have cotinine levels comparable with those of bar-workers prior to the implementation of smoke-free legislation (Akhtar et al., 2007; Semple et al., 2007). In spite of not being aimed at children, smoke-free legislation has reduced childhood exposure to SHS as a result of more stringent voluntary restrictions in the home (Akhtar et al., 2007). Nonetheless, childhood exposure to SHS remains unacceptably high. Even following smoke-free legislation, 27% of children are exposed to SHS in their homes and 7% in cars

(Akhtar et al., 2007). Smoking in cars produces very high levels of PM_{2.5} within 5 min and neither opening car windows nor use of forced ventilation can prevent concentrations exceeding the WHO indoor air quality guidance (Rees & Connolly, 2006; Semple et al., 2012). A number of countries are now considering child-specific interventions and targets. Several jurisdictions in the United States have already prohibited smoking in privately owned vehicles containing children (California Tobacco Control Program, 2008). The results of our study suggest that policies that reduce childhood exposure to SHS could reduce the population burden of childhood asthma.

SUPPLEMENTARY MATERIAL

A supplementary appendix can be found online at <http://www.ntr.oxfordjournals.org>

FUNDING

None.

DECLARATION OF INTERESTS

None.

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