

8. ASSESSMENT OF INCREASED RISK FOR RESPIRATORY ILLNESSES IN CHILDREN FROM ENVIRONMENTAL TOBACCO SMOKE

In the preceding chapter, a review was presented of recently published studies regarding the association between respiratory illnesses in children and environmental tobacco smoke (ETS) exposure. The biological plausibility and the possible pathogenetic mechanisms involved in each group of illnesses included in the chapter also were discussed. The purpose of this chapter is to consider the weight of the evidence as a whole, to analyze in detail possible sources of systematic bias or confounding that may explain the observed associations, and to estimate the population impact of ETS-associated respiratory illnesses.

8.1. POSSIBLE ROLE OF CONFOUNDING

In the review of the available evidence indicating an association (or lack thereof) between ETS exposure and the different outcomes considered in this report, the possible role of several confounding factors was analyzed in detail (see Chapter 7). Such analysis will only be summarized here.

- Other indoor air pollutants (wood smoke, NO₂, formaldehyde, etc.) have not been found to explain the effects of ETS but may interact with it to increase the risk of both respiratory illnesses and decreased lung function in children.
- Many of the studies reviewed in this report and in those of the National Research Council (NRC, 1986) and the Surgeon General (U.S. DHHS, 1986) used either multivariate statistical methods of analysis or poststratification of the sample to control for the possible confounding effects of socioeconomic status. Others controlled for this effect by study design. It can be concluded that socioeconomic status does not explain the reported effects of ETS on children's health, although children belonging to some social groups may be at an increased risk of suffering the effects of passive smoking (see also Section 8.3).
- The effect of parental symptoms on the association between ETS and child health also has been extensively analyzed. It can be concluded that, although parents with symptoms may be more aware of their children's symptoms than are parents without symptoms, it is unlikely that this fact by itself explains the association. In fact, objective parameters of lung function, bronchial responsiveness, and atopy, which are not subject to such sources of bias, have been found to be altered in children exposed to ETS.
- The effects of passive smoking may be modified by several characteristics of the exposed child. Increased risk has been reported in premature infants and infants of low birthweight, infants who are not breast-fed, infants who are kept at home with smoking mothers and not sent to day-care centers, asthmatic children, and children who are active smokers.

- Maternal smoking during pregnancy has significant effects on fetal growth and development and may affect lung growth as well as the immunologic system. However, reports of important effects of paternal smoking on the child's health and studies in which ETS exposure was found to have effects that were independent of in utero exposure indicate that maternal smoking during pregnancy does not explain the relation between passive smoking and child health, but modifies the effects of ETS.

In summary, there are no single or combined confounding factors that can explain the observed respiratory effects of passive smoking in children.

8.2. MISCLASSIFICATION OF EXPOSED AND UNEXPOSED SUBJECTS

The importance of misclassification of exposed and unexposed children has not been addressed and will be analyzed in detail below.

Two possible sources of systematic bias related to subject misclassification are considered. The first is upward bias from the effect of active smoking in children; the second is downward bias due to misreporting and background exposure. Both have also been considered in the assessment of ETS and lung cancer in adults. Adjustment for background exposure will be similar to that presented in Chapter 6, except that data for increased incidence of some ETS-associated respiratory diseases show some evidence of thresholds that must also be taken into account.

8.2.1. Effect of Active Smoking in Children

The possibility needs to be considered that some children may be smokers themselves and that this may happen more often among children of smoking parents than among those of nonsmoking parents. This would bias the results upwards or against the null effect. This source of bias is only applicable to studies of older children; regular active smoking may occur but is rare before early adolescence. A study of third graders in Edinburgh, Scotland, by Strachan and coworkers (Strachan et al., 1989, see Section 7.4.1, for example) showed that salivary cotinine levels compatible with active smoking were found in 6 of 770 children ages 6-1/2 to 7-1/2 years, suggesting only a small potential for bias. Consideration should also be given to the fact that some of the effects described in Chapter 7 (for example, the increased risks for acute respiratory illnesses [Section 7.3] and for cough, phlegm, and wheezing [Section 7.5]) have been found to be stronger in younger children (i.e., those less likely to be active smokers) than in older children. This observed reduced effect with increasing age may be in part due to an age-related increase in misclassification of exposed subjects as "unexposed" (see below), but it is clear that these specific effects of ETS *do not increase with age*, as would be expected if active smoking biased the results of studies of ETS effects in older children. It can thus be concluded that the association between respiratory health in children and ETS is not attributable to active smoking by some children. It has been suggested that active and passive smoking may interact to increase the effects of either exposure separately (Lebowitz and Holberg, 1988). This interaction is biologically

plausible, because it is likely that active smoking may be more harmful in children whose lungs have been previously affected by ETS (see Section 7.1).

8.2.2. Misreporting and Background Exposure

Various investigators have measured cotinine levels in body fluids in infants and children and correlated the results with parental reports of ETS exposure. Coultas and coworkers (1987) reported that 37% of children under 5 years of age whose parents were nonsmokers had a salivary cotinine level greater than 0, compared with 32% of children ages 6 to 12 and with 35% of children ages 13 to 17. These authors did not ask parents to report possible sources of ETS exposure for their children other than their own tobacco consumption. Strachan and coworkers' study in 6-1/2- to 7-1/2-year-old children in Scotland (Strachan et al., 1989) showed that 73% of children from households with no smokers had detectable concentrations of cotinine in saliva, whereas only 1 in 365 children from households with one or more smokers had no detectable salivary cotinine. The assay used by Strachan and coworkers was 10 times more sensitive than that used by Coultas and coworkers, and this may explain the larger number of subjects with detectable levels in the former study when compared with the latter.

Greenberg and coworkers (1984) studied cotinine levels in 32 infants in North Carolina with reported exposure to tobacco smoke within the previous 24 hours and in 19 unexposed infants. All subjects were under 10 months old. Urine samples of all exposed infants contained cotinine, whereas all unexposed infants except 2 (11%) had undetectable urine cotinine or levels below those of exposed infants with the lowest levels of urine cotinine. This same group of researchers reported results for a larger sample (433 infants at a mean age of 18 days) of the same population (Greenberg et al., 1989). They found that, of 157 infants who reportedly lived in nonsmoking households and were also not in contact with smokers the previous week, 37 infants (24%) had cotinine in their urine. They concluded that these infants had contact with tobacco smoke during the previous week and that this contact was unknown to or was not reported by their mothers.

Greenberg and coworkers (1991) followed 152 of the 433 infants originally enrolled and reassessed exposure to ETS (through maternal interviews) and urine cotinine levels when the child was 12.3 ± 0.6 months old. They found a significant increase in the prevalence of tobacco smoke absorption, indicated by excretion of cotinine, during the first year of life (from 53% at a mean age of 3 weeks to 77%). The interviews showed that this was mainly due to an increased exposure to nonhousehold sources of smoke (from 14% to 36%). The proportion of infants who reportedly had no contact with smokers but had cotinine in their urine increased from 24% at 3 weeks to 49% at 1 year of age.

These results indicate that studies relying exclusively on parental questionnaires to ascertain ETS exposure in children may misclassify many exposed subjects as nonexposed. Moreover, the degree of misclassification may increase with the child's age.

The possible consequences of this misclassification of exposure need to be discussed in detail. Nondifferential misclassification (i.e., exposure classification that is incorrect in equal proportions of diseased and

nondiseased subjects) biases the observed results toward a conclusion of no effect (Rothman, 1986). The effect of differential misclassification depends on the direction in which misclassification occurs. If true ETS exposure is preferentially reported by parents of diseased subjects (i.e., there is reporting bias), an excess of disease prevalence would be found among exposed subjects when compared with unexposed subjects that is unrelated to any biological effect of ETS. The evidence available clearly indicates that this is a very unlikely explanation for the reported misclassification of ETS exposure in infants and children. In fact, reporting bias cannot explain the substantial increase in "underreporting" of exposure with age. The logical explanation is provided by the finding that exposure to nonhousehold smokers increases significantly with age and parallels the increase in the proportion of subjects who have cotinine in their urine (Greenberg et al., 1991). There is no reason to believe that exposure to smokers may occur preferentially among diseased children, and the contrary may be more reasonable; the increased awareness of the ill effects of ETS inhalation may induce parents to limit contact between their diseased children and nonhousehold smokers. Thus, the net effect of misclassification of exposure, both nondifferential and differential, should be a systematic downward bias or bias toward observing no effect. A correction for the nondifferential misclassification bias of background exposure is made in Section 8.3.

8.3. ADJUSTMENT FOR BACKGROUND EXPOSURE

An important conclusion of the previous discussion is that studies based on parental questionnaires may underestimate the health risk from ETS in children due to underreporting of ETS exposure. The NRC (1986) report on passive smoking adopted the use of cotinine measures to correct for misreporting of ETS exposure for lung cancer effects, and this approach was adapted for use in Chapter 6 of this report. It will also be employed here, with the cotinine ratios, however, based on exposure data in children rather than in adults. The method is based on several assumptions: (1) cotinine concentrations in body fluids of nonsmokers are linearly related to ETS exposure, (2) the excess risk of respiratory illness in subjects exposed to ETS is linearly related to the dose of ETS absorbed, (3) the relationship between ambient and absorbed ETS is linear, and (4) one cotinine determination may adequately represent average childhood exposure to ETS.

As support for assumptions 1 and 2, three recent studies have used body cotinine levels as biomarkers for ETS exposure in children. All three have found significant associations between cotinine levels and respiratory effects in children. Etzel et al. (1992) found a significant relationship between serum cotinine levels and otitis media with effusion for children who attended a day-care facility during the first 3 years of life. Ehrlich et al. (1992), in a study that used questionnaires on maternal caregiver smoking as well as urinary cotinine levels to assess ETS exposure, found that by either measure ETS exposure was significantly associated with both acute and nonacute asthma in children. Furthermore, urinary cotinine levels in asthmatic children showed a highly significant correlation with maternal caregiver smoking status. In the third study, Reese et al. (1992) found urinary cotinine levels significantly ($p < 0.02$) elevated in children admitted to the hospital with bronchiolitis compared with a group of similarly aged children admitted with nonrespiratory illnesses. There was also a highly significant correlation ($p <$

0.0005) between urinary cotinine levels and maternal smoking as determined by questionnaire. Thus, the evidence suggests that questionnaire ascertainment of childhood exposure to ETS and cotinine biomarkers in children are highly correlated with each other and that both correlate with childhood diseases. This information is used to develop the risk assessment models below.

While considerable evidence exists for assumptions 1 through 3 (see also Chapter 3), there is some evidence that assumption 4 may not be entirely warranted, at least for older children. Coultas and coworkers (1990b), in a small study of 9 children from 10 homes with at least 1 smoker, reported that there is considerable variability in cotinine levels in body fluids within individuals exposed to ETS when such levels are repeatedly measured on different days. However, Henderson et al. (1989), doing repeated urinary cotinine measures in preschool children, found stable levels over 4 weeks. Thus, while the method of adjustment is based on group mean body cotinine levels, which apparently reflect household ETS levels well, the intraindividual variability, at least in older children, may subject these means to some error.

Application of the method proposed by the NRC requires some knowledge of Z , the ratio between the operative mean dose level in the "exposed" group, d_E , and the mean dose level in the "unexposed" group, d_N . $RR(d_E)$, the relative risk for the group identified as "exposed" compared with the group identified as "unexposed," is thus given by

$$RR(d_E) = (1+Z*\beta d_N)/(1+\beta d_N) \quad (8-1)$$

where β is the amount of increase per unit dose and $Z > RR(d_E) > 1$. (The "unexposed" group actually contains those with background exposure plus those truly unexposed.)

Several studies are available that could be used for the purpose of estimating Z . Jarvis and coworkers (1985) studied 569 nonsmoking schoolchildren ages 11 to 16 in Great Britain. The investigators reported that, when compared with salivary cotinine levels in children of nonsmoking parents ($N = 269$), mean levels of salivary cotinine were 3.0 times as high in children whose father smoked ($N = 96$), 4.4 times as high in children whose mother smoked, and 7.7 times as high in children whose parents were both smokers. Pattishall and coworkers (1985) reported that children from homes with smokers ($N = 20$) had 4.1 times as high mean levels of serum cotinine as children from nonsmoking families. Black children in the same study, however, had lower values of Z (2.8) than did white children. Coultas and coworkers (1987) found that, among 600 U.S. children up to age 17 years, mean salivary cotinine levels were between 1.3 and 2.6 times as high among subjects exposed to one cigarette smoker at home as among unexposed subjects, and between 2.9 and 3.5 times as high among subjects exposed to two or more smokers at home as among subjects not exposed to cigarette smokers at home. Strachan and coworkers (1989) reported separate results for 6-1/2- to 7-1/2-year-old Scottish children belonging to families living in their own homes and for those belonging to families living in rented homes. In the former, geometric mean salivary cotinine was 6 times as high among subjects exposed to one cigarette smoker at home as among unexposed subjects and 16 to 17 times as high among subjects

exposed to two or more smokers at home as among unexposed subjects. For children belonging to families living in rented homes, the same ratios were 3 to 5.5 times and 4 to 7 times, respectively.

While these studies show consistent relationships between mean body cotinine levels in children and home smoker occupancy, there is also a wide variability in the estimated Z ratios, ranging from 1+ to 17. These different estimates may have very important effects on the background exposure adjustment and, thus, on the calculation of adjusted relative risks for different studies (see also Chapter 6). For example, for a study in which the observed relative risk (RR) is 2.0 but for which the Z ratio is 3, equation 8-1 can be solved for β_{d_N} , which is the estimated increase in relative risk for the group called "unexposed" but who in fact have been exposed to some recent ETS. Solving, $\beta_{d_N} = 1$. Thus, the adjusted RR for the group identified as "unexposed" would be 2, and the adjusted RR for an "exposed" group compared with a truly unexposed group would be $1 + (3*1) = 4$, i.e., twice the observed risk. For a similar example (observed RR = 2) but with Z = 5, $\beta_{d_N} = 0.3$, the RR for a group identified as "unexposed" in this case would be 1.3, and the adjusted RR for an "exposed" to a truly unexposed group would be 2.67. Finally, if the observed RR is still 2 but Z = 17, $\beta_{d_N} = 0.07$, RR for "unexposed" would be 1.07 and the adjusted RR for exposed children would be 2.13. These results are shown in Table 8-1.

These calculations show that when use of parental questionnaires significantly underestimates their children's exposures to other sources of ETS (other than via the parental ETS) and values of Z are lower (as found in black children by Pattishall and coworkers [1985], and in children of lower socioeconomic status by Strachan and coworkers [1989]), the "true" RR of children exposed to ETS may be considerably underestimated. But perhaps the most important conclusion that may be derived from the above analysis is that exposure to ETS from sources other than smoking parents may be high enough to constitute a significant risk for their health. This may be particularly consequential for children of lower socioeconomic levels, whose nutritional status, crowded conditions at home, and opportunity for contact with biological agents of disease make them a part of the population that is particularly susceptible to respiratory illnesses during infancy and childhood. Available data show that ETS exposure via nonhousehold members in these children, as measured by cotinine levels in body fluids, may be as much as one-third that of children exposed to one smoking parent (Z = 3). In the example presented above (observed RR = 2), the estimate of the adjusted relative risk is 4 for children of smoking parents to the truly unexposed children. However, using the same assumptions, children of *nonsmoking parents* who are exposed to ETS (at background levels found in some of the studies) would have twice as high a risk of developing the illness under study as children truly unexposed to ETS.

A cautionary note about the model is appropriate. Table 8-1 shows that, for observed RR = 2 and Z = 3, the adjusted relative risk is 4. However, as the observed RR and Z get closer together, the behavior of the model becomes erratic. This is shown in Table 8-2. In fact, the model (equation 8-1) becomes undefined if Z is less than or equal to the observed RR, and it reaches some stability only as Z becomes at least 30% to 50% greater than the RR.

Table 8-1. Adjusted relative risks for "exposed children." Adjusted or background exposure based on body cotinine ratios between "exposed" and "unexposed" and equation 8-1

		<u>Z Ratio of body cotinine levels ("exposed"/"unexposed")</u>							
		1.50	2.00	3.00	5.00	7.00	10.00	13.00	17.00
Observed	1.0	1	1	1	1	1	1	1	1
	1.50	-	3.00	2.00	1.71	1.64	1.59	1.57	1.55
Relative	1.75	-	7.00	2.80	2.15	2.00	1.91	1.87	1.84
	2.00	-	-	4.00	2.67	2.40	2.25	2.18	2.13
Risks	2.50	-	-	10.00	4.00	3.33	3.00	2.86	2.76
	3.00	-	-	-	6.00	4.50	3.86	3.60	3.43
(RR)									

Table 8-2. Behavior variations in adjusted relative risks from equation 8-1 when the observed relative risks and Z ratios are close together

		<u>Z ratio</u>							
		1.50	1.75	2.00	2.25	2.50	2.75	3.00	10.00
Observed	1.50	-	4.50	3.00	2.50	2.25	2.10	2.00	1.59
	1.75	-3.5	-	7.00	4.38	3.50	3.06	2.80	1.91
Relative	2.00	-2.0	-6.00	-	10.00	6.00	4.67	4.00	2.25
	2.25	-1.5	-3.38	-9.00	-	13.50	7.88	6.00	2.62
Risks	2.50	-1.25	-2.50	-5.00	-12.50	-	17.50	10.00	3.00
(RR)									

Fortunately, the estimates of Z presented above are appreciably greater than the observed relative risk estimates seen in Chapter 7, and in the observed range of both RR and Z, the model yields relatively stable estimates of the adjusted RR. Furthermore, as discussed in Chapter 6, the values of RR and Z are expected to be correlated for each study, i.e., the greater the Z ratio between exposed and unexposed groups in each study, the greater should be the observed RR and the less the effect of the (equation 8-1) adjustment.

If the above model is correct, then exposure of children to ETS other than at home (parental smoking) may be an important risk factor for respiratory illness in childhood. On the other hand, it is also possible that for at least some respiratory illnesses, outside exposure to ETS has relatively little effect, either because outside exposures in younger children tend to be less than those of older children or because there may be a threshold of exposure below which certain respiratory effects may not be expected to occur. For this latter case, equation 8-1 is not an appropriate model, and the observed relative risk would be taken to be the true risk. Both models are addressed in the sections that follow.

8.4. ASSESSMENT OF RISK

Neither the NRC report (1986) nor the Surgeon General's report (U.S. DHHS, 1986) attempted to assess the population or public health impact of the increased risk of respiratory disorders in children attributable to ETS exposure. In this section, estimates will be derived for the number of ETS-attributable lower respiratory tract infections in infants and for the induction and exacerbation of childhood asthma. Quantifying the public health impact of other conditions, such as reduced lung function, coughing, wheezing, and middle ear effusion, is difficult, either because of the lack of overt symptoms or because some necessary U.S. population health statistics are not available. Estimates of sudden infant death syndrome (SIDS) occurrences attributable to ETS will not be made but will be discussed in Section 8.4.3.

For the following quantitative analyses, estimates will be developed in terms of ranges. The ranges are derived by the use of both threshold and nonthreshold (equation 8-1) models, different estimates for population incidence and prevalence, and estimated values of Z and RR from studies reviewed above. Various differences in design, disease definition, and conduct among these studies make them less adaptable to meta-analysis techniques than were the lung cancer studies. To the extent that a less rigorous statistical analysis is attempted here, the ranges should reflect that uncertainty.

8.4.1. Asthma

From the analysis of studies regarding risk for asthma and ETS exposure, it was concluded that passive smoking increases both the number and severity of episodes in asthmatic children. It was further concluded that ETS is a risk factor for new cases among previously asymptomatic children, since the evidence is suggestive, but not conclusive, of a causal association (see Section 7.6). Relative risks for asthma ranged from 1.0 to 2.5 in the studies analyzed, but methodologies differed considerably among studies, and effects were often found only in children of mothers who smoke heavily. Of the four large studies, totaling more than 9,000 children (Burchfield et al., 1986; Sherman et al., 1990;

Weitzman et al., 1990; Martinez et al., 1991b), three showed statistically significant risk estimates ranging from 1.7 to 2.5, with the two largest ratios, 2.5 (Martinez et al., 1991b) and 2.1 (Weitzman et al., 1990), coming from comparisons using children of heavily smoking mothers (≥ 10 cig./day) as the exposed group. The third study (Burchfield et al., 1986) had OR = 1.7 for males with two smoking parents, but results were not significant either for girls or for children with one parental smoker. The fourth study (Sherman et al., 1990) (770 children) did not find an effect, but made no effort to assess the effect of heavy smoking by parents, nor was there control for socioeconomic status. Thus, assigning a range of 1.75 to 2.25 for the estimated relative risk of developing asthma for children of mothers who smoke 10 or more cigarettes per day appears reasonable and is within the ranges of observed risk.

The above results suggest two possible scenarios. One scenario is that relatively heavy exposure to ETS is needed to bring on asthma, i.e., there is a threshold of exposure below which effects will not occur. Alternatively, lesser exposures may merely induce fewer effects, not detectable statistically with these study designs. The choice of scenario does not affect the observed relative risk but will affect whether or not an adjustment for background exposure (Z ratio) is appropriate. Under the first (threshold) scenario, the estimates of RR = 1.75 to 2.25 need no adjustment; under the alternative (nonthreshold) scenario, equation 8-1 applies.

Considering the nonthreshold model first, from the discussion in Section 8.3, it can be assumed that values of 3 to 10 may be a reasonable range for estimates of Z (i.e., the ratio of body cotinine levels in children whose mothers smoke heavily to those of children whose mothers do not smoke). Lower values of Z would yield significantly larger estimates of asthma cases attributable to ETS. Based on the above estimates for a range of Z and RR and use of the nonthreshold model, the estimated range of adjusted relative risks for children of mothers who smoke 10 or more cigarettes per day would be approximately 1.91 to 6.00 (see Table 8-3). Transforming relative risks to

Table 8-3. Range of estimates of adjusted relative risk and attributable risk for asthma induction in children based on both threshold and nonthreshold models, and different values for Z.

	Threshold model ¹		Nonthreshold model ²				
Observed relative risk	1.75	2.25	1.75	2.25	1.75	2.00	2.25
Z = Cotinine ratio (exposed/unexposed)	-	-	10	10	3	3	3
Adjusted relative risk ³	-	-	1.91 ⁴	2.62 ⁴	2.80 ⁵	4.00 ⁵	6.00 ⁵
AR _E ⁶	0.43	0.56	0.48	0.62	0.64	0.75	0.83
AR _T ⁷ (P _T ⁸ =0.17)	0.07	0.09	-	-	-	-	-
AR _T (P _T ⁹ =0.26)	-	-	0.12	0.16	0.17	0.20	0.22
ETS-attributable population impact ¹⁰	8,000 to 20,000	10,000 to 26,000	13,000 to 34,000	18,000 to 45,000	19,000 to 46,000	22,000 to 54,000	24,000 to 60,000

¹Threshold model assumes that heavy ETS exposure (i.e., mothers smoking ≥ 10 cig./day) is required to induce new cases.

²Nonthreshold model assumes that all ETS exposure can produce some new cases of asthma.

³Equation 8-1 for the nonthreshold model; no adjustment for the threshold model.

⁴Ratio of mean body cotinine levels: Z = 10.

⁵Ratio of mean body cotinine levels: Z = 3.

⁶Attributable risk fraction for the exposed population.

⁷Attributable risk fraction for the total (mixed) population.

⁸Proportion of women of reproductive age who smoke at least 10 cigarettes per day (0.26×0.65).

⁹Proportion of women of reproductive age who smoke cigarettes.

¹⁰Range based on 2 million to 5 million asthmatic children under 18 years old in the United States, and assumes that the number of ETS-attributable new cases at each age is constant.

attributable risks (Rothman, 1986), 48% to 83% of all cases of asthma among children of mothers who smoke 10 or more cigarettes per day may be attributable to passive smoking based on

$$AR_E = 100 * (1 - [1/RR]) \quad (8-2)$$

where AR_E is the attributable risk (%) for the exposed population.

Under the assumptions of the threshold model, $RR = 1.75$ to 2.25 for children of heavily smoking mothers, and the $AR_E = 43\%$ to 56% (see Table 8-3); for children of light-smoking mothers, $RR = 1$ and the $AR_E = 0$.

To calculate the percentage of all cases occurring in a mixed population of exposed and unexposed individuals that is attributable to exposure (AR_T), knowledge of the prevalence of mothers smoking 10 or more cigarettes per day is needed because

$$AR_T = AR_E * P_1 \quad (8-3)$$

where P_1 is the proportion of cases that is exposed (Rothman, 1986). It has been reported that approximately 26% of the population of women of childbearing age smoked in the United States in 1988 (CDC, 1991b) and in 1990 (CDC, 1992b). For the number of cigarettes smoked, Weitzman and coworkers (1990), using the 1981 National Health Information Survey (NHIS), found that approximately 50% of smoking mothers of children ages 0 to 5 years smoke 10 or more cigarettes per day. The 1990 NHIS reports that 78% of smoking women ages 18 to 44 smoke at least 10 cigarettes per day (data courtesy of Dr. Gary Giovino, CDC). We have used an average of 65% to derive the estimates in Table 8-3. Based on these figures and the threshold model, it can thus be estimated that approximately 7% to 9% of all cases of asthma may be attributable to exposure to ETS from mothers who smoke 10 or more cigarettes per day. Estimates of the prevalence of asthma among U.S. children less than age 18 vary from 5% to 10% (Clark and Godfrey, 1983) to 3% to 8% (R. Evans et al., 1987), depending on disease definition. This latter paper uses the data from the 1979-1981 NHIS and derives a population asthma prevalence of 2 million to 5 million. A more recent estimate from the 1989 NHIS is 3.9 million (U.S. DHHS, 1990b). Use of these population prevalence figures and the threshold model provides a range of 8,000 to 26,000 as the annual number of new cases of childhood asthma attributable to mothers who smoke 10 or more cigarettes per day. The confidence in this estimate is medium and is dependent on the conclusion that ETS is a risk factor for asthma induction.

If the nonthreshold model applies, use of the same prevalence figures leads to a range of 13,000 to 60,000 new cases per year attributable to all ETS exposures (Table 8-3).

While the range of 8,000 to 60,000 is plausible, the existing data are more supportive of the threshold model, which assumes that rather heavy exposures to ETS are required to induce asthma in previously asymptomatic children (Section 7.6.2). Thus, the range of 8,000 to 26,000 will be adopted as the more probable range of new cases among children per year attributable to ETS exposure.

In view of the increased number and severity of asthmatic episodes also caused by ETS, the public health impact of ETS on asthmatic children is considerably greater than the range of estimates for new cases presented above. Shephard (1992), after reviewing several studies, concludes that ETS exposure (from any source) exacerbates preexisting asthma in approximately 20% of patients. If this figure is correct, up to 1 million asthmatic children could be affected. Also, in an earlier study, O'Connell and Logan (1974) found that parental smoking aggravated clinical symptoms of 67% of 265 asthmatic children in the Midwest versus 16% of 137 controls ($p < 0.0001$) and that 10% of 400 asthmatic patients (of both smoking and nonsmoking parents) considered tobacco smoke a major aggravating factor. D. Evans and coworkers (1987) found that passive smoking by asthmatic children in New York City (via presence of smokers in the household) was associated with a mean annual increase of 1.34 emergency room visits per year for asthmatic symptoms, an increase of 63% over asthmatic children from nonsmoking households. Ehrlich et al. (1992), in a study not reviewed by Shephard (1992), found that asthmatics with clinically significant symptoms had both higher cotinine levels than controls ($p = 0.04$) and an OR = 2.0 ($p = 0.03$) for maternal caregivers who smoke. Using this estimate of 2.0 with equation 8-1 and a $Z = 3$ also leads to an attributable risk fraction, AR_T , of 20% (equation 8-3). Multiplying this 20% by the 2 million to 5 million asthmatic children in the United States yields estimates of 400,000 to 1,000,000 whose condition is aggravated by exposure to ETS. Thus, exposure to ETS in general and especially to parental ETS adversely affects hundreds of thousands of asthmatic children.

8.4.2. Lower Respiratory Illness

From the assessment of available data (see Section 7.3), it was concluded that exposure of infants and young children to ETS causes an increased incidence of lower respiratory illness (LRI). An examination of the data in the referenced studies of both Tables 7-1 and 7-2 leads to the conclusion that the observed risk of having LRIs is approximately 1.5 to 2.0 times as high in young children whose mothers smoke as in those whose mothers do not smoke and that the risk is probably higher in infants than in toddlers.

This estimate is also consistent with that of the NRC (1986), which estimated a relative risk of up to 2 for infants who have one or more parents who smoke. The more recent evidence reviewed here strongly suggests that the increased risk due to ETS exposure lasts for at least the first 18 months and decreases after that. Based on this evidence, this chapter estimates a relative risk range of 1.5 to 2.0 for infants and children up to 18 months old who have smoking mothers. It will assume that the increased risk is zero after 18 months.

Based on these findings, and following equation 8-1 with a range of $Z = 3$ to 10 and $RR = 1.5$ to 2.0, the adjusted relative risk range becomes 1.6 to 4.0, and AR_E takes the range 38% to 75%. As in the previous section, for equation 8-3, the mixed population attributable risk AR_T takes the range 10% to 20%, again based on 1988 and 1990 estimates of approximately 26% women of childbearing age who smoked (CDC, 1991b, 1992b). Because the estimated mean number of cigarettes smoked by these women is approximately 17 to 20 per day (CDC 1991b,

1992b), it is reasonable to assume that most children of smoking mothers will be exposed. Therefore, the proportion of cases exposed, P_i , is estimated to be 0.26.

It has recently been shown that the incidence of LRIs early in life is approximately 30% (Wright et al., 1991). When the analysis is limited to the first 18 months of life, the population at risk is approximately 5.5 million children. A slight modification of the same algorithms described above yields 150,000 to 300,000 cases of LRIs annually in children under 18 months old attributable to exposure to ETS generated mostly by smoking mothers. For $RR = 1.5$ and $Z = 10$, the attributable risk fraction for the exposed population, AR_E , is 0.38, and the attributable risk fraction for the total population, AR , is 0.10. Assuming 3.7 million children less than 1 year old and a 30% incidence of LRI, the ETS-attributable population risk is 110,000. In order to get the incidence rate for the 1.8 million children aged 12 to 18 months, also with 30% incidence, the 110,000 must be subtracted from the 540,000 before multiplying by 0.10. The product of 43,000 is then added to 110,000 to determine the total annual incidence of 150,000 LRIs. For $RR = 2.0$ and $Z = 3$ the total annual incidence is about 300,000. Approximately 5% of these LRIs require admission to a hospital (Wright et al., 1989); therefore, it is estimated that 7,500 to 15,000 hospitalizations yearly for LRIs may be attributable to ETS exposure.

While these estimates may appear large, three factors suggest that they are on the low side. First, although these estimates are calculated only for children less than 18 months old, Section 7.3 presents evidence that these ETS-attributed increased risks extend at a decreasing rate up to 3 years of age. Second, no estimates have been calculated for exposure in a smoking father-nonsmoking mother household. Third, these numbers do not take into account the fact that many infants and young children have recurrent LRIs, and therefore, more than one episode of such illnesses may be attributable to ETS in each exposed child.

8.4.3. Sudden Infant Death Syndrome

Because this report concludes that there is an association between maternal smoking and SIDS but is unable to determine the contribution that ETS makes to that association (see Section 7.7), no estimate of ETS-attributable SIDS deaths will be calculated. The Centers for Disease Control (CDC, 1991a) provides an estimate of 702 SIDS deaths attributable to maternal smoking, based on a relative risk of 1.5 for infants of actively smoking mothers. While this report concurs with the numbers and the methodology used to determine that estimate, it is unable to apportion the in utero, lactation, and ETS exposure components of the risk.

8.5. CONCLUSIONS

This chapter has attempted to estimate the impact on the U.S. population of ETS exposure on childhood asthma and lower respiratory tract infections in young children. For new cases of asthma in previously asymptomatic children under 18 years of age, we estimate that 8,000 to 26,000 is a probable range of new cases per year that are

attributable to ETS exposure from mothers who smoke at least 10 cigarettes per day. The confidence in this range is medium and is dependent on the conclusion that ETS is a risk factor for asthma induction.

While the data are most supportive of a situation in which heavy exposures to ETS are required to induce new cases of asthma, two other scenarios would lead to larger estimates. The first is that even in the absence of smoking mothers, a child could receive heavy ETS exposure from other sources. The second is that lesser ETS exposures induce fewer numbers of new cases, and the increase is not statistically detectable. Under this latter (nonthreshold) scenario, the range of new cases of asthma annually attributable to ETS exposure is 13,000 to 60,000.

This report concludes that, in addition to inducing new cases of asthma, ETS exposure increases the number and severity of episodes among this country's 2 million to 5 million asthmatic children. This chapter considers exposure to parental smoking to be a major aggravating factor to approximately 10%, or 200,000, asthmatic children. Estimates of the number of asthmatics whose condition is aggravated to some degree by ETS exposure are very approximate but could run well over 1 million.

This chapter also estimates that 150,000 to 300,000 cases annually of lower respiratory tract infections in children up to 18 months old are attributable to ETS exposure, most of which comes from smoking parents (mostly mothers). These ETS-attributable cases are estimated to result in 7,500 to 15,000 hospitalizations annually. Confidence in these estimates is high based on the conclusion of a causal association and the strong validity of parental smoking as a surrogate of temporally relevant ETS exposure in infants and young children. Additional cases and hospitalizations are expected to occur in children up to 3 years old in decreasing numbers, but this report makes no further quantitative estimates.

Infants' exposure to ETS may also be responsible for a portion of the more than 700 deaths from SIDS attributable to maternal smoking by the CDC (1991a), but this report is unable to determine whether and to what extent these deaths can be attributed specifically to ETS exposure.

The estimates of population impact presented above are given in ranges and approximate values to reflect the uncertainty of extrapolating from individual studies to the population. As with the lung cancer population impact assessment (Chapter 6), these extrapolations are all based on human studies conducted at true environmental levels. Therefore, they suffer from none of the uncertainties associated with either animal-to-human or high-to-low exposure extrapolations.

In addition to the estimates presented above, ETS exposure in children also leads to reduced lung function, increased symptoms of respiratory irritation, and increased prevalence of middle ear effusion, but this report does not provide estimates of the population impact of ETS exposure for these conditions.