Environmental tobacco smoke

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Environmental tobacco smoke is an important contaminant of indoor air. For a non-smoker living with a smoker the exposure is equivalent to about 1% of that from actively smoking 20 cigarettes a day (based on plasma cotinine). There is strong and consistent evidence that passive smoking increases the risk of lung cancer. It is estimated that there is an increase in risk of 24% (95% confidence interval 11—38%) compared to unexposed non-smokers, and several hundred lung cancer deaths per year in Britain are attributable to environmental tobacco smoke exposure. Passive smoking is associated with an increase in risk of chronic respiratory disease in adults of 25% (10—43%), and increases the risk of acute respiratory illness in children, by 50—100%. It is likely that passive smoking increases the risk of ischaemic heart disease, and that exposure in pregnancy lowers birthweight, but there is inconsistency between different estimates of the magnitude of risk. The overall hazard is sufficient to justify measures to restrict smoking in public places and workplaces, and to discourage people from smoking in their homes.

Environmental tobacco smoke is probably the most important contaminant of indoor air. It consists mainly of 'sidestream' smoke given off directly from the burning end of the cigarette; exhaled mainstream smoke is a minor component. The smoke differs in certain ways from active smoking: sidestream smoke is unfiltered (since it does not pass through the column of tobacco or the filter of the cigarette), and the nicotine is mainly in the gaseous phase in sidestream smoke and the particulate phase in mainstream smoke. These differences notwithstanding, it is reasonable to expect in general that environmental tobacco smoke exposure, or passive smoking, would cause the same diseases as active smoking, but at a risk reduced approximately in proportion to the considerable dilution of the smoke. This expectation is secure in the case of smoking-related cancers because of the evidence that carcinogens in general have no threshold. For other smoking related diseases there may plausibly be a threshold exposure level such that passive smoking constitutes too low a dose to convey any excess risk, or conceivably (though less plausibly) a near maximal response at low dose such that passive smoking conveys a risk of the same order of magnitude as active smoking.
There is a reasonable basis for conducting epidemiological studies of exposure to environmental tobacco smoke for conditions in which the relative risk in active smokers compared to non-smokers is relatively large. In non-smokers married to smokers, the exposure to tobacco smoke is about 1% that of actively smoking 20 cigarettes per day\textsuperscript{2,3} (based on concentrations of cotinine, the principal metabolite of nicotine). In the case of a disease for which actively smoking 20 cigarettes per day conveyed a 20-fold excess risk, the expected excess risk from passive smoking would be 20% (1% of 20) and the relative risk 1.2. This could be detected in a large epidemiological study (or a meta-analysis of several smaller studies). The difficulty in assessing and quantifying the health effects of environmental tobacco smoke is that for many other smoking-related diseases the expected increase in risk is not large enough to be detected in epidemiological studies. For several diseases the risk in those who smoke 20 cigarettes per day is about double that in lifelong non-smokers\textsuperscript{1}. It would be hopeless to attempt to demonstrate the expected excess risk associated with passive smoking of 1% (1% of the excess risk of 100% associated with active smoking).

Simple measures of household exposure, assessing spousal smoking in studies of non-smoking adults or parental smoking in studies of children, are commonly used to define an exposed group in epidemiological studies of passive smoking. It is difficult to quantify exposure in the workplace and other environments using questionnaires. Spousal smoking is also indicative of exposure outside the home as it categorises a non-smoker as likely to be tolerant of environmental smoke and hence less likely to avoid it. Animal studies are available for some smoking-related conditions but they cannot quantify the risk of disease from typical exposure levels in humans.

**Evidence on specific diseases**

The evidence on the association between passive smoking and the major smoking related diseases is discussed below. Two issues not discussed are the simple irritant effects of environmental tobacco smoke (important because they affect many people) and the fire hazards associated with smoking.

**Lung cancer**

The observation that carcinogens have no threshold indicates that inhaled tobacco smoke must increase the risk of lung cancer. A reasonable
expectation is that it will do so at a level proportional to the dilution. The last 20 years follow-up in the British Doctors Study demonstrated an excess risk of about 20-fold associated with actively smoking 20 cigarettes per day\textsuperscript{1}. As discussed above, since the average exposure in passive smokers is about 1\% that in active smokers of 20 cigarettes per day\textsuperscript{2,3}, the expected excess risk in non-smokers passively exposed, from linear dosimetry, would be 20\%, and the relative risk 1.2.

Direct evidence from epidemiological studies confirms this estimate. Figure 1 shows the relative risk for spousal (or cohabitant) smoking in 34 published prospective and case-control studies of passive smoking and lung cancer\textsuperscript{4-36}, updating an earlier published meta-analysis\textsuperscript{37}. The combined relative risk estimate from all studies is 1.24 (95\% CI 1.11–1.38; \( p < 0.001 \)). Figure 1 shows that the estimate from each individual study is consistent with the overall estimate, and that no one study is critical in influencing the combined estimate.

**Biases in the epidemiological studies** There are two important biases in quantifying the risk. Misclassification bias arises because current smokers or former smokers, at increased risk of lung cancer, may falsely claim to be non-smokers. Smokers tend to marry other smokers, so these misclassified active smokers would be more prevalent in the group of exposed non-smokers than in the unexposed group, thereby spuriously increasing the risk estimate\textsuperscript{37}. The second bias arises because individuals in the reference group, non-smokers living with non-smokers, are
exposed to environmental tobacco smoke outside the home, and will not have zero exposure. This will decrease the risk estimate. Previous calculations have shown, however, that these two factors approximately cancel each other out\textsuperscript{37}.

There is potential for confounding because the dietary intake of antioxidant vitamins (carotenes/vitamin A and vitamin C) is lower in non-smokers married to smokers than in non-smokers married to non-smokers\textsuperscript{38,39}, and low levels of these vitamins may increase the risk of lung cancer independently of smoking. However, three epidemiological studies of passive smoking and lung cancer controlled for the effect of diet and showed that the risk estimate for environmental tobacco smoke exposure was not materially altered\textsuperscript{28,30,40} (the third\textsuperscript{40} being a further analysis of data from a previously published study\textsuperscript{6}).

**Additional confirmatory evidence** The isolation of a tobacco-specific lung carcinogen from the urine of non-smokers exposed experimentally to environmental tobacco smoke confirmed that the carcinogens are indeed inhaled and metabolised\textsuperscript{41}. A study of autopsy findings in individuals who died from causes other than cancer showed that premalignant changes in the bronchial mucosa were more common in non-smokers married to smokers than in those married to non-smokers\textsuperscript{42}.

**Range of acceptable estimates of risk** There has been disagreement over the magnitude of the association between passive smoking and lung cancer. In a model which employed quadratic rather than linear extrapolation to estimate the risk equivalent to 1% of the exposure from 20 cigarettes per day, the estimate of relative risk from spouse smoking in adulthood was 1.09, or 1.14 with exposure from parental smoking during childhood in addition\textsuperscript{43}, compared to the above estimate of 1.2. The estimate from the epidemiological studies might tally with these lower estimates if the effect of the misclassification bias had been underestimated\textsuperscript{43}. The quadratic dosimetry estimates were based on the first 20 years follow-up of the British Doctors Study and should be increased a little to allow for the observation that the first 20 years of follow-up underestimated the full extent of risk compared to the second 20 years of follow-up\textsuperscript{1}. Moreover, the large prospective studies of smoking and lung cancer show a dose-response relationship that is linear, or approximately linear, over doses that encompass passive smoking and active smoking up to 20 cigarettes per day. Precise correlation cannot in any case be expected between dosimetry estimates from active smoking and direct estimates from epidemiological studies. The content and activity of carcinogens may differ between the smoke from freshly combusted tobacco inhaled on actively smoking and the relatively stale...
environmental smoke for example. The broad consistency between estimates is encouraging.

Overall the best estimate of the excess risk of lung cancer attributable to passive smoking is about 20%, and the lower limit of the range of acceptable estimates is about 10%.

Conclusions The evidence confirms beyond reasonable doubt that a causal relationship exists between environmental tobacco smoke exposure and lung cancer. The dosimetry evidence (reducing the known risk of active smoking in proportion to the exposure) and the direct epidemiological evidence are consistent, both indicating a relative risk of about 1.2. The best estimate of the increase in the risk of lung cancer attributable to environmental tobacco smoke exposure in non-smokers is about 20%.

Other smoking related cancers

The dosimetry considerations apply equally to lung cancer and to other smoking-related cancers. An excess risk in non-smokers equivalent to 1% of that in active smokers of 20 cigarettes per day would be expected, corresponding to relative risks of about 1.2 for cancers at upper respiratory sites, 1.1 for oesophageal cancer, etc. The direct epidemiological data on passive smoking and cancers other than lung cancer, reviewed by Lee, are too few to support any independent conclusion.

Chronic respiratory disease in adults

Figure 2 shows the relative risk estimates in eight epidemiological studies of chronic respiratory disease in non-smoking adults exposed to environmental tobacco smoke, compared to those not exposed. These studies are less satisfactory than those of lung cancer because of the difficulty in always distinguishing asthma from chronic bronchitis and emphysema, and the variation between studies in disease definition (as the certified cause of death in prospective studies or of hospital admission in case-control studies or as a history of frequent infected sputum or frequent wheezing in cross-sectional studies). In all eight studies the cases fall into the broad category of chronic obstructive lung disease however.

Seven of the eight studies showed an increase in risk, but none was statistically significant. The combined estimate from all studies is highly significant—relative risk 1.25 (95% CI 1.10–1.43; p<0.001). This direct
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Fig. 2 Relative risk estimates with 95% confidence intervals from 8 prospective (open circles) and case-control or cross-sectional (solid circles) studies of spouse smoking and chronic respiratory disease in non-smokers with summary estimate. Reference numbers to individual studies are shown; separate data are shown for females (F) and males (M) where available.

The conclusion that passive smoking causes chronic respiratory disease in adults is further supported by studies showing impaired lung function (peak expiratory flow rate and spirometry) in exposed compared to unexposed never-smokers. Environmental tobacco smoke is irritant and likely to exacerbate asthma. However, there are few published data on adults shown to have asthma (reversible airways obstruction) beyond the above studies in which the subjects mostly had chronic bronchitis and emphysema. There is by contrast a large body of evidence on asthma in children, discussed below.

Respiratory illnesses in children

Cotinine measurements have shown that infants and children whose parents smoke absorb the constituents of the environmental smoke. As with adult non-smokers who live with smokers, the exposure is approximately equivalent to actively smoking one fifth of a cigarette per day. Conclusions on environmental tobacco smoke and childhood illness are necessarily based on epidemiological studies alone, however; dosimetry calculations from studies of active smoking and adult diseases are inappropriate (see also the section by Charlton, page 98).
The epidemiological studies of parental smoking and childhood respiratory disease have been reviewed in detail by the US Environmental Protection Agency\textsuperscript{52}, whose documentation of the evidence is summarised here. The studies were considered in five groups. There is diagnostic overlap, and the first three groups might all be termed asthma.

**Acute respiratory illnesses** Review of 20 studies of acute respiratory illness in infants and older children (identified predominantly as hospital admissions with bronchiolitis or asthma) showed a greater risk in children exposed to tobacco smoke at home\textsuperscript{52}. The association was independent of birthweight and socioeconomic factors. The evidence supports a cause-and-effect relationship. The risk associated with maternal smoking was greater than that with parental smoking, favouring a causal interpretation (since exposure to maternal smoking is greater\textsuperscript{53}, as infants spend more time with their mothers than their fathers) but inconsistent with an interpretation of confounding by social class (which should apply equally to both parents). Infants aged up to 6 months were at higher risk (about 3-fold) than older infants and preschool children (50–100% excess risk) while in older children the risk was smaller still; this declining effect with age also favours a causal interpretation, since infants spend more time at home with their mothers than older children.

**Cough, sputum and wheezing** Results of 26 studies of the prevalence of cough, sputum and wheezing in children showed that parental smoking increased risk, more so in infants (about two-fold risk) than school age children (about 50% excess risk)\textsuperscript{52}.

**Asthma** Ten studies have shown that passive smoking increases the frequency and severity of episodes of asthma in children who already have the disease, and increases the number of new cases (again by 50–100%)\textsuperscript{52}. The demonstration of reduced lung function (spirometry and peak flow rate) in children of mothers who smoked, compared to children whose mothers did not smoke, supported the conclusion. The effect was not attributable merely to the irritant nature of tobacco smoke because decreased lung function was apparent long after the last exposure.

**Acute and chronic middle ear disease** Results of 15 epidemiological studies suggested that the association between parental smoking and middle ear disease was likely to be one of cause and effect\textsuperscript{52,55}, with an increase in risk of 50%. The finding of a linear dose-response relationship
between salivary cotinine levels and the presence of abnormal tympanometry was persuasive.

**Sudden infant death syndrome** Eleven published studies have examined the effect of maternal smoking on the risk of sudden infant death syndrome (SIDS) and together they show an approximate doubling in risk. In most of the studies, however, exposure was defined as maternal smoking during the pregnancy. While exposure is likely to continue after birth in almost all cases, it is difficult from such studies to distinguish the effects of exposure before or after birth. If one-third of women smoked during and after pregnancy, and smoking doubled the risk of SIDS, then 25% of all cases would be attributable to smoking; this ‘attributable proportion’ will decline as the prevalence of maternal smoking during and after pregnancy declines.

**Conclusions** There is diagnostic overlap between the above five groupings, but the fact that a positive association was observed within each grouping weights against any diagnostic bias. The evidence strongly supports a conclusion that parental smoking increases the risk of respiratory illness in infancy and childhood. The consistent association in epidemiological studies (prevalence of illness increased by 50–100% in infants and preschool children) is confirmed by the stronger relationship with maternal than paternal smoking and in younger than older children, the linear relationship between cotinine and tympanometry and the demonstration of reduced lung function in children of parents who smoke.

**Passive smoking in pregnancy**

Active smoking by pregnant women reduces birthweight (by about 200 g on average) with an associated increase in perinatal mortality of about 28%\(^5\). In three studies comparing the birthweight of babies born to non-smoking women exposed and unexposed to other people's tobacco smoke, the difference in birthweight was 24 g\(^5\). This difference is greater than would be expected from linear dosimetry (reducing the above estimate of 200 g by the ratio of tobacco smoke exposure associated with passive and active smoking). The three studies may therefore have failed to adequately control for confounding factors. Despite this uncertainty, however, some effect is likely and the Independent Scientific Committee on Smoking and Health recommended the avoidance as far as practicable of exposure to other people's smoke during pregnancy.\(^5\)
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Fig. 3 Relative risk estimates with 95% confidence intervals from 12 prospective (open circles) and case-control or cross-sectional (solid circles) studies of spouse smoking and ischaemic heart disease in non-smokers, with summary estimate. Reference numbers to individual studies are shown; separate data are shown for females (F) and males (M) where available.

Ischaemic heart disease

The evidence on environmental tobacco smoke exposure and ischaemic heart disease (IHD) is difficult to interpret. Figure 3 shows the relative risk estimates from 12 prospective and case-control or cross-sectional studies of passive smoking and IHD15,27,44,48,49,51,58-64. The combined estimate is 1.3 (95% CI 1.2–1.4; p<0.001), and each individual study is consistent with this overall estimate of 1.3. The effect of the misclassification bias is negligible in the case of IHD because the relative risk with active smoking is much smaller for IHD than lung cancer.

Simple dosimetry considerations are inconsistent with this estimate of 1.3. Actively smoking 20 cigarettes per day approximately doubles the risk of IHD at the age of 60–65 years (the average age at death in the above 12 studies). It is implausible that an exposure equivalent to 1% of this should produce nearly half the mortality effect. The expected relative risk of IHD associated with passive smoking from linear dosimetry would be 1.01 (1% of the excess risk of 100%).

In view of this inconsistency, the association observed in the epidemiological studies might be attributed to confounding. Dietary antioxidant vitamins (markers for fruit and vegetable consumption) are associated with the risk of IHD in observational studies, the association is independent of serum cholesterol and other risk factors for IHD, and dietary intake of the vitamins differs between non-smokers married to smokers and to non-smokers38,39. Attributing all of the observed
association to bias is as implausible as attributing it all to cause and effect, however, because it is difficult to envisage any confounding or other bias that would apply to passive smoking but not to active smoking. The dietary differences between smoking and non-smoking households would affect studies of active smoking as well as passive smoking. Attributing the relative risk estimate of 1.3 for passive smoking to dietary confounding implies that about half of the association with active smoking is also spurious. Yet a great deal of evidence indicates that this is not the case: the excess risk is largely reversed several years after stopping smoking for example. Also, experimental exposure of animals to environmental tobacco smoke has produced atheromatous disease\textsuperscript{65,66}, to an extent that would suggest a moderate increase in the risk of IHD in humans.

Glantz has proposed a causal mechanism whereby active and passive smoking might increase the risk of IHD to a similar extent\textsuperscript{65,66}. It is likely that active smoking increases the risk of IHD in part by increasing platelet adhesiveness, and he cites evidence suggesting similar effects of passive and active smoking on platelet adhesiveness—a maximal response at very low exposure. This proposal cannot be definitively accepted, if only because of the absence of any evidence that the measurements of platelet adhesiveness reflect platelet behaviour \textit{in vivo}, or of any epidemiological evidence directly relating these measures of platelet adhesiveness to the incidence of IHD. But they lend some support to an acceptance of the results from the epidemiological studies.

The best interpretation may be that the association is partly due to confounding (hence a small part of the association between active smoking and IHD is also due to confounding), and partly indicates a causal relationship (hence at least one mechanism whereby smoking increases the risk of IHD is maximal at very low dose). However, no definitive conclusion is possible.

\textbf{Other smoking related diseases}

Active smoking increases the risk of several other important conditions including stroke, aortic aneurysm, peripheral vascular disease, peptic ulcer, hip and other age related fractures, cataracts and periodontal disease. The mortality and morbidity attributable to these conditions is so great that an excess risk attributable to passive smoking of even 1 or 2\% (as predicted from linear dosimetry) would be important. However, the direct data from epidemiological studies are too limited to support any conclusion\textsuperscript{44}. The dosimetry may be non-linear—there could be a threshold effect with no excess risk at low dose, or there could be a
maximal response at very low dose as has been proposed for IHD\textsuperscript{65}. No conclusion can be made in relation to these diseases.

**Conclusions**

There is strong and consistent evidence that passive smoking increases the risk of lung cancer and the risk of respiratory diseases in children and in adults. Several hundred lung cancer deaths per year in Britain\textsuperscript{57}, and about 3,000 in the USA\textsuperscript{52}, could be attributable to environmental tobacco smoke exposure, as well as a great deal of morbidity from asthma in children. There is inconsistency between direct estimates and projected estimates from studies of active smoking based on dosimetry in the evidence relating to pregnancy and to ischaemic heart disease, but some effect is likely. The overall hazard is sufficient to justify measures to prohibit or restrict smoking in public places and workplaces, and health education campaigns to discourage people from smoking in their homes.

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