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Original Articles

Meta-Analysis on the Association Between Environmental Tobacco Smoke (ETS) Exposure and the Prevalence of Lower Respiratory Tract Infection in Early Childhood

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Summary. The aim of this study was to obtain quantitative information from published data on the association between environmental tobacco smoke (ETS) exposure and the prevalence of serious lower respiratory tract infections (LRTI) in infancy and early childhood. We identified 21 relevant publications on the relation between ETS and the prevalence of serious LRTI by reviewing reference lists in relevant reports and by conducting manual and computer searches (Medline database; Dissertation abstracts index of Xerox University Microfilms) of published reports between 1966 and 1995. Thirteen studies were included in a quantitative overview using random effects modeling to derive pooled odds ratios.

Sensitivity analyses were conducted to test the decision rules used in extracting odds ratio data. The results of community and hospital studies are broadly consistent and show that the child of a parent who smokes is at approximately twice the risk of having a serious respiratory tract infection in early life that requires hospitalization. This association was pronounced in children younger than age two and diminished after the age of two. The combined odds ratio for hospitalization for lower respiratory tract infections in infancy or early childhood is 1.93 (95% CI 1.66–2.25); the combined odds ratio of prevalence of serious LRTI at age less than 2 years, between 0 and 6 years, and between 3 and 6 years were 1.71 (95% CI 1.33–2.20); 1.57 (1.28–1.91), and 1.25 (0.88–1.78), respectively. There was no evidence of heterogeneity across the studies in these combined odds ratios. We conclude that this meta-analysis provides strong evidence that exposure to ETS causes adverse respiratory health outcomes such as either a serious LRTI or hospitalization for LRTI. New public health campaigns are urgently needed to discourage smoking in the presence of young children. **Pediatr Pulmonol. 1999; 27:5–13.**

Key words: meta-analysis; epidemiology; environmental tobacco smoke; passive smoking; lower respiratory tract infection.

INTRODUCTION

The health consequences of exposure to environmental tobacco smoke (ETS) have been a cause of scientific and public health concern because of increasing evidence showing that acute respiratory illness, chronic respiratory symptoms, and the initiation and exacerbation of asthma in children are associated with exposure to ETS.[1] Although ETS exposure is important in many childhood disorders,[1–5] most interest has focused on respiratory illness because these effects are clinically important, and there is a plausible causal relationship. In addition, acute respiratory illness is the most common cause of morbidity in childhood throughout the world, and it is also a major cause of mortality in many countries.[6] Although

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clinical recovery from acute respiratory illness in childhood is usual,[7] there may be important long-term sequelae with increased susceptibility to illness and diminished respiratory function following lower respiratory infection in infancy.[8,9]

Between 1974 and 1995, seven prospective, nine case-control, and seven cross-sectional studies reported the possible effects of exposure to parental tobacco smoke on the frequency and severity of acute respiratory illness in young children. Although different research designs were used, the results have consistently demonstrated increased frequency of both upper and lower respiratory problems among young children of smoking parents compared with children of nonsmoking parents. As early as 1974, the Israeli researchers Harlap and Davies[10] reported an increase of 27.5% in hospital admission rates for pneumonia and bronchitis in infants of smoking mothers, with a dose–response relation with respect to the amount of cigarettes a mother consumed. Researchers in Britain[11,12] showed a significant increase of 32% in bronchitis and pneumonia during the first year of life, but not in the subsequent 4 years, in children exposed to parental smoking and with a dose–response relation with respect to the number of parents who smoked. The finding persisted after controlling for parental respiratory symptoms, the gender of the child, the number of siblings, and any sibling history of respiratory illness. American researchers[13] found a significantly increased frequency of tracheitis (89%) and bronchitis (44%) in infants whose parents smoked, with most of the attributable risk derived from maternal smoking. New Zealander researchers[14,15,16] showed a dose-related effect of maternal smoking on the prevalence of pneumonia, bronchitis, and bronchiolitis. Infants of smoking mothers were twice as likely to see a doctor for respiratory illness as those of nonsmokers. In China, where women do not smoke, admission rates for respiratory illness in infancy maintained a significant correlation with cigarette consumption in the household, indicating that postnatal passive smoking by the mother has an influence that is not explained by maternal smoking during pregnancy.[17,18,19]

In this article, we combine the current evidence using meta-analysis techniques to measure the association between ETS exposure and specific respiratory outcomes, that is, hospitalization frequency due to LRTI or diagnosed serious LRTI in infancy and early childhood.

Abbreviations

CI	Confidence interval
ETS	Environmental tobacco smoke
LRTI	Lower respiratory tract infection
OR	Odds ratio
SES	Social economic status

METHODS

To find studies examining potential associations between exposure to ETS and respiratory illness in infancy or early childhood, a search of the scientific literature using MEDLINE, review of bibliographies from previously retrieved articles, and hand searches of selected journals (American Review of Respiratory Disease, 1985–1995) and conference meeting handbooks (Annual Meeting of Thoracic Society of Australia and New Zealand, 1990–1995) was conducted. A search of Dissertation Abstracts Index (Xerox University Microfilms; Ann Arbor, Michigan) identified two additional unpublished relevant studies of ETS exposure on early childhood respiratory illness. A MEDLINE computerized bibliographic search was conducted between the years of 1966 and 1995, using subheading key words: tobacco smoke pollution, infant, respiratory tract disease/epidemiology, ethnology, genetics, pneumonia/epidemiology, ethnology, genetics and respiratory tract infections/epidemiology, genetics.

To be eligible for inclusion in the meta-analysis, studies had to: i) be primary studies, not reanalyses or reviews; ii) be of case-control, cohort, or cross-sectional design, using individual level exposure and health outcome information; iii) examine either serious LRTI or hospitalization for a respiratory illness in infancy or in early childhood as outcomes; iv) examine exposure to environmental tobacco smoke; v) report an odds ratio (OR) and its variance or sufficient data to estimate them; and vi) be published or reported between 1966 to 1995. The definitions of serious LRTI and respiratory illness varied among different authors, as noted in Table 1. The extracted OR and confidence intervals are listed in Table 2. Table 3 shows a list of studies and the reasons for their exclusion from the OR for children who had been hospitalized related to respiratory illness, and prevalence of serious LRTI, i.e., pneumonia, bronchitis, or bronchiolitis, in association with ETS exposure were used. Ninety-five percent confidence intervals (95% CI) were either extracted directly from the original papers or calculated by the standard approximation to a normal distribution on a logarithmic scale. Since not all the studies provided sufficient data to construct contingency tables, the pooled estimation by Mantel-Haenszel was not appropriate. Therefore, the DerSimonian-Laird method,[20] which is a random effect model, was used in this pooling procedure. Briefly, this involved taking a weighted average of the log OR from each study, with the weight assigned to each log OR proportional to the inverse of its variance. The variance was made up of the variance calculated within each study, and the variability in log ORs among studies is also incorporated. In the presence of substantial inter-study variability (heterogeneity), this method produces wider CIs than a simple inverse-variance weighted aver-

TABLE 1—Studies Included in the Meta-analysis

First author	Country of study	Definition of respiratory outcome	Exposure level of ETS	Age focus	No. of cases	Study type	Variables controlled for by the authors
Ekwo (1983)	USA	Hospitalization for a respiratory illness: chest colds and other respiratory illnesses <2years	Paternal smoking, maternal smoking, either of the parents smoke	<2 year	1,138	Cross-sectional	Nil
Chen (1986)	China	Inpatient admissions for respiratory illness from birth to 18 months	Cigarette consumption of fathers and other family members: none, <10, >10/day	1–2 years	1,066	Cross-sectional	Gender, feeding method, birthweight, paternal education, maternal age at birth, whether coal was used for cooking, average living area per person, family income
Taylor (1987)	UK	Hospitalization for lower respiratory tract illnesses and bronchitis in the children's first 5 years of life	Paternal smoking, maternal smoking, smoking during pregnancy: none, <15, >15/day	0–5 years	12,727	Cross-sectional	Parental SES, mother's age, whether baby was breastfed, birthweight
Chen (1988)	China	1. Hospitalization for lower respiratory tract illnesses and bronchitis during first 18 months of life 2. Incidence of medically diagnosed bronchitis or pneumonia during first 18 months of life	Cigarette consumption of fathers and other family members: none, <20, >20/day	0–2 years	2,227	Cross-sectional	Gender, birthweight, feeding type, father's educational status
Stern (1989)	Canada	Hospitalization for a chest illness <2 years of age	Maternal smoking: during pregnancy, during the child's first 2 years of life	<2 years	301	Cross-sectional	City of residence, parental education, gas cooking at home, history of chronic respiratory illness in either parent
Weitzman (1990)	USA	Hospitalization for a respiratory illness from 0–5 years	Maternal smoking: none, <0.5 pack/day, >0.5 pack/day	0–5 years	4,099	Cross-sectional	Gender, race, presence of both biological parents, family size, number of rooms in household, and maternal education
Chen (1994)	China	Episodes of hospitalization for respiratory disease in the first 18 months of life: bronchitis, bronchiolitis, pneumonia, and other other respiratory infections	Cigarette consumption by household members: none, <20/day, >20/day	<2 years	3,285	Cross-sectional	Gender, feeding type, parental education, maternal age at child's birth, monthly income per capita, number of household members, average living space per capita, cooking fuel
Colley (1974)	UK	Incidence of bronchitis or pneumonia in the first year of life	Paternal smoking, maternal smoking: none, <15/day, >15/day, >25/day	1 year	2,205	Cohort	Social class, family size, birthweight
Pedreira (1985)	USA	Incidence of bronchitis, pneumonia, or bronchiolitis in the first year of life	Paternal smoking, maternal smoking: none, <11/day, >11/day	1 year	1,144	Cohort	Nil

TABLE 1—Continued

First author	Country of study	Definition of respiratory outcome	Exposure level of ETS	Age focus	No. of cases	Study type	Variables controlled for by the authors
Ferguson (1985)	NZ	Incidence of bronchitis, bronchiolitis or pneumonia reported for medical consultation during each year of life	Paternal smoking, maternal smoking: none, <11/day, >11/day	0–2 years 3–4 years 5–6 years	1,115	Cohort	Birthweight, gestational age, maternal age, family size, maternal educational level, family SES, family atopy, duration of breast feeding, exposure to pets at home
McConnachie (1986)	UK	Incidence of bronchiolitis in the first 2 years of life	Paternal smoking, maternal smoking, or other household members smoking No exposure levels	2 years	159	Case-control	Nil
Forastiere (1992)	Italy	Incidence of pneumonia or bronchitis in the first years of life	Paternal smoking, maternal smoking No record of exposure levels	2 years	2,929	Cross-sectional	Gender, age, length of residence in the area, heating system, paternal education, number of siblings
Rylander (1993)	Sweden	Incidence of wheezing bronchitis in the first 4 years of life	Paternal smoking, maternal smoking: none, <10/day, >10/day	0–4 years	550	Case-control	Gestational age, breastfeeding, gender, parental atopy, and other indoor environmental factors

TABLE 2—Odds Ratios Associated With ETS

Reference	Country	Age	Sample size	OR(95% CI)
Hospitalization for lower respiratory illness				
Ekwo (1983)	USA	<2 years	1,138	2.1 (1.1–3.8)
Chen (1986)	China	1–2 years	1,066	1.9 (1.1–3.4)
Taylor (1987)	UK	0–5 years	12,727	2.0 (1.5–2.8)
Chen (1988)	China	0–2 years	2,227	2.2 (1.5–3.4)
Stern (1989)	Canada	<2 years	301	1.9 (1.5–2.2)
Weitzman (1990)	USA	0–5 years	4,099	1.0 (0.5–2.5) asthmatics
				1.9 (1.2–3.0) nonasthmatics
Chen (1994)	China	<2 years	3,285	4.5 (2.1–9.7) birthweight <2.5 kg
				1.6 (1.1–2.4) birthweight >2.5 kg
Community studies: lower respiratory tract infections				
Colley (1974)	UK	1 year	2,205	2.3 (1.4–3.6)
Pedreira (1985)	USA	1 year	1,144	1.26 (1–1.59)
Fergusson (1985)	NZ	0–2 years	1,115	2.0 (1.2–3.2)
		3–4 years		1.3 (0.8–2.2)
		5–6 years		1.0 (0.5–1.8)
McConnachie (1986)	UK	2 years	159	3.2 (1.4–7.3)
Chen (1988)	China	0–2 years	1,746	1.2 (1.0–1.46)
Forastiere (1992)	Italy	2 years	2,292	1.7 (1.1–2.7)
Rylander (1993)	Sweden	0–4 years	550	2.6 (1.4–4.8) <age 18 months
				1.5 (0.7–3.2) >age 18 months

age. For each summary OR, a χ^2 with K-1 (K = number of studies) degrees of freedom was computed under the null hypothesis of homogeneity across studies at $P < 0.05$. A significant value of χ^2 indicated differences among the combined studies in the strength of association between ETS exposure and respiratory health outcomes.

A random effects model was preferred because it allowed heterogeneity from sampling methods and other unexplained variation due to unreported study characteristics.[21] Such heterogeneity is important from the perspective of generalizability of results. The random model also implicitly assumes that there is a population of studies from which those included in the meta-analysis were sampled, and it anticipates the possibility of future studies being conducted. On the other hand, a fixed effect model assumes that only the studies included in the meta-analysis are of interest, and that there is no interest in

TABLE 3—Studies of ETS and Hospitalization for LRTI/Incidence of Serious LRTI Excluded From the Meta-analysis

Author	Year	Outcome variable	Reason for exclusion
Anderson*	1988	Hospitalization for LRTI	Possible selection bias and insufficient results (missing 95% CI)
Schenker*	1983	Serious chest illness	Insufficient results to calculate 95% CI for OR
O'Connell**	1990	Hospitalization for LRTI, incidence of RTI	Abstract only; insufficient results
Burchfiel**	1984	Prevalence of respiratory conditions	Abstract only; insufficient results
Leeder	1976	Prevalence of bronchitis or pneumonia	The same study population as Colley, 1974
Fergusson	1980	Prevalence of bronchitis or pneumonia	The same study population as Fergusson, 1981 and 1985
Fergusson	1981	Prevalence of bronchitis or pneumonia	The same study population as Fergusson, 1985
Zmirou	1990	Prevalence of chronic infections of lower respiratory tract	A systematic review article, not original study

*Have tried to contact the primary investigator to get sufficient data for OR and 95% CI, but had no response so far.
**No correspondence details on the electronic abstract and therefore attempt to contact the primary investigator is impossible.

generalizing the result to other studies.[22] The random effects model was chosen therefore, because of the association between ETS exposure and respiratory health outcomes throughout the general population from which the studies' subjects were drawn.

RESULTS

Meta-analysis

Thirteen studies met our study inclusion criteria. These comprised three cohort studies, two case-control studies, and eight cross-sectional studies. Seven studies[11,13,16,17,19,23,24] contributed information on bronchitis and pneumonia, four studies[18,25,26,27] on admission related to unspecified lower respiratory illness, one concentrated on illness diagnosed as bronchiolitis,[23] and one focused on wheezing bronchitis.[29] Seven studies were excluded from the meta-analysis (Table 3) because of insufficient results to estimate 95% CI for OR or because the paper used the same study population as other studies. The OR estimates contributed by each study for each respiratory health outcome and the combined ORs are shown in Figures 1 and 2. Results of the analyses are summarized in Table 4.

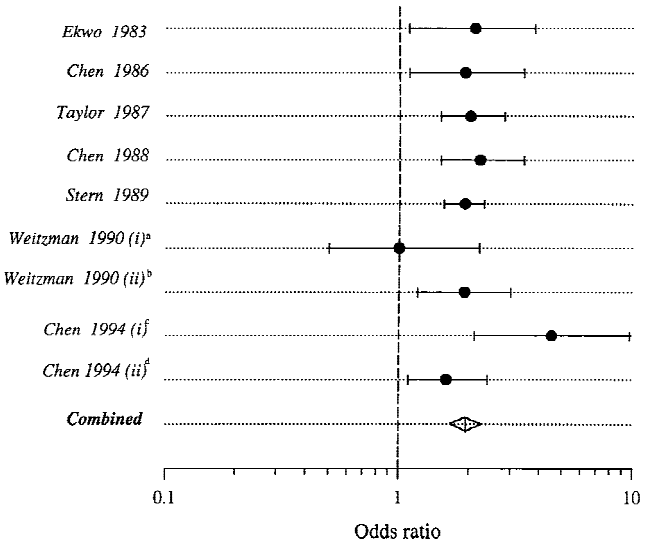

Fig. 1. Odds ratios and 95% confidence intervals for hospitalization for a respiratory illness in infancy or early childhood if exposed to ETS. Abbreviations: [a]Odds ratio for asthmatic subjects in Weitzman's study.[27] [b]Odds ratio for non-asthmatic subjects in Weitzman's study.[27] [c]Odds ratio for children with birthweight less than 2.5 kg in Chen's study.[17] [d]Odds ratio for children with birthweight more than 2.5 kg in Chen's study.[17]

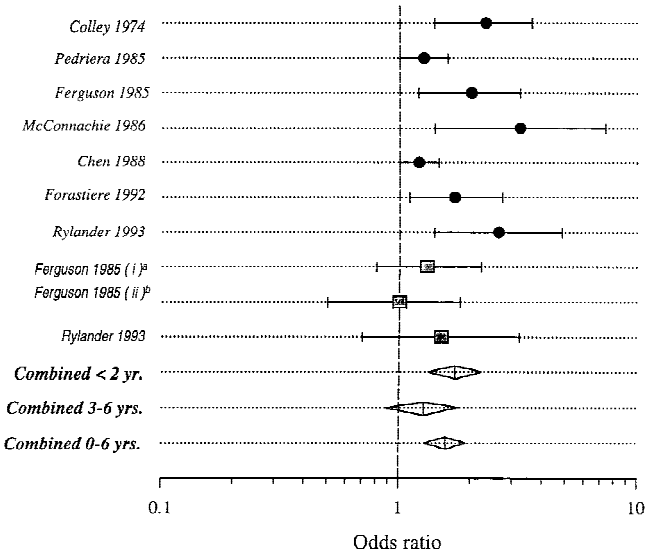

Fig. 2. Odds ratios and 95% confidence intervals for serious lower respiratory tract infections in infancy or early childhood if exposed to ETS. Individual studies are denoted: circles = studies of children less than 2 years old; square = studies of children between 3–6 years old. Abbreviations: [a]Odds ratio for children between 3–4 years in Fergusson's study.[16] [b]Odds ratio for children between 5–6 years in Fergusson's study.[16]

Based on seven studies, the meta-analysis showed a statistically significant association between ETS expo-

TABLE 4—Combined OR, 95% CI and Homogeneity Tests From Meta-analyses

	OR & 95% CI	df	Homogeneity χ^2	*P* value	Sample size
ETS & hospitalization for respiratory illness	1.93 (1.66–2.25)	8	8.9	>0.25	28,873
ETS & LRT infection 0–2 years	1.71 (1.33–2.20)	6	6.4	>0.1	16,242
ETS & LRT infection 0–6 years	1.57 (1.28–1.91)	9	16.92	>0.05	16,242
ETS & LRT infection 3–6 years	1.25 (0.88–1.78)	2	0.64	>0.5	1,665

sure and hospitalization for respiratory illness in infancy or in early childhood. Weitzman et al.[27] presented two ORs, one for asthmatics and one for nonasthmatics, and Chen[17] presented two ORs, one for birthweight less than 2.5 kg and one for birthweight greater than 2.5 kg. These additional two ORs were considered to have two degrees of freedom. The combined OR for such association was 1.93 (95% CI 1.66–2.55). When individual studies were compared, there was no significant heterogeneity among the studies ($\chi^2 = 8.9$, df = 8, $P > 0.05$).

The seven studies that contributed data on the risk of serious respiratory infection in early childhood showed a significant risk association between ETS exposure and serious LRT infection, in which bronchitis, bronchiolitis, and pneumonia were included (combined OR = 1.71; 95% CI 1.33–2.20). A heterogeneity test of risk association across studies did not achieve statistical significant ($\chi^2 = 6.4$, df = 6, $P > 0.05$).

Based on the seven studies that examined the risk of respiratory infection, we found a statistically significant increase in risk of serious respiratory infection (bronchitis, bronchiolitis, or pneumonia) associated with ETS exposure among children of 0–6 years old: combined OR = 1.57 (95% CI 1.28–1.91). Fergusson and Horwood[16] presented three ORs for the following age groups: 0–2, 3–4, and 5–6 years. Rylander et al.[29] presented two ORs for wheezy bronchitis: one for less than 18 months of age and the other for greater than 18 months of age. Each of these additional ORs was counted as one degree of freedom. There was no significant heterogeneity of risk association across the studies ($\chi^2 = 16.92$, df = 9, $P > 0.05$).

The two studies that contributed data on the risk of serious LRT infection among children 3–6 years old also showed an increased risk of serious LRT infection (bronchitis, bronchiolitis, or pneumonia) associated with ETS exposure (combined OR = 1.25), but it was not statistically significant (95% CI 0.88–1.78). Fergusson and Horwood[16] presented two ORs, one for 3–4 years and one for 5–6 years and each OR was counted as one degree of freedom. There was no heterogeneity of risk association across the studies ($\chi^2 = 0.64$, df = 2, $P > 0.05$).

Regarding the independence of confounding, only two studies[18,19] presented estimates of the effects of parental smoking, both before and after adjustment for potential confounding variables. Table 5 shows that the effects of parental smoking are little altered by adjustment for measured confounders.

TABLE 5—Effects of Adjustment of Potential Confounders

Hospitalization for lower respiratory illness		
Ekwo (1983)	2.1	NA
Chen (1986)	1.91	1.89
Taylor (1987)	2	NA
Chen (1988)	2.1	2.2
Stern (1989)	1.9	NA
Weitzman (1990)	1 (asthmatics)	NA
	1.9 (nonasthmatics)	NA
Chen (1994)	NA	4.5 (birthweight <2.5 kg)
	NA	1.6 (birthweight >2.5 kg)
Community studies: lower respiratory tract infections		
Colley (1974)	NA	2.3
Pedreira (1985)	1.26	NA
Fergusson (1985)	2.0 (0–2 years)	NA
	1.3 (3–4 years)	NA
	1.0 (5–6 years)	NA
McConnachie (1986)	3.2	NA
Chen (1988)	1.21	1.22
Forastiere (1992)	NA	1.7
Rylander (1993)	2.6 (<18 months)	NA
	1.5 (>18 months)	NA

Sensitivity Analyses

Sensitivity analyses were conducted to test the decision rules that were used in extracting odds ratio data. Because of differing opinions on the appropriate method for performing a particular meta-analysis, sensitivity analysis becomes a useful instrument to demonstrate whether the meta-analysis results are sensitive to the methods used.[30]

Because not all odds ratios in the seven studies were adjusted for confounders, studies with unadjusted OR (Ekwo,[25] Stern,[26] and Weitzman[27]) were omitted from the sensitivity analysis. The combined OR estimate did not change substantially (1.93 to 2.05) and neither did the statistical significance. Both Stern's and Ekwo's studies did not categorize the exposure level by the number of cigarettes. When both were excluded, the combined OR estimate did not change at all from 1.93 (1.55–2.40), and only the 95% confidence interval became wider.

Although most of studies showed an association between ETS exposure, especially maternal smoking, and LRTI in early childhood, it was difficult to differentiate prenatal from postnatal maternal smoking effects. Only the three studies by Chen et al.[17,18,19] could demonstrate

a postnatal ETS risk since smoking in women is very rare in Shanghai. By grouping results from Chen's studies together, the new combined OR became 2.13 (1.52–3.00), which was a 10% increase.

Only four studies were adjusted for potential confounders[11,16,19,23] with regard to the association between ETS and respiratory infection in early childhood. The new combined OR was 1.56 (1.19–2.05) in children less than 2 years, a 8.8% of decrease.

In the subgroup of children 0–6 years of age, it was interesting to note a diversification in study types. When the cohort studies were combined, the OR became 1.49 (1.13–1.96) indicating a 5% decrease, but when the non-cohort studies were combined, the OR became 1.75 (1.20–2.53), an 11% increase.

Not all the studies estimated an OR by measuring exposure level by total cigarette consumption per day. Forastiere[23] measured exposure with a dichotomous variable for mother only, father only, or both parents, and McConnochie[28] defined passive smoking as a parent who smoked at least 20 packs of cigarettes or 12 oz of tobacco while living in the home, but no further categorization of smoking level was made. Without actual ETS exposure measures, the estimated risk may not be accurate. When McConnochie and Forastiere's results were excluded, the combined OR became 1.61 (1.22–2.13) in the group age less than 2 years, and the combined OR for the group age 0–6 years became 1.49 (1.20–1.84), or a 5% decrease in effect.

DISCUSSION

The results of this meta-analysis confirm that the child of a parent who smokes is at approximately twice the risk of having a serious respiratory infection in early life that requires hospitalization. This association was very pronounced in children younger than age two, but diminished after the age of two. The direction of the association between parental smoking and lower respiratory illness is generally consistent across different study designs and methods of case ascertainment. Only one study[70] from the U.S. found an insignificant association (with hospitalization for a respiratory illness of asthmatic subjects). This finding must be viewed with caution, because with only 117 children in the sample, its statistical power to detect a small effect is low.

Although the studies reviewed differed in terms of study population, levels of exposure, and methods of data collection, the odds ratio estimates in individual studies were generally comparable, and were not statistically heterogeneous, giving strong evidence of the consistency of the pooled results. Both adjusted and unadjusted estimates were considered in the computation of the combined OR. These criteria allowed more eligible studies to be retained in the meta-analysis. A sensitivity analysis showed that the difference between adjusted and unadjusted estimates was acceptably modest.

The papers cited were selected using keywords relevant to environmental tobacco smoke exposure and children in the title or abstract. When cross-checked against previous reviews of passive smoking in children,[1,31] no major omissions were identified. However, in the interpretation of the results of the meta-analysis, publication bias is one of the major issues, but meta-analysis requires the research findings to be published in an acceptable form. It is well recognized that negative studies are less likely to be published than those with statistically significant positive findings.[32] This "file-drawer problem" could bias the meta-analysis towards finding a positive association between ETS exposure and serious lower respiratory tract infections or hospitalization due to LRTI.

In an effort to uncover unpublished studies, we searched Dissertation Abstracts Online between 1961 and 1990, but only two studies were identified. Unfortunately, both dissertations had insufficient data information to enable them to be included in our meta-analysis. Nevertheless, both studies showed a positive association between exposure to ETS and respiratory illness in children. Although O'Connell's study[33] did not present a precise relative odds estimate, it showed that infants of parents who smoke had an increased risk of hospitalization for bronchitis and pneumonia when compared with infants of non-smoking parents. Burchfiel's study[34] also had a non-negative finding, in that it found that children were 1.5 to 2.0 times as likely to have a respiratory condition when both parents currently smoked.

It is possible that a confounder, that is a factor related to both ETS exposure and the risk of serious LRTI, would explain these observed findings. It was not possible to control for such possible confounders in the meta-analysis, which relied on the primary studies reported. Fortunately, most of the included studies had put effort into controlling for confounding. Therefore, it is unlikely that such a bias plays a major role.

A possible biological mechanism for the enhancement of respiratory infections in young infants exposed to ETS is that the infant lungs undergo rapid and extensive changes in growth and development and may be particularly vulnerable to insult, especially since the immune system is relatively immature during this period.[35] Also, the defense mechanisms of the bronchial tree, such as mucociliary clearance, can be impaired by exposure to pollutants[36] such as ETS, thus increasing susceptibility to a variety of pathogens.[37]

It is reasonable to conclude that parental smoking, especially maternal smoking, is dominant in the causation of serious lower respiratory infections in young children, at least in the first two years of life. The findings of this study and the meta-analysis should encourage renewed

efforts to discourage smoking in families, especially during pregnancy and the first few years of children's lives. Because most mothers who smoke during pregnancy continue to do so after the birth of the child,[24] the process of prevention clearly needs to begin before or during pregnancy. This has implications for public health and for new directions in health promotion strategies related to parental smoking. Because lower respiratory tract illness is a major cause of hospitalization for infants and young children and because cigarette smoking by parents appears to be the risk factor most amenable to change, there is good reason from a public health perspective to develop interventions to prevent parents from smoking in the presence of their children.

REFERENCES

1. A report of the Surgeon General. The health consequences of smoking, chronic obstructive lung disease. U.S. Department of Health and Human Services, 1984.
2. Fielding JE, Phenow KJ. Health effects of involuntary smoking. New Engl J Med 1988;319:1452–1460.
3. Royal College of Physicians. Smoking and the young. London: Royal College of Physicians, 1992.
4. Poswillo D, Alberman E, eds. Effects of smoking on the fetus, neonate and child. Oxford: Oxford University Press, 1992.
5. Couriel JM. Passive smoking in childhood. In: David TJ, editor. Recent advances in paediatrics, Vol. 112. London: Churchill Livingston, 1993:107–119.
6. Leowski J. Mortality from acute respiratory infections in children under 5 years of age: Global estimates. World Health Stat Q 1986;39:138–144.
7. Leeder SR, Corkhill R, Irwig LM, Holland WW, Colley JRT. Influence of family factors on the incidence of lower respiratory illness in the first year of life. Br J Prev Soc Med 1976;30:203–212.
8. Mok JYQ, Simpson H. Outcome for acute bronchitis, bronchiolitis, and pneumonia in infancy. Arch Dis Child 1984;59:306–309.
9. Paradise JL. Otitis media in infants and children. Pediatrics 1980; 65:917–943.
10. Harlap S, Davies AM. Infant admissions to hospital and maternal smoking. Lancet 1974;March:529–532.
11. Colley JRT, Holland WW, Corkhill RT. Influence of passive smoking and parental phlegm on pneumonia and bronchitis in early childhood. Lancet 1974;1:1031–1034.
12. Leeder SR, Corkhill R, Irwig LM, Holland WW, Colley JRT. Influence of personal and family factors on ventilatory function of children. Br J Prev Soc Med 1976;30:219–224.
13. Pedreira FA, Guandolo VL, Feroli EJ, Melia GW, Weiss IP. Involuntary smoking and incidence of respiratory illness during the first year of life. Pediatrics 1985;75:594–597.
14. Fergusson DM, Horwood LJ, Shannon FT. Parental smoking and respiratory illness in infancy. Arch Dis Child 1980;55:358–361.
15. Fergusson DM, Horwood LJ, Shannon Ft, Taylor B. Parental smoking and lower respiratory illness in the first three years of life. J Epidemiol Community Health. 1981;35:180–184.
16. Fergusson DM, Horwood LJ. Parental smoking and respiratory illness during early childhood: A six year longitudinal study. Pediatr Pulmonol 1985;1:99–106.
17. Chen Y. Environmental tobacco smoke, low birth weight, and hospitalization for respiratory disease. Am J Respir Crit Care Med 1994;150:54–58.
18. Chen Y, Wanxian L, Shunzhang Y. Influence of passive smoking on admissions for respiratory illness in early childhood. Br Med J. 1986;293:303–306.
19. Chen Y, Li W, Yu S, Qian W. Chang-Ning epidemiological study of children's health. I. Passive smoking and children's respiratory diseases. Int J Epidemiol 1988;17:348–355.
20. DerSimonian R, Laird N. Meta-analysis in clinical trials. Contr Clin Trials 1986;7:177–188.
21. Dickersin K, Berlin J. Meta-analysis: State-of-the-science. Epidemiol Rev 1992;14:154–176.
22. Fleiss JL, Gross A. Meta-analysis in epidemiology, with special reference to studies of the association between exposure to environmental tobacco smoke and lung cancer: A critique. J Clin Epid 1991;44:127–139.
23. Forastiere F, Corbo GM, Michelozzi P, Pistelli R, Agabiti N, Brancato G, Ciappi G, Perucci CA. Effects of environment and passive smoking on the respiratory health of children. Int J Epid 1992;21:66–73.
24. Taylor B, Wadsworth J. Maternal smoking during pregnancy and lower respiratory tract illness in early life. Arch Dis Childh 1987; 62:786–791.
25. Ekwo EE, Weinberger MM, Lachenbruch PA, Huntley WH. Relationship of parental smoking and gas cooking to respiratory disease in children. Chest 1983;84:662–668.
26. Stern B, Raizenne M, Burnett R. Respiratory effects of early childhood exposure to passive smoke. Environ Int 1989;15:29–34.
27. Weitzman M, Gortmaker S, Walker DK, Sobol A. Maternal smoking and childhood asthma. Pediatrics 1990;85:505–511.
28. McConnochie KM, Roghmann KJ. Parental smoking, presence of older siblings, and family history of asthma increase risk of bronchiolitis. Am J Dis Child 1986;140:806–812.
29. Rylander E, Pershagen G, Eriksson M, Nordvall L. Parental smoking and other risk factors for wheezing bronchitis in children. Eur J Epidemiol 1993;9:517–526.
30. L'Abbe KA, Detsky AS, O'Rourke K. Meta-analysis in clinical research. Ann Intern Med 1986;107:224–233.
31. The report of the U.S. Environmental Protection Agency. Respiratory health effects of passive smoking: Lung cancer and other disorders. National Institutes of Health, National Cancer Institute, 1993.
32. Abramson MJ, Puy RM, Weiner M. Is allergen immunotherapy effective in asthma? A meta-analysis of randomized controlled trials. Am J Respir Crit Care Med 1995;151:968–974.
33. O'Connell LC. The health consequences of passive exposure to environmental tobacco smoke on infants and children. New York Medical College MPH thesis, 1990.
34. Burchefiel CM. Passive smoking, respiratory symptoms, lung function and initiation of smoking in Tecumseh, Michigan. University of Michigan, PHD thesis, 1984.
35. Abel BL. Smoking during pregnancy: A review of effects on growth and development of offspring. Hum Biol 1980;52:593–625.
36. Spektor DM, Yen BM, Lippmann M. Effect of concentration and cumulative exposure of inhaled sulfuric acid on tracheobronchial particle clearance in healthy humans. Environ Health Perspect. 1989;79:167–172.
37. Koenig JQ. Pulmonary reaction to environmental pollutants. J Allergy Clin Immunol 1987;79:833–843.
38. Anderson LJ, Parker RA, Strikas RA, Farrar JA, Gangarosa EJ, Keyserling HL, Sikes RK. Day-care center attendance and hospitalization for lower respiratory tract illness. Pediatrics 1988;82: 300–308.
39. Binder RE, Mitchell CA, Hossein HR, Bouhuys A. Importance of the indoor environment on air pollution exposure. Arch Environ Health 1976;31:277–279.

40. Brunnemann KD, Adams JD, Ho DPS, Hoffmann D. The influence of tobacco smoke on indoor atmosphere. II. Volatile and tobacco-specific nitrosamines in main- and sidestream smoke and their contribution to indoor pollution. Proceedings of the Fourth Joint Conference on Sensing of Environmental Pollutants, New Orleans, 1977. American Chemical Society, 1978:876–880.
41. Berlin JA, Laird NM, Sacks HS, Chalmers TC. A comparison of statistical methods for combining event rates from clinical trials. Stat Med 1989;8:141–151.
42. Berry G. Analysis and interpretation. In: Epidemiology of work related diseases. McDonald JC, editor. London: BMJ Publishing group, 1995:441–462.
43. Butz AM, Rosenstein BJ. Passive smoking among children with chronic respiratory disease. J Asthma. 1992; 29:265–272.
44. Comstock GW, Meyeer JF, Helsing KJ, Tockman MS. Respiratory effects of household exposure to tobacco smoke and gas cookining. Am Rev Respir Dis 1981;124:143–148.
45. Cogswell JJ, Halliday DF, Alexander JR. Respiratory infections in the first year of life in children at risk of developing atopy. Br Med J 1982;284:1011–1013.
46. Couriel JM. Passive smoking and the health of children. Thorax 1994;49:731–734.
47. Datau D, Corberand J, Enjaume C, Rochiccioli P. Inhalation passive de fumée de tabac ches l'enfant prescolaire. Etude clinique et biologoiqque. Rev Franc de Malad Resp 1978;6:549–553.
48. Eliopoulos C, Klein J, Phan MK, Knie B, Greenwald M, Chitayat D, Koren G. Hair concentrations of nicotine and cotinine in women and their newborn infants. JAMA 1994;271:621–623.
49. Ershoff DH, Mullen PD, Quinn VP. A randomized trial of a serialized self-help smoking cessation program for pregnant women in an HMO. Am J Publ Health 1989;79:182–187.
50. Greenland S. Invited commentary: A critical look at some popular meta-analytic methods. Am J Epid 1994;140:290–296.
51. Gurwitz D, Mindorff C, Levison H. Increased incidence of bronchial reactivity in children with a history of bronchiolitis. J Pediatr 98:551–555.
52. Hanrahan J, Tager IB, Segal MR, Tosteson TD, Castile RG, Van Vunakis H, Weiss ST, Speizer FE. The effect of maternal smoking during pregnancy on early infant lung function. Am Rev Respir Dis 1992;145:1129–1135.
53. Holt PG, Keast D. Environmentally induced changes in immunological function: Acute and chronic effects of inhalation of tobacco smoke and other atmospheric contaminants in man and experimental animals. Bacteriol Rev 1977;41:205–216.
54. Howell DC. Statistical methods for psychology, third edition. Duxbury Press, California, 1992.
55. Jorm L, Blyth F, Chapman S, Reynolds C. Smoking in child family day care homes: Policies and practice in New South Wales. Med J Aust 1993;159:518–522.
55. Kattan M. Long-term sequence of respiratory illness in infancy and childhood. Pediatr Clin North Am 1979;26:525–533.
56. Lee W. Experimental design and analysis. San Francisco: WH Freeman and Co., 1975.
57. Leeder SR, Corkhill R, Irwig LM, Holland WW, Colley JRT. Influence of family factors on asthma and wheezing during the first five years of life. Br J Prev Soc Med 1976;30:213–218.
58. Lewbowitz MD, Burrows B. Respiratory symptoms related to smoking habits of family adults. Chest 1976;69:48–50.
59. Lindman HR. Analysis of variance in experimental design. New York: Springer-Verlag, 1992.
60. Montomery DC. Design and analysis of experiments, third edition. New York: John Wiley & Sons, Inc., 1991.
61. National Research Council, Committee on passive smoking board on environmental studies and toxicology. Environmental tobacco smoke—Measuring exposures and assessing health effects. Washington, National Academy Press, 1986.
62. Park JK, Kim IS. Effects of family smoking on acute respiratory disease in children. Yonsei Med J 1986;27:261–269.
63. Peat JK. Passive smoking and the respiratory health of children. Mod Med Aust 1994;1:111–114.
64. Petitti DB. Meta-analysis, decision analysis, and cost analysis. Oxford: Oxford University Press, 1994.
65. Sacks HS, Berrier J, Reitman D, Ancona-Berk VA, Chalmers TC. Meta-analysis of randomized controlled trials. N Engl J Med 1987;316:450–455.
66. Samet JM, Tager EB, Speizer FE. The relationship between respiratory illness in childhood and chronic air-flow obstruction in adulthood. Am Rev Respir Dis 1983;127:508–523.
67. Schenker MB, Samet JM, Speizer FE. Risk factors for childhood respiratory disease. The effect of host factors and home environmental exposures. Am Rev Respir Dis 1983;128:1038–1043.
68. Schilling RSF, Letai AD, Hirs SL, Beck ST, Schoenberg JB. Lung function, respiratory disease, and smoking in families. Am J Epidemiol 1977;106:274–283.
69. Searle SR. Linear models. New York: John Wiley & Sons Inc., 1971.
70. Sexton M, Hebel JR. A clinical trial of change in cigarette smoking and its effect on birth weight. JAMA 1984;251:911–915.
71. Speizer FE, Ferris BG, Bishop YMM, Spengler J. Respiratory disease rates and pulmonary function in children associated with NO_2 exposure. Am Rev Respir Dis 1980;121:3–10.
72. Ware JH, Spiro A, Dockery DW, Speizer FE, Ferris BG. Passive smoking, gas cooking, and respiratory health of children living in six cities. Am Rev Respir Dis 1984;129:366–374.
73. Washburn EP, Orza MJ, Berlin JA, Nicholson WJ, Todd AC, Frumkin H, Chalmers C. Residential proximity to electricity transmission and distribution equipment and risk of childhood leukemia, childhood lymphoma, and childhood nervous system tumors: Systematic review, evaluation, and meta-analysis. Cancer Causes Control 1994;5:299–309.
74. World Health Organization. Women and tobacco. Geneva: WHO, 1992.
75. Windsor R, Cutter G, Morris J, Reese Y, Manzella B, Barlett EE, Samuelson C, Spanos D. The effectiveness of smoking cessation methods for smokers in public health maternity clinics: A randomized trial. Am J Publ Health 1985;75:1389–1392.
76. Winer BJ, Brown DR, Michels KM. Statistical principles in experimental design, third edition. New York: McGraw-Hill, Inc., 1991.
77. Winstanley M. Tobacco in Australia, facts and issues. ASH (Australia) Ltd., 1989.
78. Zmirou D, Blatier JF, Andre E, Ferley JP, Balducci F, Rossum F, Delormas P. Tabagisme passif et risque respiratoire, une synthese quantitiative de la litterature. Rev Mal Resp 1990;7:361–371.
79. Commonwealth Department of Health; Housing and Community Services. 1991 census of child care services. Canberra: Commonwealth Department of Health; Housing and Community Services, 1992.
80. Peat JK, Toelle BG, Gray EJ, Haby MM, Belousova E, Mellis CM, Woolcock AJ. Prevalence and severity of childhood asthma and allergic sensitisation in seven regions of New South Wales. Med J Aus 1995;163:22–25.