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Prenatal and Passive Smoke Exposure and Incidence of Asthma and Wheeze: Systematic Review and Meta-analysis

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KEY WORDS

asthma, wheeze, passive smoking exposure, meta-analysis

ABBREVIATIONS

CI—confidence interval
HR—hazard ratio
NOS—Newcastle-Ottawa Quality Assessment Scale
OR—odds ratio

Drs Leonardi-Bee, Britton, Cook, and McKeever contributed to the study conception and design; Ms Burke, Dr Leonardi-Bee, Mr Hashim, Ms Pine-Abata, and Drs Chen and McKeever contributed to the identification of the studies, data collection, study selection, data extraction, and analysis and interpretation; Ms Burke and Drs Leonardi-Bee, Britton, Cook, and McKeever contributed to the drafting the article for important intellectual content; all authors approved the final version of the article.

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abstract

OBJECTIVES: Exposure to passive smoke is a common and avoidable risk factor for wheeze and asthma in children. Substantial growth in the prospective cohort study evidence base provides an opportunity to generate new and more detailed estimates of the magnitude of the effect. A systematic review and meta-analysis was conducted to provide estimates of the prospective effect of smoking by parents or household members on the risk of wheeze and asthma at different stages of childhood.

METHODS: We systematically searched Medline, Embase, and conference abstracts to identify cohort studies of the incidence of asthma or wheeze in relation to exposure to prenatal or postnatal maternal, paternal, or household smoking in subjects aged up to 18 years old. Pooled odds ratios (ORs) with 95% confidence intervals (CIs) were estimated by using random effects model.

RESULTS: We identified 79 prospective studies. Exposure to pre- or postnatal passive smoke exposure was associated with a 30% to 70% increased risk of incident wheezing (strongest effect from postnatal maternal smoking on wheeze in children aged ≤2 years, OR = 1.70, 95% CI = 1.24–2.35, 4 studies) and a 21% to 85% increase in incident asthma (strongest effect from prenatal maternal smoking on asthma in children aged ≤2 years, OR = 1.85, 95% CI = 1.35–2.53, 5 studies).

CONCLUSIONS: Building upon previous findings, exposure to passive smoking increases the incidence of wheeze and asthma in children and young people by at least 20%. Preventing parental smoking is crucially important to the prevention of asthma. *Pediatrics* 2012;129:735–744

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It has been recognized for some years that asthma and wheezing are more common in children passively exposed to cigarette smoke, though much of the available evidence to date has been derived from cross-sectional rather than cohort studies. In a meta-analysis published in 1998 by Strachan and Cook,[1] which informed the US Surgeon General's report of 2006,[2] the authors examined the effect of passive smoking on asthma and wheeze in children and found that if either parent smoked the risk of prevalent asthma in childhood was increased by around 40%, whereas postnatal maternal smoking increased the incidence of asthma or wheezing illness before the age of 6 by ~30%, and during school-age years by 13%. However, these estimates were each based on data from 4 cohort studies each. A more recent systematic review (2007) of exposure to household smoking revealed 33% increased risk of incident asthma in childhood; this estimate was based on data from only 8 studies.[3]

In recent years, several more prospective studies of this association have been reported, permitting a new meta-analysis to provide more reliable estimates and more detailed estimates of the effects of exposure to prenatal maternal and to postnatal maternal, paternal, or other household members smoking on the incidence of wheeze and asthma in childhood. We have, therefore, updated the original Strachan and Cook systematic review to provide summary estimates of the effects of passive smoking and to further expand these analyses by examining the effects in prenatal maternal and postnatal maternal, or paternal or household smoking from prospective studies of the risk of wheezing and asthma in childhood in various age groups. This work was initiated as part of a larger review on the effects of passive smoking in children for the Royal College of Physicians.[4]

METHODS

Systematic Review Methods

We used search strategies employed in the 1997 systematic review[1] to identify all prospective epidemiologic studies assessing the association between passive smoke exposure and the incidence of wheeze or asthma in childhood published between 1997 and February 2011. This included searching the Medline, Embase, Cumulative Index to Nursing and Allied Health Literature, and AMED electronic databases, published reviews, reference lists from identified publications, and abstracts from major conference proceedings (European Respiratory Society and American Thoracic Society, 2006–2009).

Search Strategy

We search for articles in all languages, but in common with the previous search strategy, we included only articles published in English.[1] Search terms were selected under guidance from the Centre for Reviews and Dissemination[4] and the Airways Group Specialist[5] search terms for wheeze and asthma. All references to passive smoking were selected by the MeSH heading Tobacco smoke pollution and/or text word combinations (passive, second hand, involuntary, parent, maternal, mother, paternal, father, or household) and (smoke, tobacco, cigarettes, or cotinine) in the title, keywords, or abstract. In addition, articles were then restricted to children or adolescents (aged 0–18 years). The results from searches were combined with studies identified in the previous review.[1]

Inclusion Criteria

We included all prospective epidemiologic studies assessing the association between passive smoke exposure and incidence of asthma or wheeze in children or young people up to the age of 18 years in which participants were free of disease (asthma or wheeze) at the start of the study and passive smoke exposure was documented at a time point before the incidence of disease was determined.

Data Extraction

Four authors (Drs Burke and McKeever, Mr Hashim, and Ms Pine-Abata) independently reviewed the titles, abstracts, and then full text excluding irrelevant articles after each stage. Disagreements were resolved by discussion. Articles were then data extracted independently by 2 authors (Ms Burke and Dr McKeever; Mr Hashim and Dr Chen; or Ms Pine-Abata and Dr McKeever) from all included text. Information on study design, methods, definitions of asthma and wheeze, passive smoke exposure (source and timing of exposure), location of study, age of study population (both when passive smoke exposure was attained and when outcome was collected) and results (adjusted estimates where possible) were obtained by using a previously piloted data extraction form. Included articles were also independently scored by 2 authors for methodological quality by using the Newcastle-Ottawa Quality Assessment Scale (NOS).[5] This scale awards points for representativeness of the cohort, ascertainment of exposure/outcome, adjustment for confounders in the analyses and follow-up (length and completeness), and has a maximum score of 9 points. Data were then entered into a standardized database and cross-checked. To ensure that no cohort was included more than once in the same meta-analysis, each article was given a study identification number relating to the birth cohort used. If 2 different full texts presented similar outcomes and exposure at the similar age in the same cohort, then the criteria for choosing which 1 to use in the analyses included the more robust definition of asthma/wheeze (for example, persistent wheeze was used over wheeze ever),

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the younger age of outcome, and multivariate results were chosen over univariate results. If a dose-response relation was reported, then the highest level of smoking was used.

Analysis: Exposure Comparisons

For each study, for a given outcome, we sought to obtain an odds ratio (OR) and its 95% confidence interval (CI) for any of the 4 exposures: prenatal maternal smoking, maternal smoking, paternal smoking, and household smoke exposure (or equivalently either parent smokes). Because the phenotype of asthma is potentially different according to age of diagnosis, we also divided the outcomes up into the following age groups: incidence of asthma/wheeze in children aged 0 to 2 years, incidence of asthma/wheeze in children aged 3 to 4 years, and incidence of asthma/wheeze in children aged over 5 years.

Meta-analyses were performed to calculate weighted effect measures and 95% CIs across studies by using random effects models using the DerSimonian and Laird method to calculate weights. Heterogeneity was expected from the analyses due to differences in study populations and exposures. The amount of heterogeneity between the studies was assessed by using I^2 and if substantial levels of heterogeneity were detected ($I^2 > 50\%$),[6] subgroup analyses were conducted to investigate potential reasons based on methodological quality score (using forest plots >6 vs ≤6) and examining differences in size of effect and heterogeneity between studies. Studies presenting data from using hazards ratios (HRs) were analyzed separately. Publication bias was examined visually by using funnel plots, where there were more than 10 studies available. The presentation of the meta-analyses adhered to the Meta-analysis of Observational Studies in Epidemiology guidelines.[7] All analyses were performed by using Stata version 10.

RESULTS

From an initial 5074 articles identified from the literature searches, 583 abstracts were reviewed and 180 full texts initially examined (Fig 1). We excluded those which did not report data on the relation between smoking and respiratory diseases, were published in non-English language, were review articles, were not prospective cohort studies, or ascertained smoking status at the same time as disease outcome. A further potential 28 articles were identified after reference list review and 9 identified as potentially eligible articles from the previous meta-analyses.[1] After excluding studies that presented similar outcomes from the same cohorts, there were 70 articles (representing 71 studies) eligible for inclusion in the systematic review and meta-analyses (Fig 1, Supplemental Tables 3 [included studies] and 4[excluded studies][8-16]). Thirty-two of the 71 studies assessed asthma as an outcome (46%), 31 assessed wheeze (44%), and 8 assessed both asthma and wheeze (11%). Thirty-seven studies assessed exposure to prenatal maternal smoking (52%), 26 assessed postnatal maternal smoking (37%), 7 assessed postnatal paternal smoking (10%), and 28 assessed household smoking (39%). Twenty-three studies presented the incidence of respiratory disease in children aged ≤2 years, 18 in children aged 3 to 4 years, and 32 studies in children aged 5 to 18 years. Only 1 analysis had more than 10 studies, and there was no evidence of publication bias when examining the funnel plot for prenatal maternal passive smoke and wheeze in children aged ≤2 years (funnel plot not presented).

The NOS scores for the 71 included studies ranged from 5 to 7 with a median of 6. Thirty-one of the 71 studies (44%) were scored as being of moderate or high level (>6) methodological quality. The main reasons for lower NOS scores were lack of an objective measure of smoking since the vast majority relied upon self-reported smoking (only 1 study provided objective data in the form of cotinine levels[17]), lack of adjustment for confounding factors, and lack of study sample representativeness due to restrictions to children whose parents had an allergic disease.

Meta-analysis Findings

Wheeze as the Outcome

All except for 2 of the pooled analyses revealed that exposure to passive smoking was associated with a significant increased risk of onset of wheeze in the child (Table 1, Supplemental Figs 3–12).

Prenatal Maternal Smoking

Exposure to prenatal maternal smoking was associated with 40% increase in risk of wheeze in children aged ≤2 years (OR = 1.41, 95% CI = 1.20–1.67, I^2 = 82.5%, 14 studies). The high levels of heterogeneity between the studies was not attributable to quality (higher quality: OR = 1.35, 95% CI = 1.13–1.61, I^2 = 85.3%, 9 studies; poorer quality: OR = 1.66, 95% CI = 0.93–2.96, I^2 = 87.7%, 5 studies). A similar magnitude of effect was observed for the relation between prenatal maternal smoking and incidence of wheeze between ages 3 and 4 (OR = 1.28, 95% CI = 1.14–1.44, I^2 = 65.5%, 8 studies). High levels of heterogeneity in this analysis was partly due to the study quality (higher quality studies: OR = 1.44, 95% CI = 0.92–2.25, I^2 = 59.5%, 3 studies; poorer quality studies: OR = 1.35, 95% CI = 1.13–1.62, I^2 = 72.6%, 5 studies). Prenatal passive smoke exposure was associated with a 52% increased risk of wheeze in children aged 5 to 18 years (OR = 1.52, 95% CI = 1.23–1.87, I^2 = 21.1%, 5 studies). We could not include 1 article in the meta-analyses because it provided no data other than *P* values; however, it

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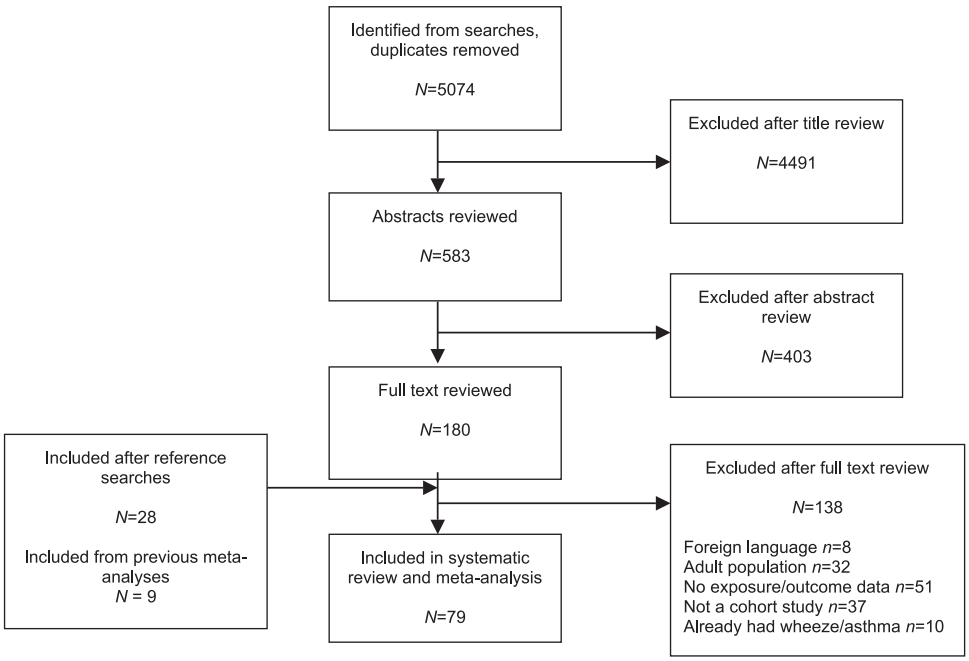

FIGURE 1
Flowchart for identifying studies.

TABLE 1 Passive Smoke Exposure and Incidence of Wheeze

Smoking Exposure	Age the Outcome Was Collected	No. of Studies	Pooled OR	95% CIs	I^2, %	Ref. Nos.
Prenatal maternal	≤2	14	1.41	1.19–1.67	87.9	17;30;38–48
Maternal	≤2	4	1.70	1.24–2.35	0.0	17;38;46;49
Paternal	≤2	0				
Household	≤2	10	1.35	1.10–1.64	64.5	39;40;42;43;46;50–53
Prenatal maternal	3–4	8	1.28	1.14–1.44	65.6	17;28;38;42;54–57
Maternal	3–4	4	1.65	1.20–2.28	48.5	17;38;54;58
Paternal	3–4	0				
Household	3–4	4	1.06	0.88–1.27	54.5	42;55;56;59
Prenatal maternal	5–18	5	1.52	1.23–1.87	21.1	29;57;58;60;61
Maternal	5–18	3	1.18	0.99–1.40	1.40	62–64
Paternal	5–18	2	1.39	1.05–1.85	0.0	60;63
Household	5–18	5	1.32	1.12–1.56	1.7	57;63;65–67

revealed that maternal smoking in pregnancy was associated significant increased risk of wheeze in the last 12 months in boys age 11 ($P = .003$) but no significant association in girls.[18]

Maternal Smoking

Exposure to postnatal maternal smoking was associated with the strongest effects on the incidence of wheeze, effects on incidence of wheeze in children aged ≤2 years (OR = 1.70, 95% CI = 1.24–2.35, I^2 = 0%, 4 studies), on incidence of wheeze in children aged 3 to 4 years (OR = 1.65, 95% CI = 1.20–2.68, I^2 = 48.5%, 4 studies), and on the incidence of wheeze in children aged 5 to 18 years (OR = 1.18, 95% CI = 0.99–1.40, I^2 = 1.4%, 3 studies).

Paternal Smoking

Data on exposure to paternal smoking were more limited; the only available estimate was for incidence of wheeze in children aged 5 to 18 years (OR = 1.38, 95% CI = 1.05–1.85, I^2 = 0%, 2 studies).

Household Smoking

Household passive smoke exposure also increased the risk of wheeze in children aged ≤2 years (OR = 1.35, 95% CI = 1.10–1.64, I^2 = 64.5%, 9 studies). There was a high level of heterogeneity between the studies, and subgroup analyses by quality score was able to account for some of the heterogeneity (higher quality: OR = 1.27, 95% CI = 1.06–1.52, I^2 = 51.7%, 6 studies; poorer quality: OR = 1.60, 95% CI = 0.77–3.33, I^2 = 76.4%, 3 studies). Exposure to household passive smoke was not significantly associated with incidence of wheeze in children aged 3 to 4 years (OR = 1.06, 95% CI = 0.88–1.27, I^2 = 54.5%, 4 studies). The moderate levels

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of heterogeneity were partly attributable to high levels of heterogeneity and in this case were attributable to study quality (higher quality: OR = 1.20, 95% CI = 1.02–1.41, I^2 = 0%, 3 studies; poorer quality: OR = 0.95, 95% CI = 0.87–1.02, 1 study). Exposure to household smoking also increased the risk of incidence of wheeze in children aged 5 to 18 years (OR = 1.32, 95% CI = 1.12–1.55, I^2 = 0%, 5 studies).

In addition, we were unable to include 1 article in the meta-analyses because the exposure was measured as per hour exposed to passive smoke, and this study revealed that increased exposure to passive smoking was associated with an increased risk of persistent wheeze in children aged 2 years (OR per hour per week exposed = 1.14, 95% CI = 1.02–1.27).[19] There was also 1 study that used an objective measure of passive smoke exposure and revealed that children with detectable cord blood levels were not at significantly increased risk of wheeze at age 1 or 3 years or of wheeze at age 3 years in relation to blood cotinine levels at age 1.[17]

Asthma as the Outcome

The effects of passive smoke exposure on the incidence of asthma tended to be weaker than those on wheeze, with exposures resulting in ~20% increased risk of asthma and most of which were statistically significant (Table 2, Supplemental Figs 13–21).

Prenatal Maternal Smoking

The strongest significant effect was for prenatal maternal smoking and incidence of asthma in children aged ≤2 years (OR = 1.85, 95% CI = 1.35–2.53, I^2 = 41.9%, 5 studies). The effect of prenatal maternal smoking became progressively weaker in relation to asthma incidence with increasing age but remained significantly associated with asthma onset between the ages of 5 and 18 years (OR = 1.23, 95% CI = 1.12–1.36, I^2 = 50%, 11 studies). In addition, the authors of 1 study examined the effect of prenatal smoking and incidence of asthma by using HRs, and therefore data could not be included in the meta-analyses, but the study revealed that prenatal maternal smoking was associated with a significant increased risk of incidence of asthma (HR = 1.5, 95% CI = 1.1–2.1).[20]

Maternal Smoking

Exposure to postnatal maternal passive smoking was not significantly associated with incidence of asthma in children aged ≤2 years or 3 to 4 years but demonstrated a borderline significant association with incidence of asthma in children aged 5 to 18 years (OR = 1.20, 95% CI = 0.98–1.46, P = .08, I^2 = 65.3%, 8 studies). Subgroup analysis by quality score accounted for only a little of the heterogeneity, which appeared to be located in the higher quality studies (higher quality: OR = 1.06, 95% CI = 0.67–1.68, I^2 = 76.5%, 4 studies; poorer quality: OR = 1.25, 95% CI = 1.00–1.57, I^2 = 55.5%, 4 studies). However, studies that presented the data by using HRs revealed that exposure to maternal smoking was associated with a 21% increased risk of incidence of asthma (HR = 1.21, 95% CI = 1.01–1.45, I^2 = 74.7%, 5 studies; Fig 2). Again, a high amount of heterogeneity was revealed that existed in the lower quality studies (poorer quality: HR = 1.17, 95% CI = 0.99–1.37, I^2 = 72.9%, 4 studies; higher quality: HR = 3.17, 95% CI = 1.42–7.04, 1 study). The age of diagnosis of incidence of asthma in these 4 studies ranged considerably from birth age 5,[21] birth until age 11,[22] or age 10 or older.[23–25]

Paternal Smoking

There were more limited data on the effect of exposure to paternal smoking with no studies with data for children aged ≤2 years and only 1 study for children aged 3 to 4 years that revealed a significant effect (OR = 1.34, 95% CI = 1.23–1.46). Paternal exposure was not associated with incidence of asthma in children aged 5 to 18 years (OR = 0.98, 95% CI = 0.71–1.36, I^2 = 0%, 4 studies). In 1 study, the authors reported HRs and found that having a father as a current smoker resulted in a significant increased risk of incidence of asthma from birth up to age 11 (HR = 1.34, 95% CI = 1.24–1.46).[22]

TABLE 2 Passive Smoke Exposure and Incidence of Asthma

Smoking Exposure	Age the Outcome Was Collected	No. of Studies	Pooled OR	95% CIs	I^2, %	Ref. No(s).
Prenatal maternal	≤2	5	1.85	1.35–2.53	41.9	31;43;46;56;68
Maternal	≤2	2	2.47	0.65–9.39	3.7	46;69
Paternal	≤2	0				
Household	≤2	3	1.14	0.94–1.38	1.7	43;46;56
Prenatal maternal	3–4	1	1.30	0.88–1.92		70
Maternal	3–4	4	1.05	0.88–1.25	0.0	70–73
Paternal	3–4	1	1.34	1.23–1.46	100	72
Household	3–4	5	1.21	1.00–1.47	72.7	55;74–77
Prenatal maternal	5–18	8	1.23	1.12–1.36	50.0	32–34;36;48;68;78–82
Maternal	5–18	8	1.20	0.98–1.44	65.3	34;35;62;78;81;83–85
Paternal	5–18	3	0.98	0.71–1.36	0.0	35;84;85
Household	5–18	6	1.30	1.04–1.62	37.7	36;66;67;81;86;87

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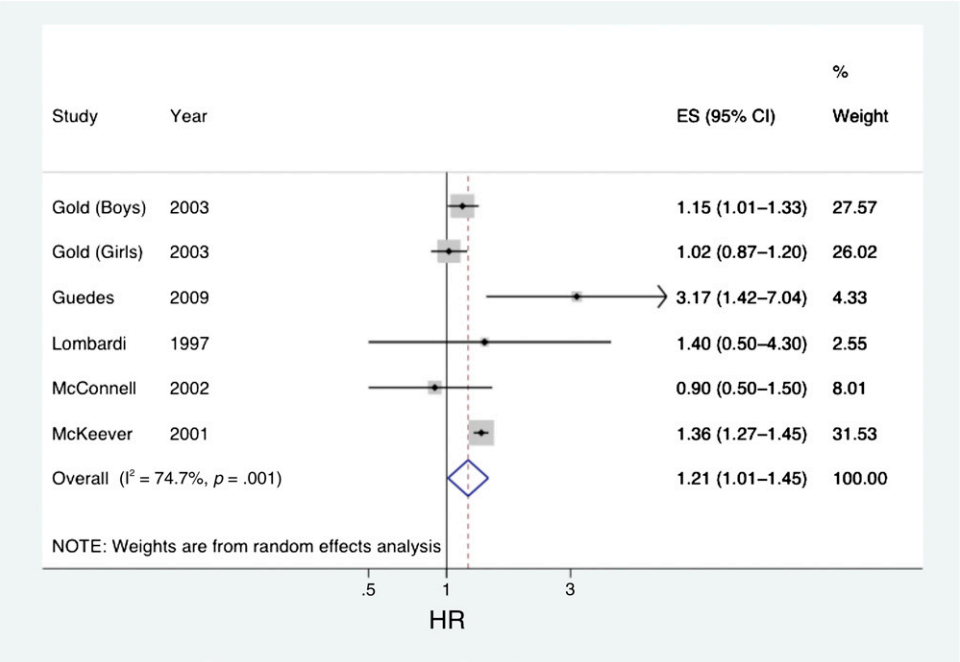

FIGURE 2
Exposure to postnatal maternal smoking and incidence of asthma.

Household Smoking

Household passive smoke exposure was not significantly associated with incidence of asthma in children aged ≤2 years (OR = 1.14, 95% CI = 0.94–1.38, I^2 = 0.1%, 3 studies) but was associated with incidence of asthma in children aged 3 to 4 years (OR = 1.21, 95% CI = 1.00–1.47, I^2 = 72.7%, 5 studies) and aged 5 to 18 years (OR = 1.30, 95% CI = 1.04–1.62, I^2 = 37.7%, 5 studies). The relation between household passive smoke exposure and incident asthma in children aged 3 to 4 years revealed a high level of heterogeneity that could be entirely explained by subgroup analyses based on quality score (higher quality: OR = 1.18, 95% CI = 0.92–1.53, I^2 = 0%, 2 studies; poorer quality: OR = 1.21, 95% CI = 0.92–1.59, I^2 = 85.8%, 3 studies). Two further studies[26,27] presented data by using HRs, and a pooled analysis of these revealed household exposure to passive smoke was not significantly related to an increased risk of incidence of asthma (HR = 1.33, 95% CI = 0.72–2.44, I^2 = 74.2%, 2 studies; Supplemental Fig 22).

Finally, 1 study that could not be combined due to its classification of exposure revealed no significant association for doctor diagnosed asthma or reactive airways disease in relation per house exposed to passive smoke (OR per hour exposed = 1.04, 95% CI = 0.94–1.15).[19]

There was insufficient data to combine the results from studies of dose-response associations; 3 studies for wheeze revealed a significant dose-response effect,[28–30] and 3 studies for asthma[31–34] revealed a significant dose-response effect; the significance could not be determined for 1 study, although the results did demonstrate increasing ORs.[32] However, 2 of the above studies also demonstrate a nonsignificant trend.[28,34]

DISCUSSION

This updated systematic review and meta-analysis, which has drawn data from over 70 studies and is thus by far the largest review of the topic reported to date, revealed that exposure to passive smoking, in particularly prenatal or postnatal maternal smoking, is associated with significantly increased risks of onset of wheeze and asthma in children. The much greater evidence base available now than at the times of previous systematic reviews of this area has permitted us to estimate effects of exposure to smoking both pre- and postnatally by the mother and by the father or any household member, on asthma or wheeze during 3 different age ranges in childhood. Our estimates update those published in the previous definitive review of these associations,[1,3] which was conducted over 10 years ago and included both cross-sectional and cohort studies and are based exclusively on prospective studies in which smoking status was documented before the development of disease, thereby minimizing reporting bias and recall biases.

Our findings indicate that the effects of passive smoking on the incidence of wheeze and asthma are substantially higher than previously estimated, particularly for the effect of maternal postnatal smoking exposure. Previous results revealed that maternal postnatal smoking exposure increased the

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risk of asthma or wheezing illness in the first 5 to 7 years after birth by 31% (4 studies), and the effect was smaller when examining the incidence during schools (13% increased risk [4 studies]).[1] The most comparable data from our study revealed that maternal smoking was associated with a 52% increased risk of wheeze and 20% increased risk of asthma at age 5 to 18 years. The other available recent systematic review revealed that maternal passive smoke exposure was associated with a 24% increased risk of incidence of asthma, and household passive smoke exposure was associated with a nonsignificant 13% increased risk of incidence of asthma in children aged 0 to 18 years.[3] Both of these estimates are at the lower ends of our estimates, as we found that passive smoke exposure was associated with a 20% to 85% increased risk of incidence of asthma. Our estimates for the effect of passive smoke on wheeze demonstrate stronger effects ranging from 28% to 70% increased risk of incidence of wheeze. This more recent meta-analyses[3] had more restrictive inclusion criteria, including postnatal exposure to smoking, asthma, and studies that allowed for the confounding effect of atopy/allergic studies. Only allowing studies that restrict the study population or controlled for atopy may be the reason their estimates are lower than the estimates that we attained. This current meta-analyses, 38 of 71 studies allowed for atopy/allergic disease in the analyses.

Our study was able to draw data from nearly 9 times more articles than the previous work and is thus more likely to reflect the true estimates of the effect of passive smoking on wheeze and asthma. We chose to separate the time of diagnoses into 3 different age categories (≤2 years, 3 to 4 years, and 5 to 18 years) to examine whether the effect of passive smoke was only an effect on disease diagnosed early in life or whether these effects were still present when the onset of wheeze or asthma presented later in childhood. In addition, this is the first time estimates for the effect of prenatal smoking on respiratory have been determined. We found estimates tended to be higher at a younger age of diagnosis, though we still found that exposure to household passive smoke still significantly increased the risk of new diagnosis of asthma after the age of 5 years.

One limitation to our systematic review is that in many of the studies we identified, the effect of smoking on asthma or wheeze was not the primary objective. It is therefore possible that we have missed other studies in which relevant data were collected but not evident in the title or abstract. Restriction of analysis to articles published in English is another potential limitation, though in practice this excluded only 8 studies. We also recognize that exposure to prenatal and postnatal smoking and smoking by the mother, father, or other household member are correlated and their effects are therefore difficult to disentangle. There was substantial heterogeneity in some of our analyses, which was not always attributable to study quality. Reasons for high levels of heterogeneity include wide range of cohort sizes, with some large cohorts providing some very tight range of effect size, some studies not allowing for confounding effect, also differences in the defined study population such as parents having allergic disease to be included into the study versus a random sample of population. Twelve of the cohort studies were selected on the basis of parents with allergic disease and of these 2 of them had ORs and 95% CIs that were outside the pooled estimate[35,36]; however, 1 was an overestimate of the effect size and 1 was an underestimate, therefore no systematic bias was revealed within these study populations. In addition, each of these 2 studies also only contributed 3% of the overall weight to the meta-analyses and therefore overall conclusions remain the same when the studies were excluded from the meta-analyses. Another factor that must be considered is the child's own smoking status, and there were only 7 studies in which the incidence of disease was after age 12 and of these only 1 of them controlled for the child's smoking behavior. Finally, we must recognize the difficulty in diagnosing asthma in young children, and therefore we chose to present the results for both wheeze and asthma; however, we must recognize that early wheeze in children will be a combination of early transient wheezers and children with early signs of asthma.

Exposure to passive smoking is an important risk factor for the incidence of wheeze and asthma throughout childhood. In the United Kingdom over 7000 or 8% of new cases of wheeze in children under the age of 2 and over 15 000 or 14% of new cases of asthma in children over the age of 3 are due to passive smoke exposure,[4] and internationally it is estimated that 651 000 disability adjusted life-years are results of exposure to passive smoking and asthma.[37] These new cases of disease pose a significant public health burden that is potentially avoidable. Therefore, it is important to limit children's exposure to passive smoke both during gestation and throughout the child's life.

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WISH UPON A TWINKLING PLANET? *Everyone knows there are billions and billions of stars. On a clear night, one can see evidence of their existence scattered across the night sky. What is a little less clear is how many planets exist. Until recently, most scientists thought planets relatively uncommon. As reported in* The New York Times *(Science: January 11, 2012), however, several new studies have shown that there may actually be more planets than stars. Scientists used a few different ways to detect the presence of planets around stars outside our solar system. NASA scientists used a space-based telescope to detect planets. This telescope can detect planets as small as Earth and planets quite close to their sun. Others examine the brightness of stars as seen by several land-based telescopes to infer the presence of planets. This method is good for detecting larger planets usually a bit farther from their sun. The surprising find is that many stars in the Milky Way have planets. Evidently, most do and very conservative estimates suggest that on average stars in the Milky Way have at least 1.6 planets. According to the article, the existence of more than 700 exoplanets, planets outside our solar system, has already been confirmed. Thousands are waiting independent confirmation. Planets have even been detected around stars thought very unlikely to have a planet. For example, planets have been found around solar systems with two stars. Somehow, the planets are not destroyed by the competing gravitational fields. Given that the Milky Way has more than 100 billion stars, the likelihood of finding a planet with similar characteristics as Earth seems much more likely. If so, scientists may have to brush up on their Greek mythology, as there will be plenty of naming opportunities.*

Noted by WVR, MD

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Prenatal and Passive Smoke Exposure and Incidence of Asthma and Wheeze: Systematic Review and Meta-analysis

Hannah Burke, Jo Leonardi-Bee, Ahmed Hashim, Hembadoon Pine-Abata, Yilu Chen, Derek G. Cook, John R. Britton and Tricia M. McKeever

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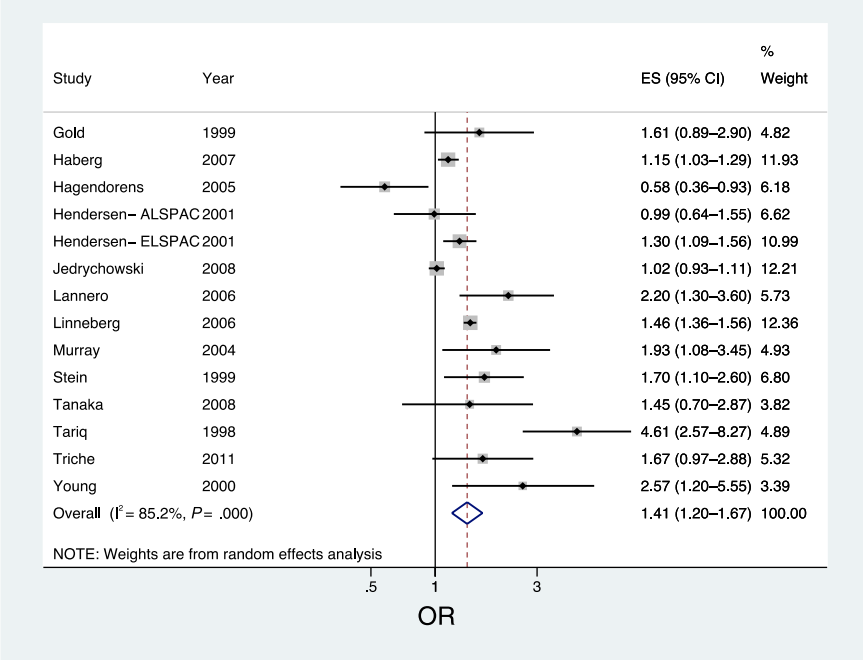
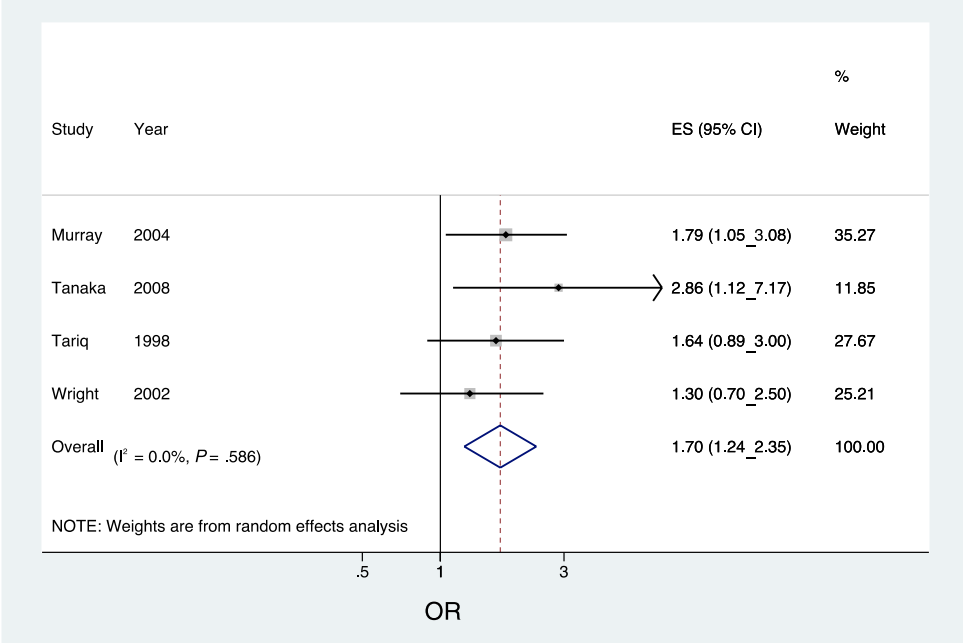
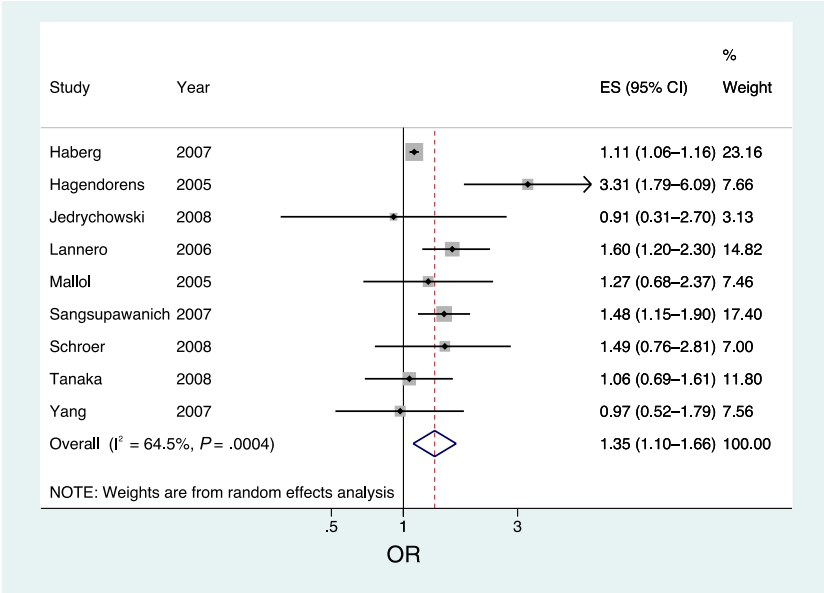


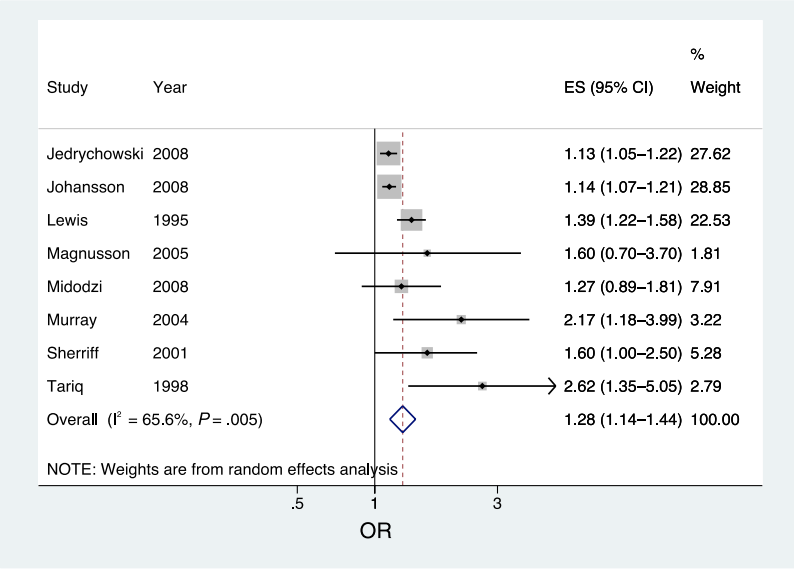
SUPPLEMENTAL FIGURE 3
Incidence of wheeze (outcome determined ≤ age 2) and exposure to prenatal smoking.



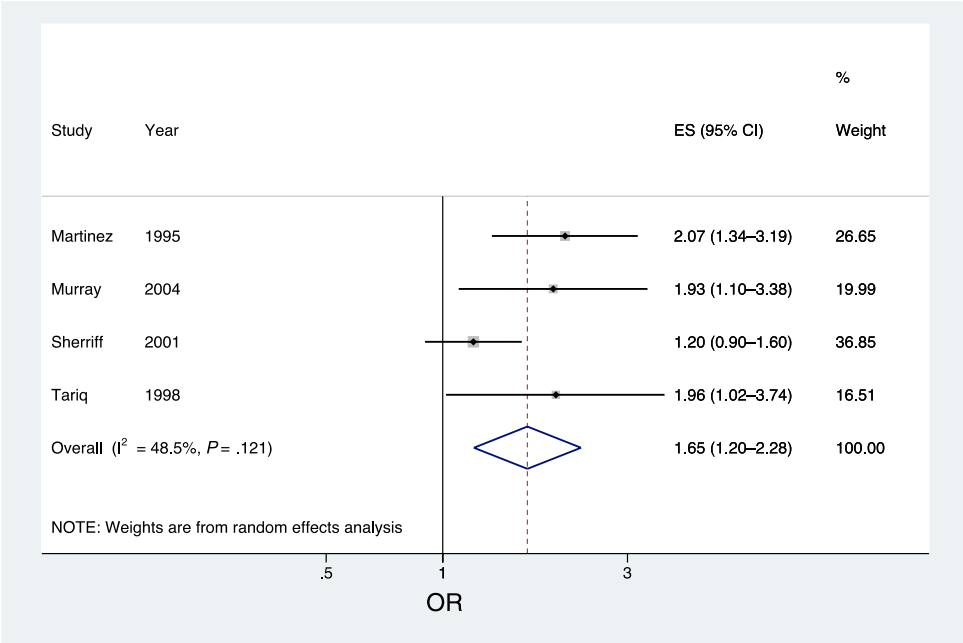
SUPPLEMENTAL FIGURE 4
Incidence of wheeze (outcome determined ≤ age 2) and exposure to maternal smoking.



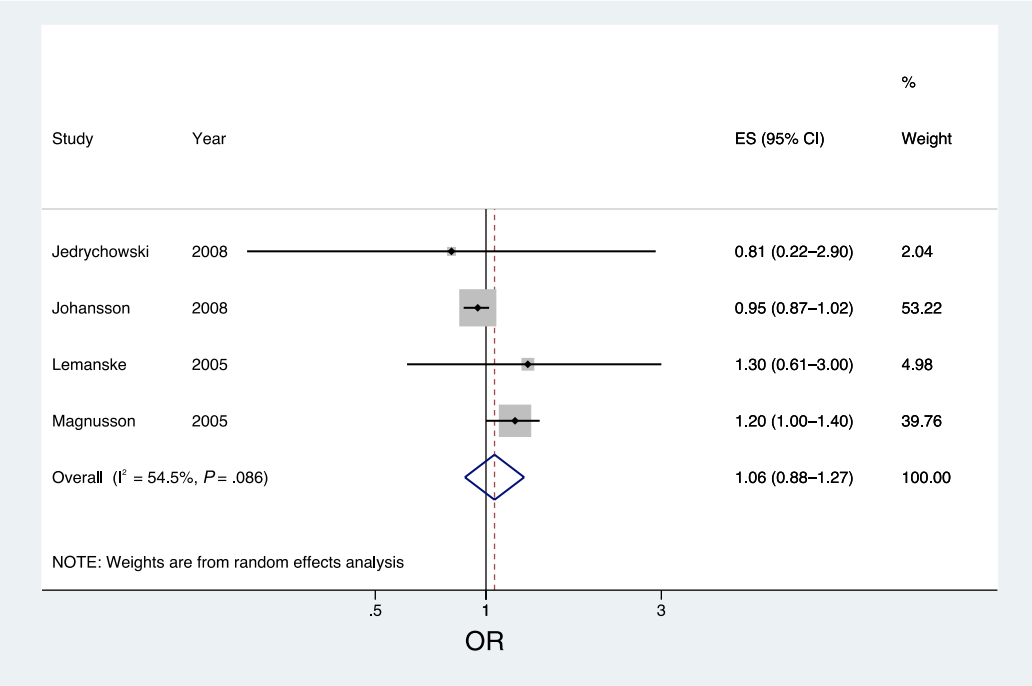
SUPPLEMENTAL FIGURE 5
Incidence of wheeze (outcome determined ≤ age 2) and exposure to household smoking.



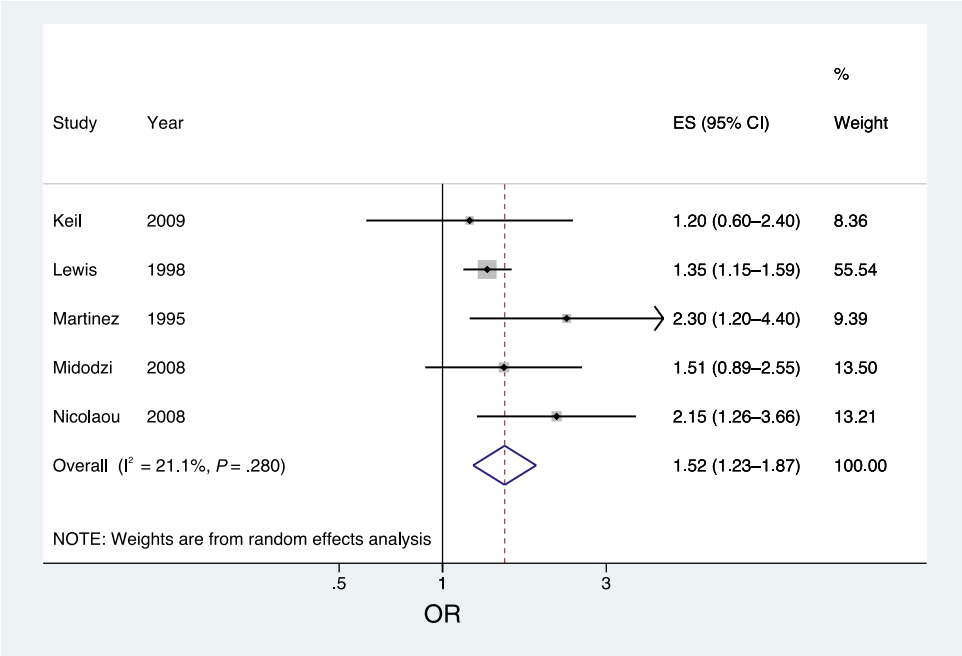
SUPPLEMENTAL FIGURE 6
Incidence of wheeze (outcome determined at ages 3–4) and exposure to prenatal smoking.



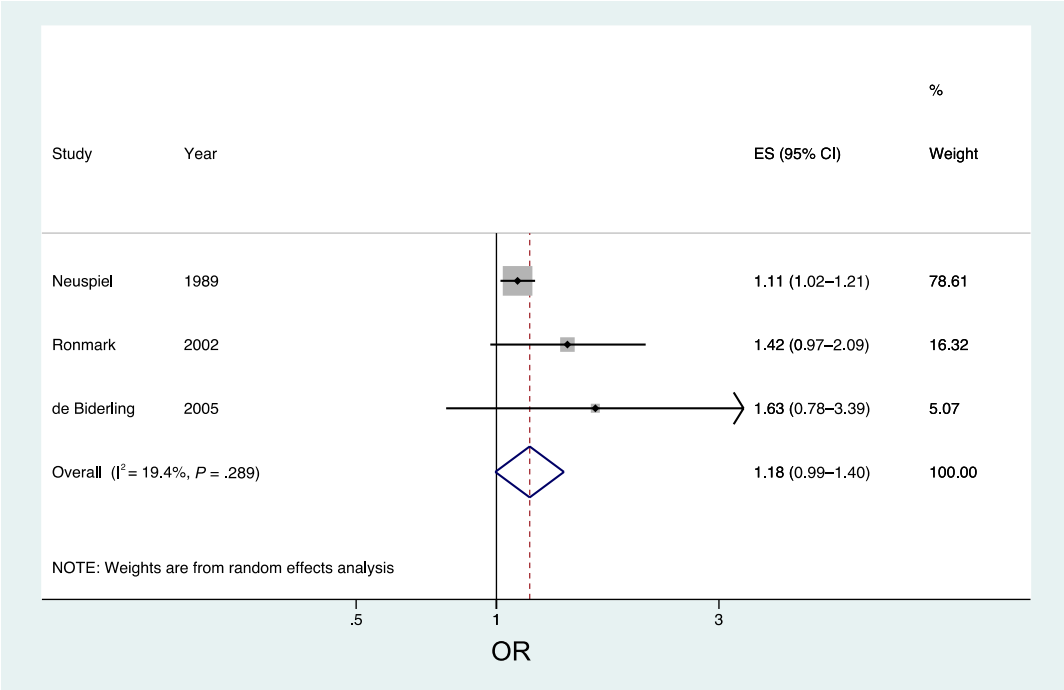
SUPPLEMENTAL FIGURE 7
Incidence of wheeze (outcome determined at ages 3–4) and exposure to maternal smoking.



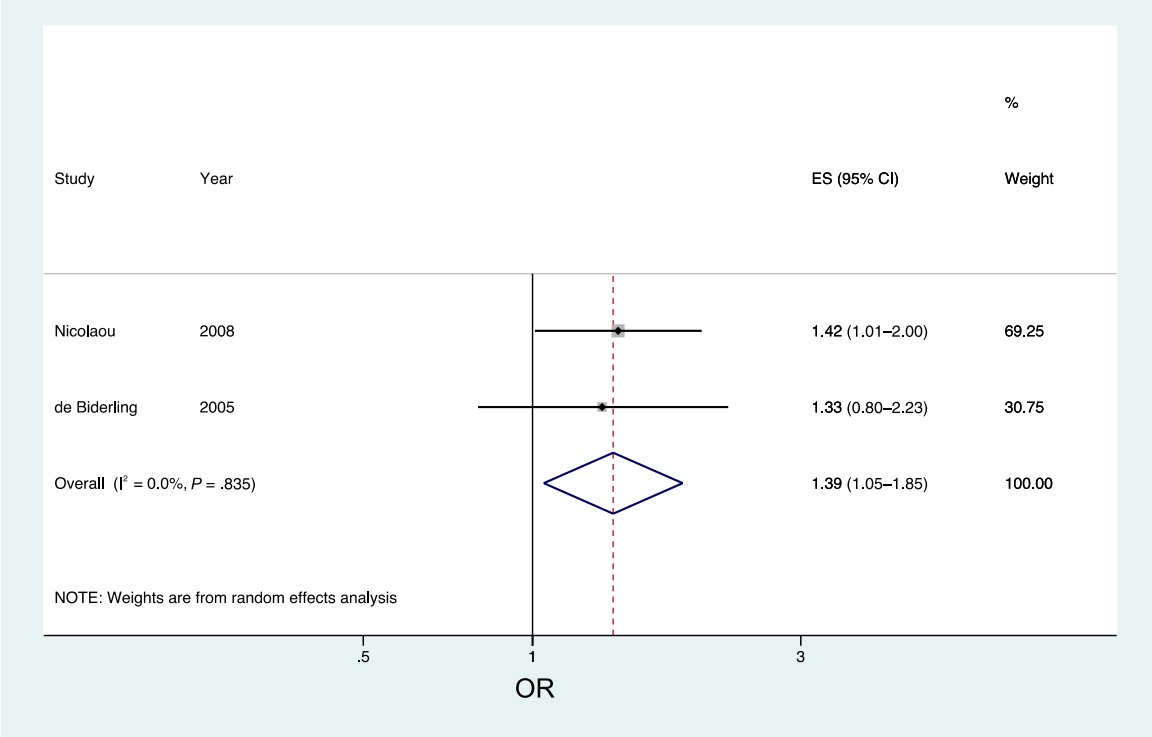
SUPPLEMENTAL FIGURE 8
Incidence of wheeze (outcome determined at ages 3–4) and exposure to household smoking.



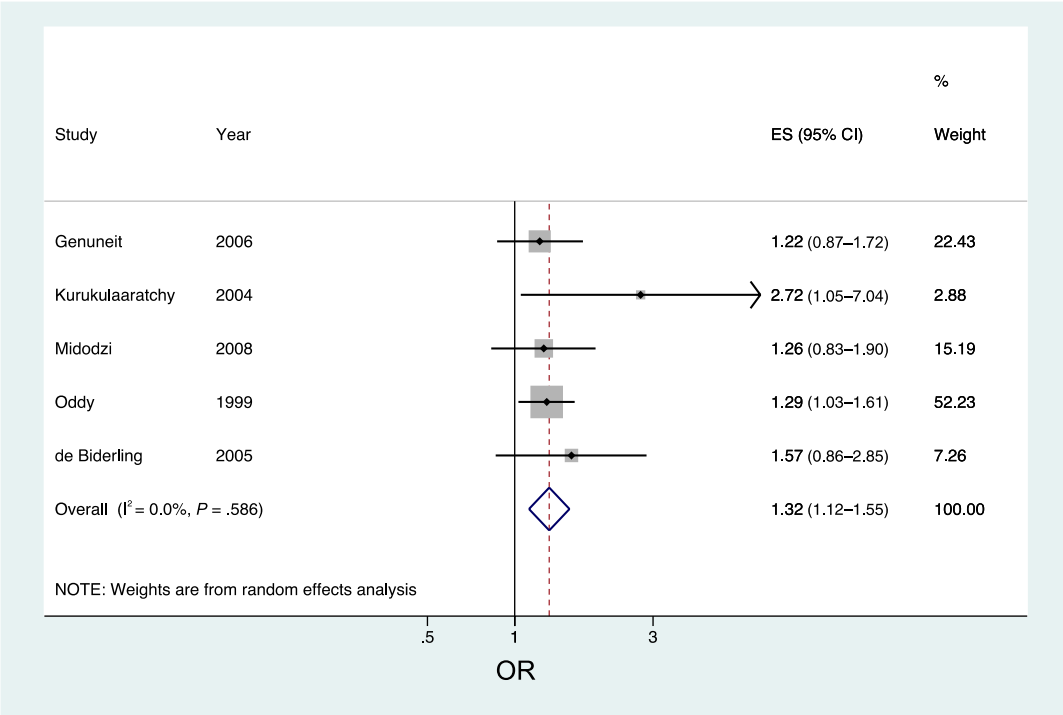
SUPPLEMENTAL FIGURE 9
Incidence of wheeze (outcome determined at ages 5–18) and exposure to prenatal smoking.



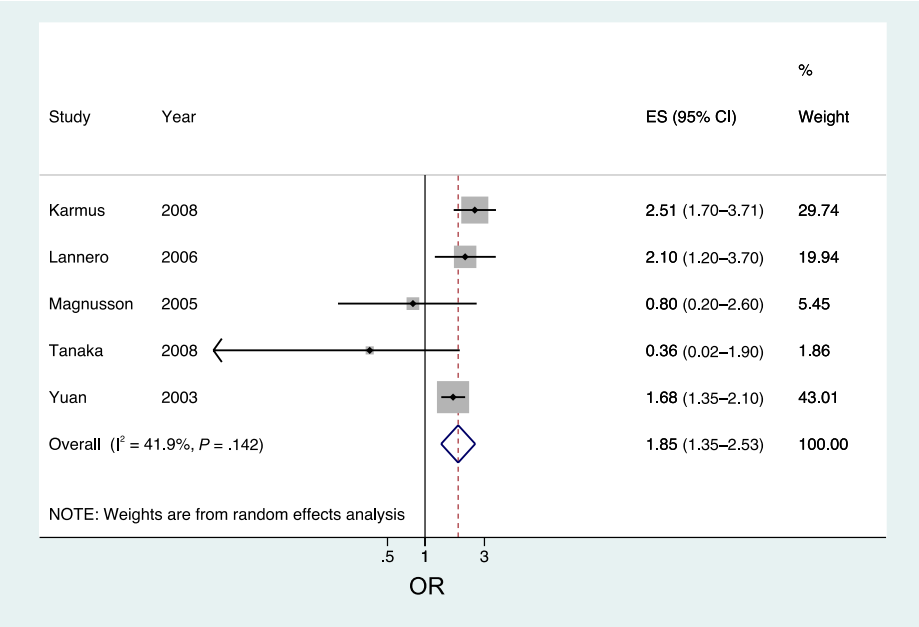
SUPPLEMENTAL FIGURE 10
Incidence of wheeze (outcome determined at ages 5–18) and exposure to maternal smoking.



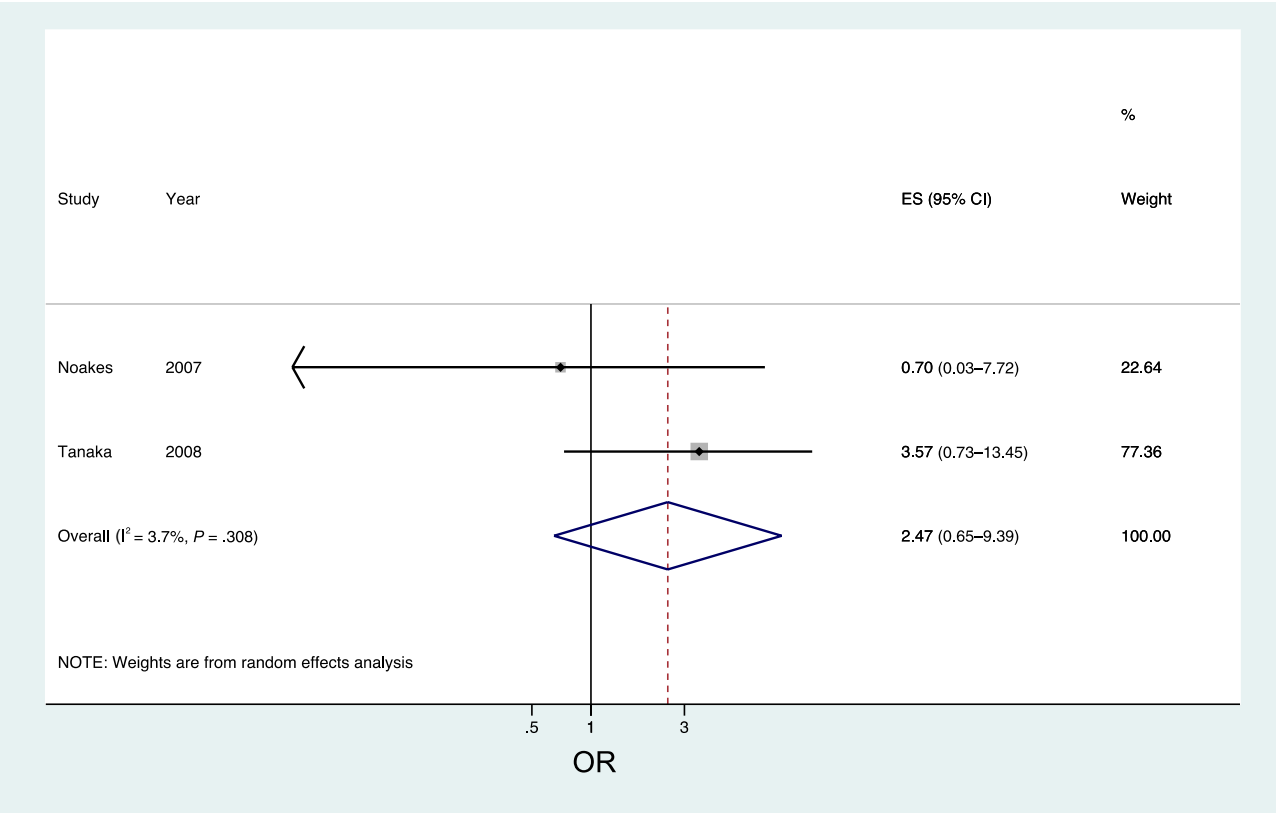
SUPPLEMENTAL FIGURE 11
Incidence of wheeze (outcome determined at ages 5–18) and exposure to paternal smoking.



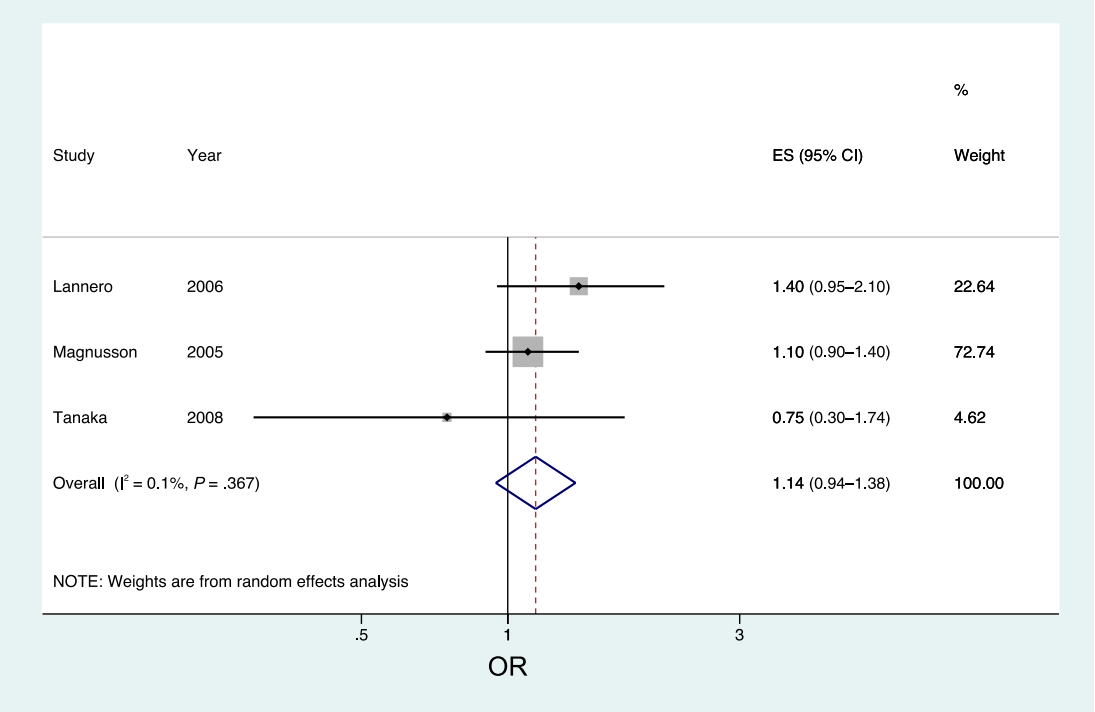
SUPPLEMENTAL FIGURE 12
Incidence of wheeze (outcome determined at ages 5–18) and exposure to household smoking.



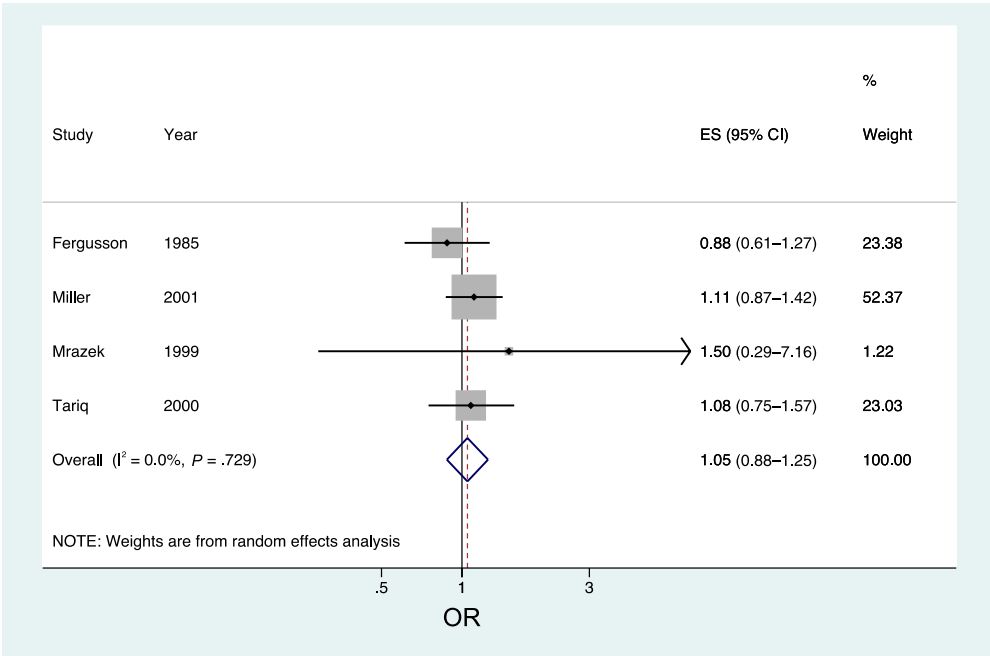
SUPPLEMENTAL FIGURE 13
Incidence of asthma (outcome determined ≤ age 2) and exposure to prenatal smoking.



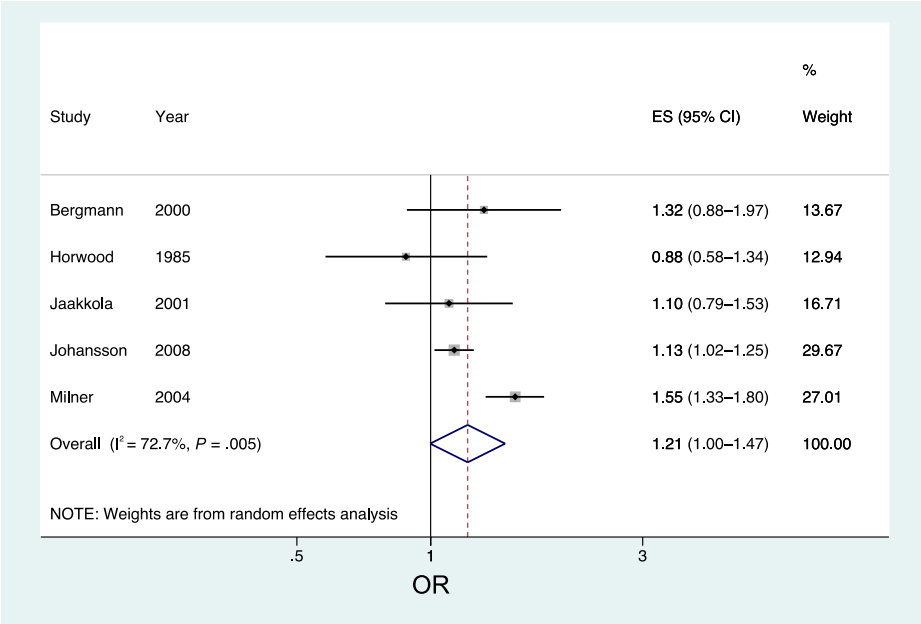
SUPPLEMENTAL FIGURE 14
Incidence of asthma (outcome determined ≤ age 2) and exposure to maternal smoking.



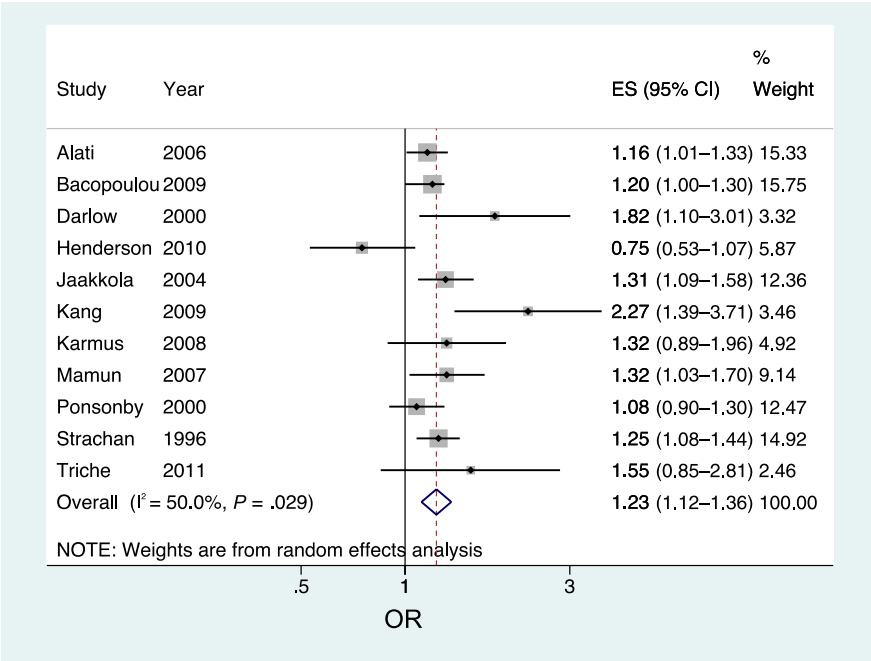
SUPPLEMENTAL FIGURE 15
Incidence of asthma (outcome determined ≤ age 2) and exposure to household smoking.



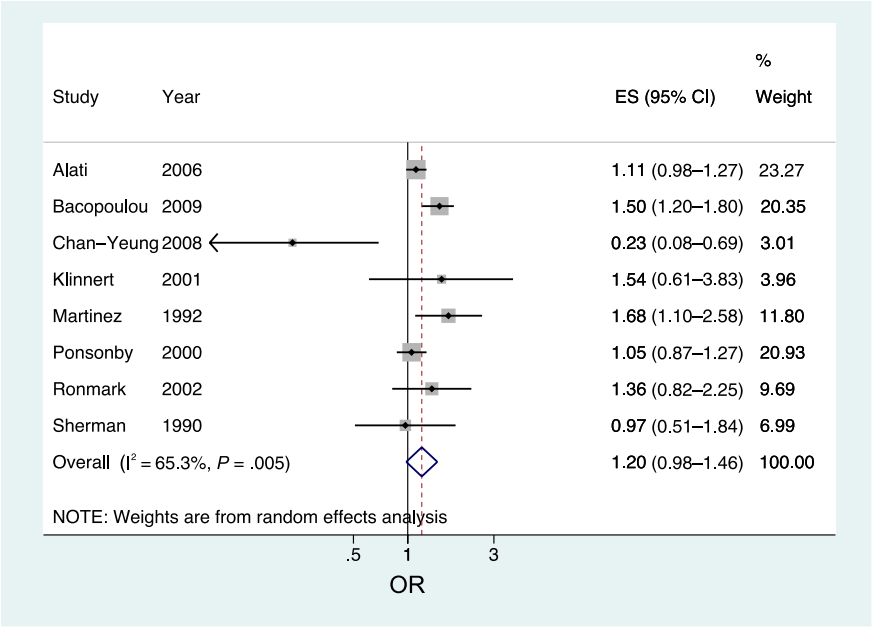
SUPPLEMENTAL FIGURE 16
Incidence of asthma (outcome determined at ages 3–4) and exposure to maternal smoking.



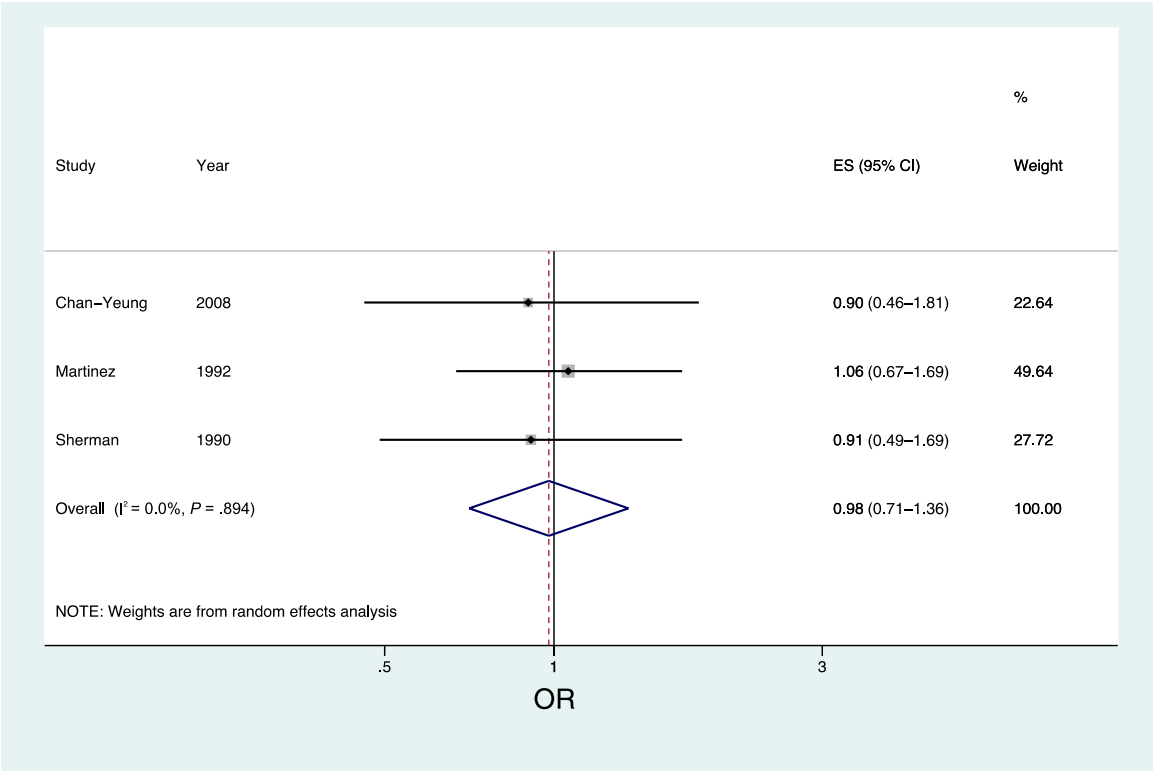
SUPPLEMENTAL FIGURE 17
Incidence of asthma (outcome determined at ages 3–4) and exposure to household smoking.



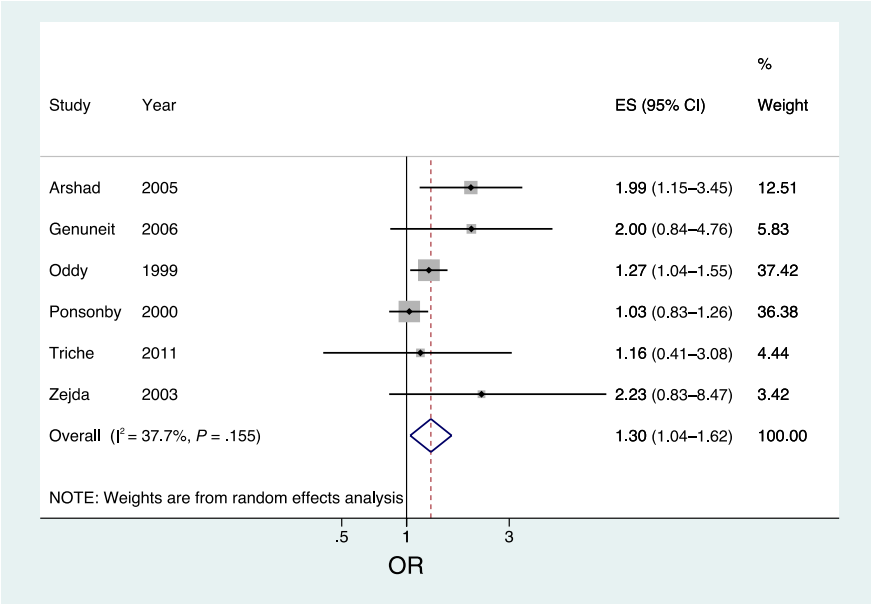
SUPPLEMENTAL FIGURE 18
Incidence of asthma (outcome determined at ages 5–18) and exposure to prenatal smoking.



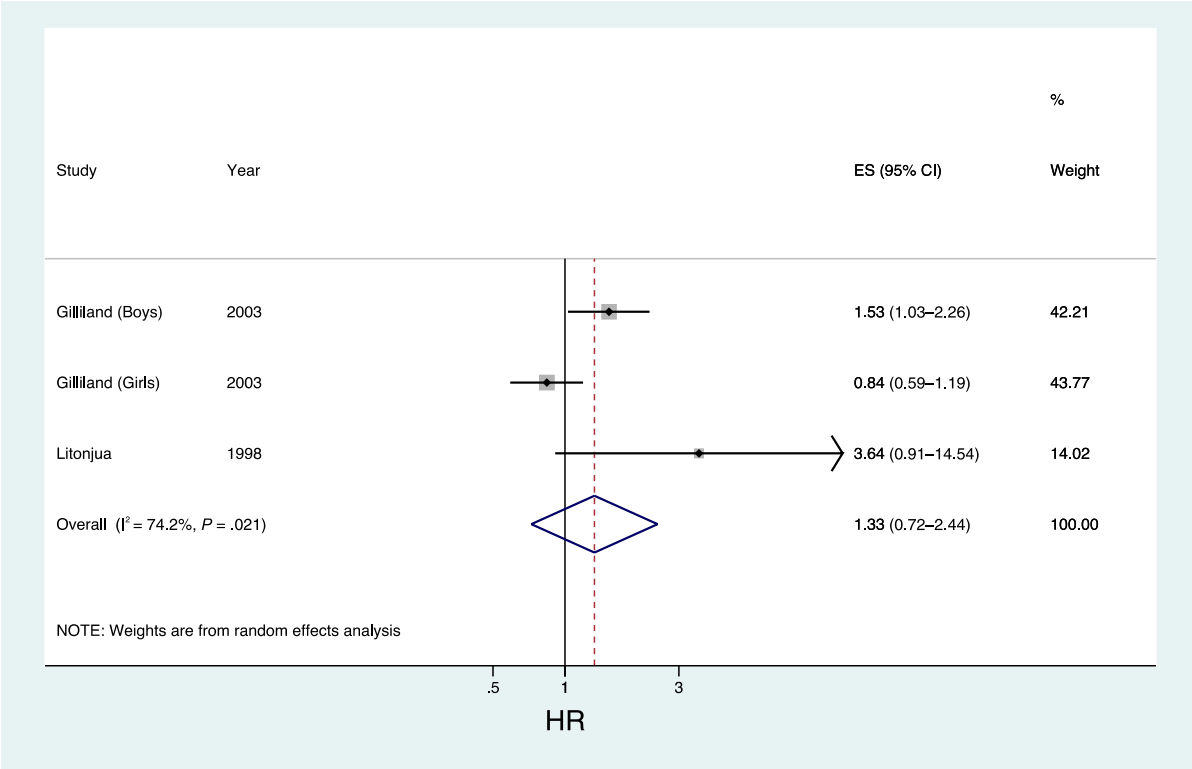
SUPPLEMENTAL FIGURE 19
Incidence of asthma (outcome determined at ages 5–18) and exposure to maternal smoking.



SUPPLEMENTAL FIGURE 20
Incidence of asthma (outcome determined at ages 5–18) and exposure to paternal smoking.



SUPPLEMENTAL FIGURE 21
Incidence of asthma (outcome determined at ages 5–18) and exposure to household smoking.



SUPPLEMENTAL FIGURE 22
Incidence of asthma (data using HRs) and exposure to household smoking.

SUPPLEMENTAL TABLE 3 Summary of Details From Articles Included in the Review and Meta-analyses

Ref. No.	Study Identification No.	Study Author	Year Published	Population Cohort	Newcastle-Ottawa Quality Assessment Score	Outcome	Exposure
1	1	Alati	2006	Mater University Study of Pregnancy 1981–1984	5	Asthma	Prenatal maternal and maternal
2	2	Arshad	2005	Isle of Wight, birth cohort	7	Wheeze and asthma	Household
3	3	Barcopoulou	2009	Greek birth cohort, 1983	6	Asthma	Prenatal maternal and maternal
4	4	Bergmann	2000	5 German cities	7	Asthma	Household
5	5	Chan-Yeung	2008	The Canadian Childhood Asthma Prevention Study	7	Asthma	Maternal and paternal
6	6	Darlow	2000	New Zealand Cohort of Very Low Birth Weight Infants 1986	7	Asthma	Prenatal maternal
7	7	de Birdeling	2005	Southampton, UK birth cohort	5	Wheeze	Maternal, paternal, and household
8	8	Fergusson	1985	Christchurch development study	5	Asthma	Maternal and paternal
9	9	Genuneit	2006	ISACC II	7	Asthma and wheeze	Household
10a	10a	Gilliland	2003	Southern California Children's Health Study 1993	5	Asthma	Household
11	11	Gold	1999	Boston Birth Cohort	7	Wheeze	Prenatal maternal
12a	12a	Gold	2003	1974–1979, 70 school communities throughout the United States	5	Asthma	Maternal
13a	13a	Guedes	2009	Brazil birth cohort	7	Asthma	Maternal
14	14	Haberg	2007	MoBa Study	7	Wheeze	Prenatal maternal
15	15	Hagendorens	2005	APO study	5	Wheeze	Prenatal maternal
16	16	Henderson	2001	Elspac–Czech	5	Wheeze	Prenatal maternal
17	17	Henderson	2001	Avon Birth Cohort (ALSPAC)	7	Wheeze	Prenatal maternal and household
18	17	Henderson	2010	Avon Birth Cohort (ALSPAC)	6	Asthma	Prenatal maternal
19	8	Horwood	1985	Christchurch development study	5	Asthma	Household
20	18	Jaakkola	2001	Oslo Birth cohort, Norway 1992	7	Asthma	Household
21	19	Jaakkola	2004	Finnish Birth Cohort, 1987	7	Asthma	Prenatal maternal
22	20	Jedrychowski	2008	Birth Cohort, Krakow	7	Wheeze	Prenatal maternal and household
23	21	Johansson	2008	ABIS	5	Asthma	Household
24	22	Kang	2009	New England birth cohort	7	Asthma	Prenatal maternal
25	2	Karmus	2008	Isle of Wight, birth cohort	6	Asthma	Prenatal maternal
26	23	Keil	2009	German multicenter study (MAS)	5	Wheeze	Prenatal maternal
27	24	Klinnert	2001	Birth Cohort Denver 1985–1987	5	Asthma	Maternal
28	2	Kurukularaaratchy	2004	Isle of Wight, birth cohort	7	Wheeze	Household
29	25	Lannero	2006	Birth cohort in Sweden 1994–1994 (BAMSE)	7	Asthma and wheeze	Prenatal maternal, maternal, and household
30	26	Lemanske	2005	Wisconsin Birth Cohort (COAST)	7	Wheeze	Household
31	27	Lewis	1995	1970 British Birth Cohort (BCS70)	5	Wheeze	Prenatal maternal
32	27	Lewis	1998	1970 British Birth Cohort (BCS70)	6	Wheeze	Prenatal maternal
33	28	Linneburg	2006	Danish National Birth Cohort	7	Wheeze	Prenatal maternal
34a	11a	Litonjua	1998	Boston Birth Cohort	7	Asthma	Household
35a	29	Lombardi	1997	Tucson Birth Cohort	5	Asthma	Maternal smoking
36	30	Magnusson	2007	2 Danish cities ("Healthy habits for 2")	7	Wheeze	Prenatal maternal and household
37	31	Mallol	2005	Santiago low income birth cohort	5	Wheeze	Household
38	32	Mamun	2007	Australia – Mater University MUSP cohort	5	Asthma	Prenatal maternal
39a	33a	Mannino	2006	National Longitudinal Survey of Youth	7	Asthma	Prenatal maternal

SUPPLEMENTAL TABLE 3 Continued

Ref. No.	Study Identification No.	Study Author	Year Published	Population Cohort	Newcastle-Ottawa Quality Assessment Score	Outcome	Exposure
40	34	Martinez	1992	Tucson study of chronic obstructive pulmonary disease	7	Asthma	Maternal and paternal
41	29	Martinez	1995	Tucson Birth Cohort	5	Wheeze	Prenatal maternal and maternal
42a	10a	McConnell	2002	Southern California Children's Health Study 1993	5	Asthma	Maternal
43a	35a	McKeever	2001	GPRD WestMidlands Birth Cohort	5	Wheeze	Maternal and paternal
44	36	Menezes	2007	Brazil Birth Cohort	5	Wheeze	Prenatal maternal
45	37	Midozi	2008	Canadian National Longitudinal Survey of Youth	5	Wheeze	Prenatal maternal and household
46	38	Miller	2001	1988 National Maternity and Infant Study	5	Asthma	Maternal
47	38	Milner	2004	1988 National Maternity and Infant Study	5	Asthma	Household
48	39	Mrazek	1999	Denver Birth Cohort	5	Asthma	Maternal
49	40	Murray	2004	Manchester Asthma and Allergy Birth Cohort (NACMASS)	5	Wheeze	Prenatal maternal and maternal
50	26	Neuspiel	1989	1970 British Birth Cohort (BCS70)	5	Wheeze	Maternal
51	40	Nicolau	2008	Manchester Asthma and Allergy Birth Cohort (NACMASS)	7	Wheeze	Prenatal maternal, paternal, and household
52	41	Noakes	2007	Perth Birth Cohort	5	Asthma	Prenatal maternal and maternal
53	42	Oddy	1999	King Edward Memorial hospital, Western Australia	7	Asthma and wheeze	Household
54	43	Ponsonby	2000	Tasmanian Infant Health Survey 1988–1995	7	Asthma	Prenatal maternal and maternal
55	44	Ronmark	2002	Northern Sweden Birth Cohort	7	Wheeze	Maternal
56	45	Sangsupawanich	2007	Prospective cohort study of Thai Children (PCTC)	7	Wheeze	Household
57	46	Schroer	2008	Cincinnati childhood allergy and air pollution study	7	Wheeze	Household
58	47	Sherman	1990	East Boston cohort	5	Asthma	Maternal and paternal
59	17	Sherriff	2001	Avon Birth Cohort (ALSPAC)	5	Wheeze	Prenatal maternal and maternal
60	29	Stein	1999	Tucson Birth Cohort	7	Wheeze	Prenatal maternal
61	48	Strachan	1996	1958 British Birth Cohort	5	Asthma	Prenatal maternal
62	49	Tanaka	2008	Osaka Maternal and Child Health Study	7	Asthma and wheeze	Prenatal maternal, maternal, and household
63	2	Tariq	1998	Isle of Wight, birth cohort	6	Asthma and wheeze	Prenatal maternal and maternal
64	2	Tariq	2000	Isle of Wight, birth cohort	6	Asthma	Prenatal maternal, maternal, and household
65a	50a	Taveras	2006	Project VIVA–Boston birth cohort	5	Asthma and wheeze	Household
66	51	Triche	2011	Asthma in Pregnancy Study and Perinatal Risk of Asthma in Infants of Asthmatics Mothers	6	Asthma and wheeze	Prenatal maternal and household
67	11	Wright	2002	Boston Birth Cohort	7	Wheeze	Maternal
68	52	Yang	2007	Taiwan Birth Cohort	5	Wheeze	Household
69	53	Young	2000	Western Australia birth cohort – Princess Margaret hospital	5	Wheeze	Prenatal maternal
70	54	Yuan	2003	Denmark birth cohort 1996–1997	7	Asthma	Prenatal maternal
71	55	Zejda	2003	Poland 1995	5	Asthma	Household

ABIS, all babies in Southeast Sweden; ALSPAC, Avon Study of Parents and Children; BAMSE, Children, Allergy, Milieu, Stockholm, Epidemiological Survey; COAST, childhood origins of asthma; ELSPAAC, European Longitudinal Study of Pregnancy and Childhood; GPRD, General Practice Research Database; ISACC II, International Study of Asthma and Allergies in Childhood, Phase II; MAS, Multicentre Allergy Study; Mamun, Mater University of Queensland Study of Pregnancy; MoBo, The Norwegian Mother and Child Cohort Study; NACMASS, National Asthma Campaign Manchester Asthma and Allergy Study; PIPO, prospective study on the influence of perinatal factors on the occurrence of asthma and allergies.

[a] Studies with HRs.

SUPPLEMENTAL TABLE 4 Summary of Details From Articles Examined but Excluded From Meta-analyses as Data From Same Cohort Present in Another Research Article

Study Identification No.	Study Author	Year Published	Population Cohort	Newcastle-Ottawa Quality Assessment Score	Outcome	Smoking Exposure
40	Calam	2005	Manchester Asthma and Allergy Birth Cohort (NACMASS)	7	Wheeze	Maternal
19	Jaakkola	2007	Finish Birth Cohort, 1987	7	Asthma	Prenatal maternal
25	Kull	2002	Birth cohort in Sweden 1994–1994 (BAMSE)	7	Asthma	Prenatal maternal
2	Kurukularaaratchy	2005	Isle of Wight, birth cohort	5	Wheeze	Prenatal maternal
2	Kurukularaaratchy	2006	Isle of Wight, birth cohort	7	Wheeze	Maternal and household
17	Lux	2000	Avon Birth Cohort (ALSPAC)	7	Wheeze	Prenatal maternal and household
11	Park	2001	Boston Birth Cohort	7	Wheeze	Prenatal maternal
2	Sadeghnejad	2008	Isle of Wight, birth cohort	5	Wheeze	Household
25	Wickman	2003	Birth cohort in Sweden 1994–1994 (BAMSE)	7	Asthma and wheeze	Prenatal maternal and maternal

ALSPAC, Avon Study of Parents and Children; BAMSE, Children, Allergy, Milieu, Stockholm, Epidemiological Survey; NACMASS, National Asthma Campaign Manchester Asthma and Allergy Study.