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Effects of environmental tobacco smoke on the respiratory health of adults

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In this paper, current knowledge on the respiratory effects of environmental tobacco smoke among adults is synthesized, and the biological basis and methodological issues are discussed. The Medline database was searched from 1966 through October 2000. All of the related respiratory effects have been linked to both home and workplace exposures. Some evidence of a dose-response relation has also been detected for all respiratory conditions. The strongest evidence of a causal relation exists for chronic respiratory symptoms. Harmful effects on lung function have also been detected, mainly in countries and occupations with high exposure levels. There is limited evidence indicating an increased risk of its causing asthma and chronic obstructive pulmonary disease, and also for poor control of established asthma. More longitudinal studies with careful assessment of exposure are needed for better risk estimates. Despite these challenges for the future, the combination of toxicologic evidence, abundant evidence on respiratory effects among children, and the studies reviewed in this paper point to an urgent need for measures to prevent exposure to environmental tobacco smoke among adults.

Key terms asthma, chronic obstructive pulmonary disease, lung function, respiratory infections, respiratory symptoms, tobacco smoke pollution.

The first report of the consequences of exposure to environmental tobacco smoke at the workplace in relation to the lung function of adults was reported in 1980 (1). Since then, the evidence has accumulated gradually for adverse noncarcinogenic respiratory effects of exposure to environmental tobacco smoke in adulthood. The aims of this review are to synthesize current knowledge on the respiratory effects of environmental tobacco smoke among adults and to discuss the related biological basis and methodological issues. Another article in this journal synthesizes the evidence on the respiratory effects of environmental tobacco smoke among children (2). A Medline database search was carried out from 1966 through October 2000 with the Mesh-terms "Tobacco smoke pollution and exp. Respiratory track diseases". Additional material was collected from the reference lists of articles and from personal knowledge of current research.

Earlier reviews suggested that environmental tobacco smoke makes an important contribution to the total burden of environmental insults on the respiratory system, but they considered the evidence on the causality of the relations as insufficient, except for lung cancer (3–8). More recent reviews, including additional studies, have concluded that there is strong evidence of causal relations between exposure to environmental tobacco smoke and respiratory diseases in adults, especially in the case of respiratory symptoms (9, 10). Assessing exposure to environmental tobacco smoke during adulthood is more complex than such assessment in childhood, since adults are exposed from multiple sources in addition to the home environment (eg, the workplace and public places). The exposure profile may also vary considerably during different periods of adult life (11, 12). For many diseases it is important to consider the role of earlier exposures in addition to current exposure. These difficulties may have contributed to the delay in the interest in studying noncancer respiratory effects among adults.

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Biological basis for nonmalignant respiratory effects of environmental tobacco smoke

Active smoking is a well-established cause of chronic respiratory symptoms, lung function decline, and chronic obstructive pulmonary disease (COPD) (13). Its role in determining susceptibility to respiratory infections, such as pneumonia, is also strongly supported (14). The chemical similarities between mainstream and sidestream smoke support the biological plausibility of the role of environmental tobacco smoke in causing respiratory diseases. The noncarcinogenic mechanisms of exposure to environmental tobacco smoke have been studied less than the carcinogenic effects. In this section, we discuss what has been shown or speculated to be potential mechanisms leading to nonmalignant respiratory diseases in subjects exposed to environmental tobacco smoke.

Microbiological organisms are the direct causes of infectious diseases, but exposure to environmental tobacco smoke seems to be an important determinant of susceptibility to such organisms. This susceptibility has been demonstrated very clearly for children, whereas infections have been studied less among adults (2, 9, 15). The few adult studies have linked exposure to environmental tobacco smoke to severe infections, such as pneumonia and meningitis. There may be several mechanisms underlying an increased susceptibility to infections. For example, tobacco smoke impairs host defense mechanisms by weakening immunologic responses and mucociliary clearance (13, 16, 17), and it has been shown to enhance bacterial adherence and to disrupt respiratory epithelium (18, 19).

Tobacco smoke is known to contain several irritative compounds, such as ammonia, sulfur dioxide, nitrogen oxides, acrolein, and formaldehyde (5, 20). It is biologically plausible that exposure to these substances may cause inflammatory or irritative reactions in the airways and therefore lead to respiratory symptoms and lung function impairment. Tobacco smoke has been demonstrated to induce inflammatory reactions in the airways and lung parenchyma of active smokers (21–23), and the biological effects of environmental tobacco smoke are likely to be similar to those of mainstream smoke. In addition, the impairment of host defense mechanisms and the mucociliary clearance of airways increase vulnerability to infections, and repeated respiratory infections may then predispose a person to the development of COPD (13, 17). It is also likely that lung function deficit in newborns and children attributable to exposure to environmental tobacco smoke increases the vulnerability of the lungs to additional insults later in life (2, 9).

There are several biologically plausible mechanisms through which environmental tobacco smoke could cause and exacerbate asthma. It has been shown to increase the susceptibility to respiratory infections in childhood, and such infections have been associated with both early-onset asthma and exacerbations of underlying disease (24, 25). A more direct mechanism is also plausible, since tobacco smoke contains several irritant substances that could cause an inflammatory response in the airways, as has been shown in the case of irritant-induced occupational asthma (26). The effect of environmental tobacco smoke on asthma seems to occur via irritative rather than allergic mechanisms, and skin test positivity to tobacco is rare (6, 7, 27). Tobacco smoke may also increase epithelial permeability to environmental allergens and thus enhance allergic reactions to other inhalable allergens (28). In line with this hypothesized mechanism, passive smoking has been observed to increase total immunoglobulin E (IgE) among children and adults (29–31).

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Respiratory symptoms

Acute symptoms. The role of environmental tobacco smoke in producing acute irritative symptoms of the eyes, nose, throat, and lower airways is well established (3, 6, 7). Some experimental studies have shown significant increases in objective measurements related to symptoms, such as eye blink rate and nasal airway resistance, in response to exposure to environmental tobacco smoke (32, 33). Atopic subjects appear to be more sensitive to environmental tobacco smoke than nonatopics (7, 33, 34).

Chronic respiratory symptoms. The role of exposure to environmental tobacco smoke in the development of chronic respiratory symptoms in adults has been addressed in 12 cross-sectional (35–46) and 2 longitudinal studies (47, 48). Tables 1 and 2 summarize these studies. In addition, a study on the effects of exposure cessation on respiratory symptoms in bartenders has been reported (49). Most of the studies assessed household exposure, three studies assessed workplace exposure, and four studies assessed exposure in both of these environments. Two additional studies assessed the effects on a composite symptom score (50) and symptom severity (51).

The results of the studies are somewhat inconsistent. This inconsistency may be explained partly by methodological differences, for example, the exposure assessment approach used. In summary, the studies with a stronger power, either due to a large sample size or

Table 1. Cross-sectional studies on environmental tobacco smoke and chronic respiratory symptoms among adults. (95% CI = 95% confidence interval, OR = odds ratio, PR = prevalence ratio, RR = risk ratio)

Study	Study population, age	Exposure assessment	Measure of effect	Exposure category compared to no exposure	Results
Lebowitz & Burrows 1976, United States (35)	1258 men and women, never smokers, ≥15 years	Household member's report of current smoking	PR	Current exposure	PR 0.66 [a], 1.0 [a], & 1.02 [a] for cough, phlegm & wheezing, respectively
Schilling et al 1977, United States (36)	178 men, 212 women, nonsmokers	Spouse's report of current smoking	PR	Spouse smoking	Not significant for cough, phlegm or wheezing
Comstock et al 1981, United States (37)	426 men, 113 women, never smokers, ≥20 years	Household member's report of smoking 2 years earlier	RR	Smoking co-habitees	Men: RR [b] 0.96, 0.90, 1.04, & 1.08 for cough, phlegm, wheezing & dyspnea, respectively Women: RR [b] 0.17, 0.72, 1.45 & 1.79 for cough, phlegm, wheezing & dyspnea, respectively
Schenker et al 1982, United States (38)	4156 women, nonsmokers, 17–74 years	Self-report of spouse's current smoking	OR	Spouse smoking	Not significant for cough, phlegm or wheezing; OR 1.56 [c] for dyspnea
Hole et al 1989, United Kingdom (39)	671 men, 1784 women, never smokers, 45–64 years	Household member's report of ever smoking	OR (95% CI)	Ever exposed at home	OR 1.19 (95% CI 0.85–1.67) & 1.09 (95% CI 0.82–1.45) for phlegm & dyspnea, respectively
Kauffmann et al 1989, United States and France (40)	726 American women, 25–69 years; 2298 French women, 25–59 years, never smokers	Spouse's report of current smoking	OR (95% CI)	Spouse smoking	American: OR 1.14 (95% CI 0.62–2.09), 1.65 (95% CI 0.72–3.78), 1.35 (95% CI 0.97–1.87) & 1.35 (95% CI 0.68–2.61) for cough, phlegm, wheezing & dyspnea, respectively French: OR 1.35 (95% CI 0.78–2.36), 0.77 (95% CI 0.29–2.03), 1.03 (95% CI 0.77–1.38) & 1.17 (95% CI 0.87–1.57) for cough, phlegm, wheezing & dyspnea, respectively
White et al 1991, United States (41)	80 men and women, never smokers, 38–65 years; subjects with home exposure excluded	Self-report of workplace exposure, verified with observations and carbon monoxide measurements in the workplace	PR	Exposed at work for ≥1 years	PR 2.8 [d], 3.4 [d] & 4.5 [d] for cough, phlegm, & dyspnea, respectively
Pope & Xu 1993, China (42)	973 women, never smokers, 20–40 years	Self-report of household members' current smoking	OR (95% CI)	1 smoker, ≥2 smokers, ≥2 smokers + coal heating	1 smoker: OR 1.02 (95% CI 0.60–1.75), 1.43 (95% CI 0.85–2.40), 0.93 (95% CI 0.50–1.75) & 1.17 (95% CI 0.61–2.25) for cough, phlegm, wheezing & dyspnea, respectively ≥2 smokers: OR 1.87 (95% CI 0.71–4.88), 2.07 (95% CI 0.85–5.01), 1.00 (95% CI 0.27–3.71) & 1.46 (95% CI 0.39–5.52) for cough, phlegm, wheezing & dyspnea, respectively ≥2 smokers + coal heating: OR 3.07 (95% CI 1.23–7.65), 3.64 (95% CI 1.56–8.52), 1.07 (95% CI 0.29–4.00) & 3.55 (95% CI 1.20–10.5) for cough, phlegm, wheezing & dyspnea, respectively
Ng et al 1993, Singapore (43)	1282 women, never smokers, 20–74 years	Self-report of household members' ever smoking	OR (95% CI)	≥1 light [e] smokers, ≥1 heavy [e] smokers	≥1 light smokers: OR 2.84 (95% CI 1.29–6.24), 1.50 (95% CI 0.83–2.71), 0.95 (95% CI 0.38–2.39) & 1.23 (95% CI 0.87–1.74) for cough, phlegm, wheezing & dyspnea, respectively ≥1 heavy smokers: OR 3.79 (95% CI 1.76–8.14), 1.36 (95% CI 0.72–2.57), 2.69 (95% CI 1.23–5.88) & 1.83 (95% CI 1.30–2.58) for cough, phlegm, wheezing & dyspnea, respectively
Leuenberger et al 1994, Switzerland (44)	1674 men, 2523 women, never smokers, 18–60 years	Self-report of exposure at home and work during the past 12 months	OR [f] (95% CI)	Any exposure, workplace exposure	Any exposure: OR 1.69 (95% CI 1.23–2.31), 1.99 (95% CI 1.41–2.82) & 1.44 (95% CI 1.18–1.75) for phlegm, wheezing & dyspnea, respectively Workplace exposure: OR 1.67 (95% CI 1.23–2.28), 2.05 (95% CI 1.42–2.96) & 1.62 (95% CI 1.29–2.03) for phlegm, wheezing & dyspnea, respectively

(continued)

Table 1. Continued.

Study	Study population, age	Exposure assessment	Measure of effect	Exposure category compared to no exposure	Results
Piitulainen et al 1998, Sweden (45)	95 men, 110 women, severe α_1-antitrypsin deficiency, never smokers, ≥20 years	Self-report of exposure ever at home and work (days/week, years of exposure)	OR (95% CI)	Exposure at home and work for ≥10 years	OR 1.6[g] (95% CI 1.3–2.4), 1.1 (95% CI 0.7–1.6) & 1.2 (95% CI 0.8–1.8) for phlegm, wheezing & dyspnea respectively
Lam et al 2000, Hong Kong (46)	4468 men, 728 women, never smokers, 18–58 years, police officers	Self-report of current exposure at home and work (number of smokers, number of cigarettes smoked by co-workers, hours of daily exposure)	OR (95% CI)	Exposure at home or work	Men (home): OR 1.03 (95% CI 0.68–1.56), 1.29 (95% CI 0.91–1.82) & 1.41 (95% CI 1.08–1.85) for cough, phlegm, & wheezing, respectively Men (work): OR 2.61 (95% CI 1.50–4.55), 2.05 (95% CI 1.35–3.11) & 1.76 (95% CI 1.26–2.45) for cough, phlegm, & wheezing, respectively Women (home): OR 0.52 (95% CI 0.18–1.48), 0.62 (95% CI 0.25–1.51) & 1.07 (95% CI 0.57–2.03) for cough, phlegm & wheezing, respectively Women (work): OR 1.00 (95% CI 0.29–3.47), 2.57 (95% CI 0.67–9.90) & 0.55 (95% CI 0.26–1.19) for cough, phlegm & wheezing, respectively

[a] Statistically nonsignificant.
[b] All were statistically nonsignificant.
[c] Statistically significant at P = 0.001.
[d] Statistically significant at P<0.001.
[e] Light smoker = household member who smokes or has smoked <20 cigarettes/ day, heavy smoker = household member who smokes or has smoked ≥20 cigarettes/day.
[f] The OR values for any exposure have been taken from analyses excluding subjects with end-expiratory carbon monoxide levels of ≥7 ppm in order to reduce the misclassification of exposure; the OR values given for phlegm are actually for chronic cough and phlegm combined.
[g] Chronic bronchitis defined as daily cough with phlegm for at least 3 months/year.

Table 2. Longitudinal studies on environmental tobacco smoking and chronic respiratory symptoms among adults. (95% CI = 95% confidence interval, OR = odds ratio)

Study	Study population, age, length of follow-up	Exposure assessment	Measure of effect	Exposure compared with no exposure	Results
Schwartz & Zeger 1990, United States (47)	100 women, 18% smokers, age not given, 3 years	Self-report of presence of a smoking roommate	OR (95% CI) (controlled for personal smoking)	Smoking roommate	Not significant for cough, OR 1.41 (95% CI 1.08–1.85) for phlegm
Jaakkola et al 1996, Canada (48)	60 men, 57 women, never smokers, 15–40 years at the baseline, 8 years (1980/1981–1988/1989)	Self-report of household members' smoking and exposure at work during the follow-up	OR (95% CI) per 10 cigarettes/ day	Total exposure (home+ work)	OR 1.55 (95% CI 0.61–3.90), 0.69 (95% CI 0.21–2.26), 1.15 (95% CI 0.64–2.06) & 2.37 (95% CI 1.25–4.51) for cough, phlegm, wheezing & dyspnea, respectively

longitudinal follow-up, have shown a significantly increased risk of chronic respiratory symptoms in relation to exposure to environmental tobacco smoke among adults (38, 43, 44, 46–48). In addition, some other cross-sectional studies have shown a tendency towards an increased risk of symptoms related to exposure to environmental tobacco smoke, although the effects did not reach statistical significance (39, 40) or they were significant only in a sensitive subgroup (42). The excess risk of symptoms related to exposure to environmental tobacco smoke has varied between 40% and over 300%. Five studies found significant relations between workplace exposure and the occurrence of chronic respiratory symptoms when workplace exposure was assessed separately or as part of total exposure (41, 44–46, 48).

A dose-response relation was demonstrated between exposure to environmental tobacco smoke and the risk of symptoms in five studies (42–44, 46, 48). In a Swiss study (44) of nonsmoking men and women, the following symptoms showed a statistically significant relation

to the quantitative estimate of exposure to environmental tobacco smoke: bronchitis symptoms, wheezing and dyspnea with the hours of daily exposure, bronchitis symptoms and dyspnea with the number of smokers to whom the subject was exposed, and wheezing with the years of exposure. In an 8-year follow-up study of nonsmoking young adults in Canada, the risk of developing dyspnea increased significantly with increasing total exposure to environmental tobacco smoke, the odds ratio (OR) being 2.37 for average exposure to 10 cigarettes/day (48). An increasing trend with increasing total exposure to environmental tobacco smoke was detected also for wheezing and cough, but the relations did not reach statistical significance.

In a study from San Francisco, California, 53 bartenders responded to an interview and performed spirometry about 1 month before and after a bill prohibiting smoking in bars and taverns came into effect (49). Workplace exposure to environmental tobacco smoke was reported to decline from a median of 28 to 2 hours per week. This decline was accompanied by a significant reduction in the prevalence of lower respiratory symptoms (wheezing, dyspnea, cough, and phlegm production) from 74% to 32% and in the prevalence of upper airway irritation symptoms (eye, nose and throat symptoms) from 77% to 19%.

A study from China showed synergistic effects of passive smoking and coal heating on the occurrence of respiratory symptoms (42). A study of a potentially susceptible group consisting of 205 never-smoking persons with severe α_1-antitrypsin deficiency (with PiZZ genotype) from Sweden reported effects on chronic bronchitis, but not on wheezing, dyspnea, or lung function (45).

In a cross-sectional study of 2992 adults from the United Kingdom, an increasing trend for symptom severity was found across the smoking categories, the median score being 2.8 for never smokers, 4.2 for passive smokers, 3.7 for past smokers, and 5.6 for current smokers (51). The adjusted odds ratio was 1.4 [95% confidence interval (95% CI) 1.0–1.8] for severe symptoms in relation to current household exposure to environmental tobacco smoke. Another cross-sectional study of 3405 nonsmoking women from Hong-Kong reported the effects of household smoking on a composite symptom outcome, including sore throat, morning and evening cough, phlegm production during day or night, and phlegm for 3 months (50). The risk of occurrence of any symptom increased with the number of smokers at home (OR 1.16, 95% CI 0.83–1.62, for exposure to one smoker and 1.80, 95% CI 1.15–2.83, for exposure to two or more smokers).

In summary, abundant evidence from different countries indicates that exposure to environmental tobacco smoke causes chronic respiratory symptoms in adults. A dose-response relation has been shown in several studies, and the effects are biologically plausible. Exposure misclassifications due to active smoking or confounding are not likely explanations for the observed relations. Several of the studies took into account potential confounders, such as age, gender, socioeconomic status, atopy, occupational exposures, and other indoor sources of pollutants, either in the study design or in the statistical analyses. The large Swiss study excluded subjects with end-expiratory carbon monoxide over 7 parts per million (ppm) in order to exclude active smokers, but the exclusion did not essentially change the relations between exposure and chronic respiratory symptoms (44). However, more longitudinal studies are needed to throw light on temporal relations and to exclude recall bias as a potential explanation.

Lung function

Studies on the effects of environmental tobacco smoke on the lung function of adults have focused mainly on ventilatory lung function. Altogether 18 cross-sectional studies (1, 36, 37, 39, 40, 43, 52–63), 1 case-referent study (64), and 4 longitudinal studies (55, 63, 65, 66) have addressed these relations. These studies are summarized in tables 3 and 4. In addition, a study of the reduction of exposure among Californian bartenders (table 4) and another study among Canadian bartenders on workshift changes have reported lung function effects (49, 67). Three studies have addressed the effects of environmental tobacco smoke on airway hyperresponsiveness, measured with peak expiratory flow (PEF) variability or methacholine challenge (61, 62, 68).

The results of the studies have been somewhat inconsistent. Among the cross-sectional and case-referent studies, 10 studies detected significant adverse effects on forced expiratory volume in 1 second (FEV_1), indices of small airway function, or both of these parameters (1, 39, 43, 52, 55–59, 63), while 6 did not find any significant associations (36, 37, 40, 53, 60, 64). The FEV_1 deficit related to the exposure to environmental tobacco smoke was estimated to be from –50 ml in the Singapore study (43) to –257 ml in the China study (when adjusted for confounders) (59). In a meta-analysis including nine cross-sectional studies, the effect of environmental tobacco smoke on FEV_1 was –2.7% (95% CI –4.1% – –1.2%) (63). All the cross-sectional studies but one assessed exposure from household members' smoking, while workplace exposure was assessed in eight studies (1, 53, 54, 57–59, 61, 62). Significant lung function impairment related to workplace exposure was detected in five studies (1, 54, 57–59). Four cross-sectional studies showed a significant dose-response relation between the amount of household smoking and the reduction in lung function, either FEV_1 or forced expiratory flow rate at 25–75% of forced vital capacity

Table 3. Cross-sectional and case-referent studies on environmental tobacco smoke exposure and lung function among adults. (95% CI = 95% confidence interval, cig = cigarettes, DL_{CO} = carbon monoxide diffusing capacity of the lung, FEF_{25-75} = forced expiratory flow rate at 25–75% of the FVC, FEF_{75-85} = mean forced expiratory flow during 75% to 85% of the FVC, FEV_1 = forced expiratory volume in 1 second, FVC = forced vital capacity, MEF_{25} = maximal expiratory flow at 75% of the FVC, MEF_{50} = maximal expiratory flow at 50% of the FVC, MEF_{75} = maximal expiratory flow at 25% of the FVC, MMEF = mean forced expiratory flow during the middle half of the FVC, $PaCO_2$ = arterial blood carbon monoxide tension, PaO_2 = arterial blood oxygen tension, PEF = peak expiratory flow, TET = total expiratory time, VC = vital capacity)

Study	Study population, age	Exposure assessment	Lung function outcomes	Results
Schilling et al 1977, United States (36)	178 men, 212 women, nonsmokers, age not given	Spouse's report of current smoking	Level of FVC (l), FEV_1 (l), PEF (l/s), MEF_{50} (l/s), MEF_{25} (l/s)	No significant relation between exposure and lung function
White & Froeb 1980, United States (1)	400 men, 400 women, nonsmokers, mean age 46-49 years, no home exposure	Self-report of exposure at work for ≥20 years	Level of FVC (l), FEV_1 (l), FEF_{25-75} (l/s), FEF_{75-85} (l/s)	Men (unexposed): FEV_1 3.72, FEF_{25-75} 3.78, FEF_{75-85} 1.22 Men (exposed): FEV_1 3.54, FEF_{25-75} 3.30 [a], FEF_{75-85} 0.97 [a] Women (unexposed): FEV_1 2.63, FEF_{25-75} 3.17, FEF_{75-85} 1.03 Women (exposed): FEV_1 2.47, FEF_{25-75} 2.72 [a], FEF_{75-85} 0.78 [a]
Comstock et al 1981, United States (37)	369 men, never smokers, ≥20 years	Household member's report of smoking 2 years earlier	Prevalence ratio of FEV_1 <80% predicted, FEV_1/FVC<70%	Prevalence ratio: FEV_1 <80% 1.42, FEV_1/FVC<70% 1.19
Jones et al 1983, United States [b] (64)	205 women, nonsmokers, 20–39 years	Self-report of household members' smoking 1–2 years earlier	Odds ratio of exposure in lowest versus highest quartile of FEV_1 % predicted	Odds ratio 0.76 (P = 0.34)
Kauffmann et al 1989 (40), 1983 (52), France and United States	France: 970 men, 2306 women, never smokers, 25–59 years; United States: 726 women, never smokers, 25–69 years	Spouse's report of current smoking	Level of FVC (l), FEV_1 (l), FEF_{25-75} (l/s)	French men ≥40 years (unexposed): FVC 4.08, FEV_1 3.31, FEF_{25-75} 3.58 French men ≥40 years (exposed [c]): FVC 4.11, FEV_1 3.19, FEF_{25-75} 3.02 [a] French women ≥40 years (unexposed): FVC 2.98, FEV_1 2.43, FEF_{25-75} 2.74 French women ≥40 years (exposed [c]): FVC 2.89 [a], FEV_1 2.34 [a], FEF_{25-75} 2.57 [a] American women: no significant relation between exposure and lung function
Kentner et al 1984, Germany (53)	393 men, 198 women, never smokers, median age 36-42 years	Self-report of current smoking by household members and co-workers	Level of FVC, FEF_{25-75}, FEF_{75-85} as % predicted	Men (unexposed): FVC 99, FEF_{25-75} 99 Men (exposed): FVC 99, FEF_{25-75} 101 Women (unexposed): FVC 100, FEF_{25-75} 98 Women (exposed): FVC 99, FEF_{25-75} 95
Salem et al 1984, Egypt (54)	517 men, 79 women, never smokers, age not given	Self-report of current and past smoking by household members or co-workers or both	Level of TET (s), FEV_1 (l), PEF (l/min), PaO_2 (mm Hg), $PaCO_2$ (mm Hg)	Unexposed: TET 2.53, FEV_1 2.97, PEF 488, PaO_2 93.0, $PaCO_2$ 37.0 Exposed [d]:TET 3.31 [a], FEV_1 2.80, PEF 473, PaO_2 91.5, $PaCO_2$ 39.0 [a]
Brunekreef et al 1985, The Netherlands (55)	97 women, nonsmokers, 25–60 years	Self-report of household members' smoking since1965	Level of FVC (l), FEV_1 (l), PEF (l/s), MEF_{75} (l/s), MEF_{50} (l/s), MEF_{25} (l/s), MMEF (l/s)	40- to 60-year-olds (unexposed): FVC 3.45, FEV_1 2.82, PEF 8.12, MEF_{75} 6.96 40- to 60-year-olds (exposed [e]): FVC 3.34, FEV_1 2.63, PEF 6.79 [a], MEF_{75} 5.89 [a]
Svendsen et al 1987, United States (56)	1245 men, never smokers, 35–57 years	Self-report of spouse's current smoking	Level of FEV_1 (l)	Unexposed: FEV_1 3.59 Exposed: FEV_1 3.49 [a] for all, FEV_1 3.41 for 1–19 cig/day, FEV_1 3.55 for ≥20 cig/day
Masi et al 1988, Canada (57)	133 men, 160 women, never smokers, 15–35 years	Self-report of lifetime exposure at home and work, cumulative exposure indices	Estimated effect on VC (l), FVC (l), FEV_1 (l), PEF (l/s), FEF_{25-75} (l/s), DL_{CO} [ml/(min · mm)]	Men (home, per person-years): VC 0.004, FEV_1 –0.002 FEF_{25-75} –0.020,[a] DL_{CO} 0.020 Men (work, per pack/day-years): VC –0.045,[a] FEV_1 –0.022, FEF_{25-75} 0.024, DL_{CO} –0.202 Women (home, per person-years): VC 0.001, FEV_1 –0.001, FEF_{25-75} –0.003, DL_{CO} –0.007 Women (work, per pack/day-years): VC –0.006, FEV_1 –0.011, FEF_{25-75} –0.023, DL_{CO} –0.258 [a]
Hole et al 1989, United Kingdom (39)	671 men, 1784 women, never smokers, 45–64 years	Household member's report of ever smoking	Level of FEV_1 (l)	Unexposed: FEV_1 2.31 for men + women, FEV_1 1.88 for women Exposed: FEV_1 2.23 [a] for men + women, FEV_1 1.89 for women (<15 cig/day), FEV_1 1.83 [a] women (≥15 cig/day)

(continued)

Table 3. Continued.

Study	Study population, age	Exposure assessment	Lung function outcomes	Results
Masjedi et al 1990, Iran (58)	167 men, 108 women, never smokers, 18–65 years	Self-report of current smoking by household members and co-workers	Level of FVC, FEV_1, PEF, $FEF_{25–75}$ % predicted	Men (unexposed): FVC 102.1, FEV_1 102.6, PEF 100.9, $FEF_{25–75}$ 104.3 Men (exposed [f]): FVC 97.5,[a] FEV_1 96.9,[a] PEF 98.8 $FEF_{25–75}$ 94.4 [a] Women (unexposed): FVC 98.9, FEV_1 99.3, PEF 100.6, $FEF_{25–75}$ 98.4 Women (exposed [f]): FVC 101.2, FEV_1 100.9 PEF 99.4, $FEF_{25–75}$ 99.8
Ng et al 1993, Singapore (43)	1008 women, never smokers, 20–74 years	Self-report of household members' ever smoking	Level of FEV_1 (l) measured with a portable spirometer	Unexposed: FEV_1 1.83 Light [g] exposure: FEV_1 1.78 [a] Heavy [g] exposure: FEV_1 1.76 [a]
Xu & Li 1995, China (59)	131 men, 371 women, never smokers, 40–69 years	Self-report of current smoking by household members and co-workers	Level of FVC (l), FEV_1 (l)	Men (unexposed): FVC 3.69, FEV_1 2.96 Men (exposed [h]): FVC 3.21 [a], FEV_1 2.61 [a] Women (unexposed): FVC 2.46, FEV_1 1.98 Women (exposed [h]): FVC 2.44, FEV_1 1.98
Frette et al 1996, United States (60)	176 men, 415 women, never smokers, 51–95 years	Self-report of current or past smoking by household members	Level of FVC (l), FEV_1 (l), $FEF_{25–75}$ (l/s)	Men (unexposed): FVC 4.10, FEV_1 3.14, $FEF_{25–75}$ 2.80 Men (exposed [i]): FVC 3.90, FEV_1 3.00, $FEF_{25–75}$ 2.66 Women (unexposed): FVC 2.71, FEV_1 2.13, $FEF_{25–75}$ 1.99 Women (exposed [i]): FVC 2.72, FEV_1 2.12, $FEF_{25–75}$ 2.00
Casale & Pasqualetti 1997, Italy (61)	30 healthy never smokers, 30 exposed nonsmokers, men, mean age 43–44years	Self-report of exposure at home or work or both for ≥3 hours/day, also urinary cotinine	Diurnal PEF (l/s): average level (mesor), amplitude as the absolute value and the % mesor	Unexposed: mesor 5.91, amplitude: absolute 0.37, % mesor 6.26 Exposed: mesor 5.52, amplitude: absolute 0.43, % mesor 7.79
Abbey et al 1998, United States (62)	519 men, 872 women, nonsmokers, 25–80 years	Self-report of exposure at home and work (in years)	Estimated effect on FEV_1 (% predicted), FEV_1/VC (%), PEF lability (%)	Men (worked 10 years with smoker): FEV_1/VC -0.5, PEF lability 0.4 [j] Women (lived 10 years with smoker): FEV_1/VC -0.2, PEF lability 0.3
Carey et al 1999, United Kingdom (63)	683 men, 940 women, nonsmokers, 18–73 years	Self-report of current smoking by household members and past smoking of parents, salivary cotinine	FEV_1 (l) deficit (95% CI) between the top and bottom quintiles of salivary cotinine	Men: FEV_1 deficit -166 ml (95% CI -295 – -37) Women: FEV_1 deficit -68 ml (95% CI -145–9) Total: FEV_1 deficit -105 ml (95% CI -174 – -37)

[a] Significantly lower values for the exposed than for the unexposed (P<0.05).
[b] Case-referent study.
[c] Exposed = living with a smoker of ≥10 grams/day.
[d] Exposed = exposure at home or work or both daily for ≥4 hours for at least 12 months.
[e] Exposed = living in a home where ≥10 cigarettes had been smoked daily since 1965.
[f] Exposed = reported exposure at home or work or both.
[g] Light exposure = ≥1 household members smoke or had smoked < 20 cigarettes per day; heavy exposure = ≥1 household members smoke or had smoked ≥20 cigarettes per day.
[h] Exposed = current smokers at home or work or both.
[i] Exposed = has ever lived in a household with a smoker.
[j] Significantly higher PEF variability in exposed than the unexposed (P<0.05).

($FEF_{25–75}$), in at least a subgroup of the population (52, 57, 59, 63). Two additional studies found a significant effect for heavy exposure on FEV_1, but they did not show a gradient across exposure levels (39, 43).

In contrast to the cross-sectional studies, none of the longitudinal studies found significant effects of exposure to environmental tobacco smoke on the change in lung function over time (55, 63, 65, 66). The follow-up ranged from 2 years (65) to 17 years (55). Jaakkola and her co-workers followed a cohort of 117 young adults aged 15 to 40 years for 8 years (66). Average exposures to environmental tobacco smoke at home and in the workplace were estimated during the study period as cigarettes/day, and cumulative exposure from home and workplace sources before the beginning of the study period was estimated as cigarette-years. No significant effects were detected on the change in FEV_1 or $FEF_{25–75}$ over time in relation to exposure from either source. In a subgroup analysis of young subjects (25 years or younger), cumulative home exposure before the study period was statistically significantly related to a decline in FEV_1. However, this effect was too small to be considered physiologically relevant.

Table 4. Longitudinal studies on environmental tobacco smoke exposure and lung function among adults. (95% CI = 95% confidence interval, $FEF_{25–75}$ = mean forced expiratory flow during the middle half of the forced vital capacity, FEV_1 = forced expiratory volume in 1 second, IVC = inspiratory vital capacity, PEF = peak expiratory flow)

Study	Study population, age, length of follow-up	Exposure assessment	Lung function outcomes	Results
Lebowitz 1984, United States (65)	229 adults, age not given, 2 years	Household member's report of current smoking	Mean PEF level during study period based on daily measurements	No significant relation between exposure and PEF
Brunekreef et al 1985, The Netherlands (55)	57 women, nonsmokers, 40-60 years (at the end of follow-up), 15–17 years (1965/1967–1982)	Self-report of household members' smoking since 1965	Change in IVC (ml/year), FEV_1 (ml/year)	Unexposed: IVC -10.1, FEV_1 -19.3 Exposed [a]: IVC -11.4, FEV_1 -13.9, not significant
Jaakkola et al 1995, Canada (66)	60 men, 57 women, 15-40 years (at the baseline), 8 years (1980/1981–1988/1989)	Self-report of average exposure at home and work during the study, lifetime exposure at home and work before the study (cumulative exposure)	Change in FEV_1 (ml/year), $FEF_{25–75}$ [l/(s·year)]	Exposure during study [b] (cigarettes/day): FEV_1 0.53 (95% CI -0.21 – 1.28) Cumulative exposure before study [b] (cigarette-years): FEV_1 -0.01, (95% CI -0.03 – 0.007) No significant relations between exposure and $FEF_{25–75}$; no evidence of modification by gender, atopy, or wheezing
Eisner et al 1998, United States (49)	38 men, 15 women, mean age 42.5 years	Self-report of workplace exposure before and 1 month after a bill prohibiting smoking in bars came into effect in California (in 1998)	Change in FVC (ml), FEV_1 (ml)	Change in lung function [c]: 326 ml (95% CI 9 – 565) for FVC & 157 ml (95% CI 1 – 303) for FEV_1 for exposure of ≥ 7 hours/week; 244 ml (95% CI 0 – 489) for FVC & 127 ml (95% CI -24 – 277) for FEV_1 for exposure of 1–6 hours/week
Carey et al 1999, United Kingdom (63)	68 men, 940 women, nonsmokers, 18–73 years at baseline, 7 years (1984/1985–1991)	Self-report of smoking by household members at baseline and follow-up, past smoking of parents	Change in FEV_1 (ml)	Exposure started during follow-up: FEV_1 -43 (95% CI -114 – 28), Exposure continued during study: FEV_1 25 (95% CI -20 – 70), Mother smoked in childhood: FEV_1 -25 (95% CI -58 – 9)

[a] Exposed = living in a home where ≥10 cigarettes had been smoked daily since 1965.
[b] Exposure during study = average home + work exposures during the study period (from 1980–1981 to 1988–1989); cumulative exposure before study = lifetime home + work exposures before the beginning of the study.
[c] Improvement in lung function among those whose exposure ceased compared with the exposure group shown.

Two studies evaluated the effects of a change in exposure to environmental tobacco smoke among bartenders. The study of Californian bartenders showed significant improvement in lung function after workplace exposure was reduced following a bill banning smoking in bars and taverns (table 4) (49). A dose-dependent improvement was noted when those with complete cessation of workplace exposure were compared with those with moderate (1–6 hours weekly) and high (≥7 hours weekly) exposure at the time of the follow-up. A study from Canada compared workshift changes in lung function between 26 nonsmoking bar workers exposed to environmental tobacco smoke and 14 nonsmoking unexposed servers (67). The bar workers experienced significant decrements in lung function over a workshift (–42 ml in FEV_1, 95% CI –83 – –0.1, and –155 ml/s in $FEF_{25–75}$, 95% CI –290 – –21), while servers working in restaurants where smoking was banned did not.

A study from California found a significantly higher variability in PEF among men who had worked for 10 years with a smoker (62). A study from Italy applied a cosinor analysis to evaluate the effects of exposure to environmental tobacco smoke at home and work on diurnal PEF variability (61). Passive smokers had a lower average level (mesor) and higher PEF amplitude than unexposed referents, but the differences were not statistically significant, probably due to the small sample size. In line with these results, a cross-sectional study of random population samples of adults from west and east Germany showed that current home exposure to environmental tobacco smoke increased significantly the risk of bronchial hyperresponsiveness (OR 1.37, 95% CI 1.05–1.78), defined as PD_{20} (cumulative dose of histamine at which FEV_1 declines from the basic value) smaller than or equal to 2.0 mg in methacholine challenge or a positive response to a bronchodilator test (68).

One cross-sectional study also assessed the effect of cumulative exposure to environmental tobacco smoke on the diffusing capacity of the lung (DL_{CO}) (57). Among young women, cumulative exposure at work was significantly related to a decrease in DL_{CO}. It was estimated that a woman who has never smoked but who has worked in an office with heavy exposure to environmental tobacco smoke for 10 years would have a DL_{CO} that is 3 units lower than if she has worked in a smoke-free office.

The inconsistency of the results between different studies may be explained partly by methodological

differences, such as the exposure assessment methods used, selection of the study population, and adjustment for potential confounders. However, these differences do not seem to explain the disparate findings completely. It appears that the effect of environmental tobacco smoke on the lung function of adults is dose-dependent and may not be seen in low exposures, whereas some countries, such as China, seem to have levels high enough to produce clinically relevant adverse effects. In addition, in some occupations with high exposure levels, such as bartending, the cessation of exposure seems to result in significant improvement in lung function. The sample size of most of the longitudinal studies has been relatively small, and therefore the sensitivity of the studies to detect small adverse effects may have been reduced, although this possibility has been partly compensated by a long follow-up period, which increases the power of the study. It is possible that the small effects on lung function detected in several cross-sectional studies in relation to exposure to environmental tobacco smoke are due to a susceptible group experiencing a more pronounced lung function deficit, and thus potential determinants of susceptibility should be studied in the future. Atopy and asthma are among important individual characteristics that may lead to sensitivity to environmental tobacco smoke.

In summary, several cross-sectional studies on environmental tobacco smoke and lung function in adults indicate small but significant reductions in ventilatory function parameters among subjects exposed at home or in the workplace. This effect seems to be dose-dependent, and it has been observed mainly in countries and occupations with high exposure levels. Exposure misclassification or confounding does not explain the observed relations. Most of the studies controlled for gender, age, height, socioeconomic status, or education or some combination of these variables. Other potential confounders that have been adjusted for included atopy (66), housing conditions and other indoor air pollutants (37, 43, 52, 55, 57, 59, 64, 65), occupational exposures (1, 52, 53, 57, 59, 66), upper respiratory infections (49, 62), and outdoor air pollutants (62). There is a need for more longitudinal studies to gain information on the potential effects of exposure to environmental tobacco smoke on the development of lung function during adulthood.

Asthma

There is abundant evidence of the role of environmental tobacco smoke in the development and prognosis of asthma among children (2), but a limited number of studies has addressed these relations among adults. The studies on adult asthma can be divided into etiologic studies and prognostic studies of the severity of established disease.

Induction of asthma. Environmental tobacco smoke has been addressed with respect to the induction of asthma in adulthood in five studies (43, 44, 69–71), summarized in table 5. Preliminary results from a population-based incident case-referent study from Finland have also been reported recently (72) (table 5). Two additional studies included asthma in their definition of obstructive lung disease, and they are reviewed with chronic obstructive pulmonary disease (73, 74). In addition to these studies of diagnosed asthma, studies on environmental tobacco smoke and respiratory symptoms and bronchial hyperresponsiveness, reviewed in the earlier sections, provide information relevant to early stages of asthma development.

All of the five etiologic studies concerning adults (table 5) found an increased risk of asthma in relation to exposure to environmental tobacco smoke, although this effect did not reach statistical significance in two studies (43, 70). All the studies assessed residential exposure to environmental tobacco smoke, and three also assessed workplace exposure. In the cross-sectional and case-referent studies, the risk of asthma increased by 40% to 200% in relation to exposure to environmental tobacco smoke. In two of the studies the risk of asthma increased in relation to workplace exposure, but not significantly in relation to home exposure (69, 70). A longitudinal study of Seventh-Day Adventists in the United States reported an odds ratio of 1.45 (95% CI 1.21–1.80) for asthma in relation to 10 years of exposure to environmental tobacco smoke at work (69). In a 15-year update of the follow-up of this same population, the odds ratio was 1.21 per 7 years of workplace exposure (95% CI 1.04–1.39) among women, while the effect was statistically nonsignificant for men (risk estimate was not given) (75). In the 15-year study, the subjects lost to follow-up were more likely to have asthma and be exposed to high levels of environmental tobacco smoke, and this selected loss of subjects may explain the decrease in the risk estimate between the two follow-up studies (10). The Finnish case-referent study included 231 never-smoking cases of new asthma and 487 never-smoking referents (72). The risk of asthma was significantly increased in relation to exposure to environmental tobacco smoke in the past year, both at work (OR 2.16, 95% CI 1.26–3.72) and at home (OR 4.77, 95% CI 1.29–17.7). Another study from Finland estimated that the attributable fraction of asthma mortality from exposure to environmental tobacco smoke at work was 4.5% in 1996 (76).

Clear evidence of a dose-response relation was found in four studies (44, 69, 71, 72, 75). In the longitudinal study from the United States, the risk of asthma was

Table 5. Epidemiologic studies on environmental tobacco smoke and development of asthma among adults. [95% CI = 95% confidence interval, NS = statisically not siginificant (value not given), OR = odds ratio, PEF = peak expiratory flow]

Study	Study design	Study population, age	Exposure assessment	Definition of asthma	Exposure category compared with no exposure	Results
Greer et al 1993, United States (69)	Longitudinal 10-year follow-up (1977–1987)	1414 men, 2500 women, nonsmokers, ≥25 years	Self-report of exposure at work and home (in years of exposure)	Self-report of incident physician-diagnosed asthma + wheezing or attacks of shortness of breath	Work exposure Home exposure	Work exposure: men & women [a] OR 1.45 (95% CI 1.21–1.80), men [a] OR 1.50 (95% CI 1.12–2.01), women [a] OR 1.50 (95% CI 1.17–1.92) Home exposure: no significant relation with asthma
Ng et al 1993, Singapore (43)	Cross-sectional	1282 women, never smokers, 20–74 years	Self-report of household members' ever smoking	Self-report of physician-diagnosed asthma with symptoms in the past year	Light exposure [b] Heavy exposure [b]	Light exposure: OR 0.86 (95% CI 0.34–2.21) Heavy exposure: OR 1.60 (95% CI 0.69–3.70)
Leuenberger et al 1994, Switzerland (44)	Cross-sectional	1674 men, 2523 women, never smokers, 18–60 years	Self-report of exposure at home and work during the past 12 months	Self-report of physician-diagnosed asthma or current asthma (physician-diagnosed asthma + wheezing or cough in past 12 months)	Any exposure [c]	Physician-diagnosed asthma: OR 1.42 (95% CI 1.05–1.91) Current asthma: OR 1.62 (95% CI 1.10–2.37)
Flodin et al 1995, Sweden (70)	Population-based case-referent study	79 cases, 304 referents, of these never smokers: 29 cases, 159 referents, 20–65 years	Self-report of exposure at work and home for ≥3 years before the diagnosis of asthma (year of diagnosis used for matched referents)	Onset in adulthood + clinical history of reversible obstruction and positive methacholine challenge or significant reversibility in beta-2 agonist test	Exposure at work and home	Exposure at work: crude OR 1.5 (95% CI 0.8–2.6), adjusted OR 1.5 (95% CI 0.8–2.5) Exposure at home: crude OR 0.9 (95% CI 0.5–1.5)
Hu et al 1997, United States (71)	Cross-sectional (exposure assessment 7 years earlier)	1469 men and women, nonsmokers, 20–22 years	Parents' report of smoking in a previous survey 7 years earlier	Self-report of physician-diagnosed asthma, or current asthma (physician-diagnosed asthma + symptoms or asthma medication in the past year)	Maternal smoking,[d] paternal smoking,[d] 1 parent smoking,[d] 2 parents smoking,[d]	Physician-diagnosed asthma: maternal smoking OR 1.8 (95% CI 1.1–3.0), paternal smoking OR 1.6 (95% CI 1.1–2.4), 1 parent smoking OR 1.3 (95% CI 0.9–2.0), 2 parents smoking OR 2.9 (95% CI 1.6–5.6) Current asthma: maternal smoking OR 1.8 (95% CI 1.0–3.2), paternal smoking OR 1.7 (95% CI 1.1–2.7), 1 parent smoking OR 1.1 (95% CI 0.7–1.9), 2 parents smoking OR 3.3 (95% CI 1.7–6.4)
Jaakkola et al 2001, Finland (72)	Population-based case-referent study	231 incident cases, 487 referents, never smokers, 21–63 years	Self-report of exposure at home and work as cigarettes/day in the past 12 months or lifetime cumulative exposure in cigarette-years	History of asthmatic symptoms +reversible airflow obstruction in lung function measurements (spirometry+bronchodilation test, diurnal PEF follow-up)	Exposure in the past 12 months at home and work	At work: OR 2.16 (95% CI 1.26–3.72) At home: OR 4.77 (95% CI 1.29–17.7)

[a] OR per 10 years of exposure.
[b] Light exposure = ≥1 household members smoke or had smoked <20 cigarettes per day, heavy exposure = ≥1 household members smoke or had smoked ≥20 cigarettes per day.
[c] Exposure at home or at work during the past 12 months, OR and 95% CI are from an analysis excluding subjects with end-expiratory carbon monoxide levels of ≥7 ppm in order to reduce the misclassification of exposure.
[d] Mother smoking >0.5 packs/day versus mother not smoking or smoking ≤0.5 packs/day, father smoking >0.5 packs/day versus father not smoking or smoking ≤0.5 packs/day, one or two parents versus no parent smoking >0.5 packs/day.

related to the duration of workplace exposure, as discussed before (69, 75). In a Swiss cross-sectional study, the risk of physician-diagnosed asthma increased in a dose-dependent relation with the hours of exposure per day, the number of smokers to whom the subject was exposed, and the years of exposure (44). In a Finnish study the risk of asthma showed a dose-dependent increase with cumulative lifetime exposure from work and home sources (72).

In summary, a limited number of etiologic studies on environmental tobacco smoke and adult-onset asthma has been published, and they indicate an increased

risk of asthma among persons exposed at home or at work. A dose-response relation between exposure and the risk of asthma has been found in several studies. Confounding or exposure misclassification does not seem to explain the observed relations. All the studies controlled for confounding, although the set of confounders varied. They included age, gender, education, occupational exposures, atopy, family history of asthma, and outdoor air pollution. The exclusion of subjects with an end-expiratory level of carbon monoxide of 7 ppm or more, to reduce the misclassification of some actual smokers as nonsmokers, did not have any major effect on the risk estimates in the Swiss study (44). Two studies based the definition of asthma on objective measurements (70, 72), while the others relied on self-reports of diagnosed asthma, the latter being vulnerable to both nondifferential and differential misclassification. More studies with a longitudinal design and objectively examined incident cases of asthma are needed for better risk estimates.

Severity and exacerbations of asthma. In community- and hospital-based surveys (77–79), 69–78% of asthma patients have reported that cigarette smoke aggravates symptoms. Only five epidemiologic studies (80–84) have addressed the role of environmental tobacco smoke in aggravating asthma in adults (table 6).

In a cross-sectional study from India including 200 never-smoking asthmatics, daily exposure to environmental tobacco smoke was significantly related to an increased need for asthma medication, an increased number of acute episodes of asthma and emergency department visits, and lower FEV_1 and $FEF_{25–75}$ levels (81). Another study by this group found that, of 50 nonsmoking asthmatic women, those exposed to environmental tobacco smoke from a spouse had more severe bronchial hyperresponsiveness in histamine challenge than those unexposed (83). These two exposure groups were similar in terms of duration of asthma and exposure to biomass fuel. In a panel study of 164 asthmatic nonsmokers from the United States, daily exposure to environmental tobacco smoke was related to an increased risk of moderate or severe cough, moderate or severe breathlessness, and nocturnal asthma symptoms (80). In a health maintenance organization-based study of 619 asthmatics from the United States, regular exposure was related to worse asthma-specific quality of life, as well as to worse physical functioning and general health (82). In a 30-month follow-up, exposure to environmental tobacco smoke at the beginning of the study was related to an increased rate ratio of health care utilization due to asthma, including hospitalizations, emergency department visits, and urgency care visits. In another study of 285 nonsmoking asthmatics from northern California, self-reported regular exposure was related to greater asthma severity, worse asthma-specific quality of life, and worse physical health status (Drs Eisner and Blanc 2001, personal communication). Asthmatics regularly exposed to environmental tobacco smoke had a significantly increased risk of emergency department visits, urgent physician visits, and hospitalizations. Asthmatics whose exposure ceased during an 18-month follow-up period experienced a reduction in asthma severity, improvement in physical health status, and a decrease in health care utilization. The latter two studies assessed exposure both at home and at work. All of these studies focused on patient populations recruited from physician practices or health maintenance organizations.

In Sweden a population-based study of 2065 adults was carried out as part of the European Community Respiratory Health Survey (84). The relative risk of work-associated symptomatic asthma, defined as self-reported asthma, a methacholine test positive for nonspecific airway hyperresponsiveness and reported work-related chest tightness or wheezing, was 1.7 in relation to regular workplace exposure. Statistically significant increases in the risk of work-related chest tightness were observed for the men (prevalence ratio 4.2, 95% CI 1.8–9.8) and for subjects who were atopic according to skin prick tests (prevalence ratio 2.5, 95% CI 1.3–4.8).

In addition to the epidemiologic studies, several experimental studies have been published on the acute effects of environmental tobacco smoke on adults with established asthma. These chamber exposure studies have been reviewed earlier (6, 7). The results of the experimental studies have been somewhat inconsistent, and their interpretation is hampered by small sample sizes, differences in the selection criteria applied to recruit asthmatics, variable exposure times (ranging from 1 to 6 hours), and variable methods used to assess outcome. Controlled chamber exposure studies have the strengths of measuring exposure and outcome more precisely than is usually possible in epidemiologic studies. On the other hand, they have the following weaknesses that reduce their sensitivity to detect any effects of environmental tobacco smoke on asthma: (i) only those with stable asthma can be exposed, although asthmatics in poor control are probably more sensitive to adverse effects, (ii) asthmatics with a recent respiratory infection are often excluded, although these subjects are likely to be more sensitive, and (iii) exposure periods are often short. The experimental studies suggest that there is a subpopulation of asthmatics sensitive to environmental tobacco smoke. These asthmatics experience increased respiratory symptoms, decreased lung function, and increased bronchial hyperresponsiveness in response to exposure to environmental tobacco smoke. Physiological responses of sensitive asthmatics appear to be reproducible after 2 years, and pretreatment with bronchodilating

Table 6. Epidemiologic studies on environmental tobacco smoke and exacerbations or severity of asthma among adults. (95% CI = 95% confidence interval, FEF_{25-75} = forced expiratory flow during the middle half of the FVC, FEV_1 = forced expiratory volume in 1 second, FVC = forced vital capacity, OR = odds ratio, PD_{20} = cumulative dose of histamine at which FEV_1 declined 20% from the baseline value, QOL = quality of life.)

First author, year, country	Study design	Study population, age, diagnosis of asthma	Exposure assessment	Outcomes of asthma morbidity	Results
Ostro et al 1994, United States (80)	3 months follow-up	53 men and 111 women with asthma, nonsmokers, 18–70 years, asthma diagnosed as history and signs of airway obstruction and reversible obstruction in spirometry	Self-report in baseline questionnaire (any household smoker) and daily diary (exposure at home or exposure to irritating smoke, dust or fumes at work)	Daily diary of occurrence and severity score of respiratory symptoms and nocturnal asthma (= awakened by asthma)	Daily exposure: moderate or severe cough OR 1.21 (95% CI 1.01–1.46), moderate or severe breathlessness OR 1.85 (95% CI 1.57–2.18), nocturnal asthma OR 1.24 (95% CI 1.00–1.53) Occupational exposures [a]: moderate or severe cough OR 1.14 (95% CI 0.98–1.33), moderate or severe breathlessness OR 1.38 (95% CI 1.19–1.59), nocturnal asthma OR 1.19 (95% CI 1.00–1.42) Chronic exposure [b]: moderate or severe breathlessness OR 2.05 (95% CI 1.78–2.40)
Jindal et al 1994, India (81)	Cross-sectional	200 patients with asthma, never smokers, 15–50 years, asthma diagnosed as history of asthmatic symptoms and reversible airways obstruction in spirometry (excluded if acute severe asthma in preceding 2 weeks)	Self-report of smoking by spouse and other close contacts, minimum exposure 1 hour/day (or 7 hours/week) for at least 1 year	Self-report of use of bronchodilators, corticosteroids, number of visits to emergency department, hospitalizations, acute episodes and spirometry (FVC, $FEV_{1,0}$, FEF_{25-75} % of predicted)	Unexposed: OR 0.60, 0.33, 0.60, 8.6, 36.3 & 3.0 for visits/patient to emergency department in last year, hospitalizations/patient in last year, acute episodes/patient in last year, weeks of required steroid treatment per patient, weeks of bronchodilation maintenance in last year & weeks of absence from work in last year, respectively; mean level of % predicted for FVC, FEV_1 & FEF_{25-75} 90.9, 80.8 & 75.7, respectively Exposed [c]: OR 0.82 [d], 0.34, 1.32 [d], 11.3 [d], 38.3 & 3.6 [d] for visits/patient to emergency department in last year, hospitalizations/patient in last year, acute episodes/patient in last year, weeks of required steroid treatment in last year, weeks of bronchodilation maintenance in last year & weeks of absence from work in last year, respectively; mean level of % predicted for FVC, FEV_1 & FEF_{25-75} 89.4, 68.7 [d] & 54.3 [d], respectively
Sippel et al 1999, United States (82)	Cross-sectional and 30 months of follow-up	619 patients with asthma, smokers and nonsmokers, 15–55 years, asthma diagnosed as hospitalization for asthma within 2 years and current use of asthma medication	Self-report of regular exposure at home or work	Asthma-specific QOL, health status Follow-up (from administrative data bases): health care utilization, including hospitalizations, emergency department visits, urgency care visits	Cross-sectional (unexposed): QOL index 2.3 for breathless and 2.0 for mood, health status index 81 for physical function, 71 for bodily pain, and 65 for general health Cross-sectional (regularly exposed): QOL index 2.7 [d] for breathless and 2.5 [d] for mood; health status index 73 [d] for physical function, 65 [d] for bodily pain, and 59 [d] for general health Longitudinal (regularly exposed at baseline): RR [e] 2.34 (95% CI 1.80–3.05) for health care utilization
Jindal et al 1999, India (83)	Cross-sectional	50 women, 20–40 years, nonsmokers, asthma diagnosed as reversible airway obstruction in lung function tests	Self-report of exposure from spouse, exposure index = average daily hours×years of exposure	Bronchial hyperresponsiveness in histamine challenge, PD_{20} (mg/ml)	Unexposed: PD_{20} 6.1 Exposed: PD_{20} 1.7 [f] Exposure index <15: PD_{20} 3.2 Exposure index ≥15: PD_{20} 1.8 [f]
Blanc et al 1999, Sweden (84)	Cross-sectional, population-based + enriched with symptomatic subjects	1013 men and 1052 women, 20–44 years, 17% had self-reported asthma, smokers and nonsmokers	Self-report of regular exposure at work	Reported asthma, bronchial hyperresponsiveness in methacholine challenge and reported chest tightness or wheezing at work	Workplace exposure: prelevance ratio 1.7 (95% CI 0.9–3.3)

[a] Occupational exposures = daily exposure to irritating smoke, dust or fumes at work.
[b] Chronic exposure = report of any household smoker in the baseline questionnaire.
[c] Exposed = asthmatics with at least the minimum exposure (as defined in exposure assessment).
[d] Statistically significant difference between exposed and unexposed (P<0.05).
[e] Rate ratio related to regular exposure at baseline.
[f] Statistically significant difference between exposed and unexposed, or between high and low exposure groups (P<0.01).

medication seems to prevent these responses (27, 85). Determinants of this sensitivity are not known.

In summary, a limited number of epidemiologic studies and several experimental studies suggest that exposure to environmental tobacco smoke contributes to the severity and exacerbation of asthma among adults with established disease. More epidemiologic studies are needed, with focus on longitudinal design, better outcome and exposure assessment, and control for other factors affecting the stability of asthma. Experimental

studies are hampered by the fact that the subgroups probably most sensitive to the adverse effects of environmental tobacco smoke cannot be exposed due to safety reasons, but studies focusing on real life type of exposures can contribute to a better understanding of the potential mechanisms of effects.

Chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) develops slowly over the years. Studies of chronic respiratory symptoms and lung function have investigated the early stages of the disease, while studies on diagnosed COPD focus on later stages. Three longitudinal studies (73, 86, 87) and three case-referent studies (74, 88, 89) have evaluated the effects of environmental tobacco smoke on the development of late stage COPD. They are summarized in table 7. A longitudinal study of Seventh-Day Adventists in California has produced several reports (73, 90–92). We were not able to identify any investigation that studied the role of environmental tobacco smoke in the exacerbation of COPD directly by measuring respiratory impairment. However, two studies assessed the impact of exposure on respiratory-related activity restrictions (93, 94).

The fact that COPD was defined in different ways in the epidemiologic studies reflects the complex nature of the disease. It overlaps to some extent with asthma, and some studies included asthma in their definition of obstructive disease (73, 74, 86, 92). The definitions used in the studies were based on symptoms or diagnoses made by a physician as reported in questionnaires, lung function measurements, diagnostic codes in mortality statistics, or a combination of these variables.

An increased risk of COPD in relation to exposure to environmental tobacco smoke was found in all the longitudinal studies. The excess risk was estimated to be from 30% to over 400%. The study from California showed the highest risk of incident COPD in relation to cumulative exposure to environmental tobacco smoke from childhood and adulthood home and workplace exposures (73). One hospital-based case-referent study from Greece (89) and one population-based case-referent study from the United States (74) showed a dose-response relation between the amount of exposure to environmental tobacco smoke and the risk of COPD. A small hospital-based case-referent study from the United Kingdom observed an increased risk of COPD only in relation to the highest exposure level (88). Workplace exposure to enrironmental tobacco smoke was assessed only in the longitudinal study of the Seventh-Day Adventists (73, 92), while the others were limited to household exposures. The study of Seventh-Day Adventists was also the only study that evaluated the role of childhood exposure for COPD. A Finnish study estimated that the attributable fraction of COPD mortality from exposure to environmental tobacco smoke at work was 1.1% in 1996 (76).

In summary, the number of studies on environmental tobacco smoke and the development of late stage COPD is limited, but all the published studies show an excess risk in relation to exposure. A dose-response relation was found in three studies. Three studies were longitudinal in design and therefore indicated a meaningful temporal relation. Age and gender were taken into account as potential confounders in all of the studies, but otherwise control for confounding varied, including factors such as the participant's or spouse's occupation, housing quality, other indoor pollutants, and outdoor pollution. One study examined potential modification of the effects of environmental tobacco smoke by ambient air pollutants, but no significant interactions were found (73). More studies with better outcome and exposure assessment are needed before any definite conclusions can be drawn.

Two studies addressed the role of exposure to environmental tobacco smoke in respiratory-related activity restrictions (93, 94). Both studies were based on data collected by national health interview surveys conducted by the Census Bureau for the National Center for Health Statistics in the United States. In the first report, among nonsmokers, respiratory-related restricted activity in the past 2 weeks increased by an average of 1% per 1 cigarette smoked per day by a household member when the situation was compared with nonsmoking households (93). In the second report, respiratory disease exacerbation was defined as activity limitation or physician visit in the preceding 2 weeks because of chronic bronchitis, asthma, emphysema, or chronic sinusitis (94). Among a probability sample of never smokers, the risk of exacerbations of respiratory conditions increased significantly in relation to exposure to environmental tobacco smoke at home or work, with an OR of 1.44 (95% CI 1.07–1.95). These two studies suggest that exposure to environmental tobacco smoke contributes to the adverse consequences of COPD. However, there is a lack of studies evaluating more directly the role of environmental tobacco smoke as a potential trigger of COPD exacerbation.

Respiratory infections

There is convincing evidence that passive smoking enhances susceptibility to respiratory infections among children (2). For adults, surprisingly little data have been published on infections. Recently, a population-based case-referent study from the United States evaluated the relations of active smoking and exposure to environmental tobacco smoke with invasive pneumococcal disease in immunocompetent adults (95). Among a total of 228

Table 7. Epidemiologic studies on environmental tobacco smoke and chronic obstructive pulmonary disease (COPD). (95% CI = 95% confidence interval, OR = odds ratio)

Study	Study design	Study population, age	Exposure assessment	Definition of COPD outcome	Exposure category compared to no exposure	Results
Hirayama 1981, Japan (86)	Longitudinal, 14-year follow-up (1965–1979)	91 540 women, nonsmokers, ≥40 years	Spouse's report of smoking in the beginning of follow-up	Mortality from emphysema or asthma, based on diagnosis in death certificate	Spouse ex-smoker or smoked 1–19 cigarettes per day; spouse smoked ≥20 cigarettes/day	OR 1.29 [a] for spouse ex-smoker or smoking 1-19 cigarettes/day and OR 1.49 [a] for spouse smoking ≥20 cigarettes/day
Lee et al 1986, United Kingdom (88)	Hospital-based case-referent study	chronic bronchitis cases: 9 men, 17 women; referents: 133 men, 318 women, never smokers, 35–74 years	Self-report of spouse's current and past smoking habits and ETS exposure at work, during daily travel and during leisure time	Chronic bronchitis, diagnosed in a hospital (criteria for diagnosis not given)	Spouse's smoking during whole marriage; quantitative index [c] 2–4 and 5–12	Men [b]: OR 0.34 for spouse's smoking during whole marriage; OR 0.83 & 1.90 for quantitative index of 2–4 & 5–12, respectively Women [b]: OR 1.22 for spouse's smoking during whole marriage; OR 1.05 & 1.03 for quantitative index of 2–4 & 5–12, respectively Combined [b]: OR 0.83 for spouse's smoking during whole marriage; OR 1.00 & 1.30 for quantitative index of 2–4 & 5–12, respectively
Kalandidi et al 1987, Greece (89)	Hospital-based case-referent study	103 COPD cases, 179 referents (visitors in the hospital), women, never smokers, 40–79 years	Self-report of spouse's current and past smoking habits	COPD diagnosis, based on history of dyspnea and phlegm for ≥3 years + obstruction or mixed type reduction in spirometry (no reversibility with bronchodilator)	Spouse ex-smoker, spouse smokes ≤1 or >1 packs/day Spouse's lifelong , consumption ($x 10^3$) ≤ 300 or > 300	OR 0.7 (95% CI 0.3–1.4) for spouse ex-smoker; 2.5 (95% CI 1.3–5.0) & 1.5 (95% CI 0.8–2.7) for spouse smoking ≤1 & >1 packs/day, respectively; 1.3 (95 CI 0.7–2.3) & 1.7 (95% CI 0.8–3.4) for $\leq 300 \times 10^3$ & $> 300 \times 10^3$ of spouse's lifelong consumption, respectively
Sandler et al United States (87)	Longitudinal, 12-year follow-up (1963–1975)	4162 men, 14 873 women, never smokers, ≥25 years at baseline	Household members' report of smoking in the beginning of thestudy	Mortality from emphysema or bronchitis = underlying cause of death in death certificate	Smoking cohabitees	Men: rate ratio 0.93 (95% CI 0.16–5.32) Women: rate ratio 5.65 (95% CI 1.19–26.8)
Robbins et al 1993, United States (73)	Longitudinal, 10-year follow-up (1977–1987)	1414 men, 2500 women, nonsmokers, ≥25 years at baseline	Self-report of exposure at work and home during adulthood and at home during childhood	Incident airways obstructive disease, physician diagnosed asthma + wheezing or cough and sputum for ≥3 months/year for ≥2 years or physician-diagnosed emphysema + breathlessness	Childhood exposure only, past adulthood exposure, childhood + past adulthood exposure, current adult home + work exposure, childhood + current adult home + work exposure, reference category= never exposed	OR 1.09 (95% CI 0.69–1.68), 1.33 (95% CI 0.93–1.88),1.68 (95% CI 1.27–2.20), 1.48 (95% CI 0.95–2.23), & 2.03 (95% CI1.45–2.77) for childhood exposure only, past adulthood exposure, childhood + past adulthood exposure, current adult home + work exposure & childhood + current adult home + work exposure, respectively
Dayal et al 1994, United States (74)	Population-based case-referent study	219 cases, 657 referents, never smokers, age range not given	Household head's report of current smoking habits of household members	Household head's report of obstructive respiratory disease, defined as diagnosed asthma, chronic bronchitis or emphysema	Exposure ≤1 or >1 packs/day	OR 1.16 (95% CI 0.78–1.72) for ≤1 packs/day & 1.86 (95% CI 1.21–2.86) for >1 packs/day

[a] Risk ratio (these were statistically nonsignificant).
[b] Reference category = spouse did not smoke during whole marriage or quantitative index score 0–1. All OR values were statistically nonsignificant, but the 95% CI were not given.
[c] Quantitative index for regular exposure was calculated based on a sum of 0 = not at all, 1 = a little, 2 = average, 3 = a lot exposure at home, at work, during travel, and during leisure.

patients, 95% had bacteremia, 4% had meningitis, and 1% had infections at other normally sterile sites. Among nonsmokers, patients with invasive pneumococcal infections were 2.5 times as likely to be exposed to environmental tobacco smoke as referents (95% CI 1.2–5.1) when confounding by gender, race, presence of chronic illnesses, education, and living with children going to day care were adjusted for. The odds ratios were of similar magnitude for persons exposed to smoke at home only and for those exposed only outside the home. The population attributable risk for passive smoking was 17%. A dose-response relation was observed between the hours of daily exposure and the risk of invasive pneumococcal disease. Two earlier studies have

suggested that exposure to environmental tobacco smoke is related to the risk of meningococcal disease in adults (96, 97). In summary, for adults, exposure to environmental tobacco smoke has been associated with serious infections, such as bacteremic pneumococcal pneumonia and meningitis, but more studies examining the relations between environmental tobacco smoke and infections are needed.

Discussion of methodological issues

Avoidance of exposure to environmental tobacco smoke because of a health condition (eg, respiratory symptom or disease) could lead to an underestimation of the true effect of environmental tobacco smoke. Longitudinal studies recording exposure before the first symptoms and signs of the disease minimizes this type of selection bias, which is more difficult to avoid in cross-sectional and prevalent case-referent studies. In longitudinal studies, subjects lost to follow-up may introduce selection bias if the loss is related to both exposure and outcome. Attempts to maintain a high follow-up rate help to minimize this type of selection bias. The selection of referents in case-referent studies may introduce selection bias if the referents do not represent the exposure of the source population that produced the cases. Especially hospital-based referent selection is susceptible to this type of bias if the referents are chosen among a patient group whose disease is related to exposure to environmental tobacco smoke. Recruitment of all new cases and concurrent recruitment of a random sample of referents from the same source population will eliminate this type of bias. Recently there has been a tendency to carry out population-based case-referent studies to avoid this type of bias.

Information on outcome should be collected similarly from the exposed and unexposed subjects so that awareness of exposure does not influence the measurement of outcome. Any differences in the outcome assessment between the exposed and unexposed subjects will lead to information bias, which may either increase or decrease the studied relation. Nondifferential or random error will usually lead to an effect towards the null. Studies of subjective outcomes, such as respiratory symptoms, are susceptible to both differential and nondifferential outcome misclassification.

In case-referent studies, information on exposure to environmental tobacco smoke from cases and referents should be comparable. Retrospective, subjective exposure assessment may be problematic. Recall bias takes place if cases remember exposures differently from referents because of their disease. However, lung cancer studies have not supported empirically the occurrence of recall bias in health effect studies of environmental tobacco smoke (98). Assessment of exposure to environmental tobacco smoke may be complicated, especially in adult studies, because of multiple sources of exposure (eg, home, workplace and different types of social situations). If these multiple sources are not taken into account, the reference category classified as unexposed includes subjects who, in fact, experience substantial exposure. This misclassification dilutes the risk estimate obtained. It has been estimated that ≥80% of nonsmokers have detectable cotinine levels in their body fluids (99, 100). Recently studies have started to pay attention to other sources of environmental tobacco smoke, in addition to household smoking, to achieve better risk estimates. A potentially important source of misclassification of exposure is the misclassification of smoking status due to self-reporting. Some current and former smokers may report themselves as never smokers and be at higher risk of developing smoking-related diseases. It has been suggested that smokers are more likely to marry smokers than nonsmokers are (101). If so, a bigger proportion of those classified as exposed to environmental tobacco smoke are active smokers when a comparison is being made to persons classified as unexposed. However, the proportion of ever smoking adults (current or former) who are misclassified as never smokers has been estimated to be relatively small, 3% to 7% (5, 101–103). This magnitude of misclassification is not large enough to explain the observed risks of lung diseases related to exposure to environmental tobacco smoke. Furthermore, there is no evidence of such differential misclassification in workplace exposure.

Potential confounders are determinants of the studied disease and are therefore disease-specific. Most of the studies reviewed adjusted for several of the important confounders for respiratory diseases, including age, gender, socioeconomic status, atopy, other indoor pollutants, and occupational exposures, the more recent studies taking into account potential confounding more completely. Focus has recently been on confounding by life-style factors, such as diet. However, adjustment for dietary factors has not changed essentially the risk estimates obtained in lung cancer studies, although the relation between diet and cancer has been relatively strongly established (98, 104–109). In summary, it is not likely that confounding plays a decisive role in the respiratory effects observed in relation to exposure to environmental tobacco smoke. Interactions between other life-style factors and environmental tobacco smoke have been studied less (ie, if an accumulation of several risk factors is more dangerous than the addition of risks related to individual factors separately).

Publication bias will be introduced if scientists submit manuscripts or the journals accept them on the basis of their results, typically so that studies finding no

effects ("negative studies") are underrepresented. In 1994 Bero and her co-workers (110) carried out a review of published and unpublished studies of the health effects of environmental tobacco smoke to assess potential publication bias. The authors concluded that there is no evidence of publication bias against statistically nonsignificant results in the peer-reviewed literature on environmental tobacco smoke. Lung cancer in adults and respiratory diseases in children have been studied extensively, and this abundance reduces the likelihood of publication bias. However, for diseases that have been studied to a limited extent, it is important that all good-quality research be published so that an unbiased picture can be obtained. A more recent comparison of published and unpublished studies on passive smoking showed a publication delay for studies with nonsignificant results (111).

In summary, it is important to be aware of the many potential sources of bias in studies of the health effects of exposure to environmental tobacco smoke. However, especially recent studies have put a great deal of effort on avoiding these biases and adjusting for confounding. Thus an abundant amount of high-quality research exists that confirms many of the observed relations between exposure to environmental tobacco smoke and respiratory disease.

Summary

Sidestream smoke contains the same irritative and toxic compounds as mainstream smoke, and it is plausible that the biological effects of environmental tobacco smoke are similar to those of active smoking. All of the respiratory effects reviewed (ie, respiratory symptoms, lung function impairment, asthma, COPD, and pneumococcal infections) have been linked to both home and workplace exposure among adults. Some evidence of a dose-response relation has been detected for all of these conditions. Table 8 summarizes the information on the respiratory effects of exposure to environmental tobacco smoke among adults. In addition, the authors' judgment of causality, based on the number of studies, their validity, the evidence of dose-response relations, and biological plausibility, is presented.

The strongest evidence for a causal relation exists for environmental tobacco smoke and chronic respiratory symptoms. Several cross-sectional studies provide evidence that exposure to environmental tobacco smoke is related to deficits in ventilatory lung function, the effects usually being relatively small. However, longitudinal studies on lung function have not confirmed these findings. It is likely that the harmful effects of exposure to environmental tobacco smoke are dependent on the dose, since adverse effects on lung function have been detected mainly in countries and occupations with high exposure levels. A limited number of studies suggests that environmental tobacco smoke increases the risk of new asthma and contributes to poor control of established disease in adults. The evidence linking exposure to environmental tobacco smoke to COPD is also limited, but an adverse effect is supported by three longitudinal studies. There is a lack of studies on the role of environmental tobacco smoke as a potential trigger of COPD exacerbation. One study among adults linked exposure to environmental tobacco smoke to serious infections, including pneumococcal pneumonia and meningitis. There is a need for more longitudinal studies with careful assessment of exposure to provide better risk estimates for all of these respiratory conditions. New studies on asthma, COPD, and respiratory infections are needed before any definite conclusions can be drawn. However, despite these challenges being left for future research, the combination of toxicologic evidence, a large number of studies on environmental tobacco smoke and respiratory effects among children, and the adult studies reviewed in this

Table 8. Summary of environmental tobacco smoke and respiratory diseases and conditions among adults. (95% CI = 95% confidence interval, OR = odds ratio, COPD = chronic obstructive pulmonary disease, EF = effect estimate, FEV_1 = forced expiratory volume in 1 second)

Disease or condition	OR[a] or EF	95% CI	Causality[b]
Chronic respiratory symptoms			+++
Wheezing	OR 1.41–2.69	·	
Cough	OR 2.61–3.79	·	
Phlegm	OR 1.41–2.05	·	
Dyspnea	OR 1.44–4.50	·	
Asthma			
Induction			++
Young adults[c]	OR 1.60–3.30	·	
Adults	OR 1.42–1.62	·	
Bronchial hyperresponsiveness[d]	OR 1.37	1.05–1.78	+
Severity	Diverse outcomes, no summary estimate available		++
COPD			
Case-referent studies	OR 1.86–2.5	·	++
Longitudinal studies	OR 1.68–5.63	·	
Respiratory infections[e]	OR 2.5	1.2–5.1	+
Lung function, FEV_1			
Cross-sectional studies	EF[f] -2.7%	-4.1%– -1.2%	
Longitudinal studies	No significant effect		+

[a] The range of the OR values from the studies reviewed (that showed a significant association) or the OR and 95% CI from an individual study.
[b] Causality as judged by the authors; symbols: +++ = causal relation established, ++ = strong evidence of a causal relation, + = some evidence of a causal relation, 0 = no clear evidence of a causal relation.
[c] From reference 71.
[d] From reference 68.
[e] From reference 95.
[f] Effect estimate and 95% CI from a meta-analysis (63): the difference in the FEV_1 between the exposed and unexposed, expressed as a percentage of the level of the unexposed group.

paper point to an urgent need for measures to prevent exposure to environmental tobacco smoke among adults.

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