Effect of passive smoking on health

More information is available, but the controversy still persists

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In 1928 Schönherr proposed that lung cancers among non-smoking women could be caused by inhalation of their husbands' smoke.[1] Since then a substantial body of research has appeared, but the impact of environmental tobacco smoke on health remains under dispute.[2] The paper by Enstrom and Kabat in this week's *BMJ* will add to this debate.[3]

Given the small health risks associated with exposure to environmental tobacco smoke and thus the large study sizes required, meta-analysis has played an important part in establishing the apparent adverse health effects. A controversial issue in this regard relates to an analysis of the American Cancer Society's first cancer prevention study, funded by the tobacco industry.[4] This has not generally been included in meta-analyses, although it would contribute the largest number of events to such an analysis. The main argument advanced for not including it in meta-analyses is that the published analysis of the study was not presented in a format that allowed for the combination of equivalent effect estimates across studies.

Enstrom and Kabat have analysed the Californian subsample of the American Cancer Society's first cancer prevention study (ACSI), with considerable additional follow up, and have presented data in a format that allows inclusion in future meta-analyses. They interpret their findings as null, although, inevitably, statistical uncertainty remains. They may overemphasise the negative nature of their findings. With respect to chronic obstructive pulmonary disease—plausibly related to exposure to environmental tobacco smoke—the estimates based on the most accurately classified exposure groups give relative risks of 1.80 in men and 1.57 in women. These are said to be non-significant, but combining them—and there is no good evidence that exposure to environmental tobacco smoke has a different effect for men and women—gives a relative risk of 1.65 (95% confidence interval 1.0 to 2.73). A substantial increased risk of chronic obstructive pulmonary disease could result from exposure to environmental tobacco smoke.

Despite this it is certain that this paper will be hailed as showing that the detrimental effect of passive smoking has been overstated, and controversy will continue. What are the issues? Confounding is clearly important, and individuals exposed to environmental tobacco smoke may display adverse profiles in relation to socioeconomic position and health related behaviours. The American Cancer Society's first cancer prevention study was established in 1959, when smoking was much less associated with such factors than it currently is in the United States. It could be argued that this is why smaller risks associated with environmental tobacco smoke are seen in the first, compared to the second, American Cancer Society study (ACS II).[5] In the second study with participants recruited in 1982, women exposed to environmental tobacco smoke had less education than those unexposed,[5] as opposed to the lack of any such gradient in the first study. Similarly among men in the 1982 cohort there was little educational gradient, whereas among men in the 1959 cohort the exposed group had more education than the unexposed group. These figures reflect changing social gradients in smoking among men and women over time. Socioeconomic confounding in the second study would lead to overestimation of the effect of environmental tobacco smoke, whereas there is relatively little confounding in the first study, and what confounding there is could lead to underestimation of the effects of environmental tobacco smoke. The findings of the two studies are, in some respects, in line with this—in the second study exposure to environmental tobacco smoke was associated with increased risk of mortality due to coronary heart disease,[5] while this is not seen in the first study.[3]

Misclassification is a key issue in studies of passive smoking. It is not being married to a smoker—the indicator of exposure to environmental tobacco smoke used in the paper by Enstrom and Kabat—that leads to disease; rather, it is the inhalation of environmental tobacco smoke. As an indicator of exposure to environmental tobacco smoke the smoking status of spouses is a highly approximate measure. This will lead to the risk associated with environmental tobacco smoke being underestimated. Conversely misclassification of confounders can lead to statistical adjustment failing to account fully for confounding, leaving apparently "independent" elevated risks that are residually confounded.[6] Methods of statistically correcting for misclassification both in the exposure of interest and in confounders exist, but they are highly dependent on the validity of assessments of measurement imprecision.[6] In the field of passive smoking the tobacco industry has eagerly discussed measurement error that would lead to the effect of passive smoking being overestimated, and it relies on the work of its consultants in this regard[7] while ignoring misclassification that would lead to underestimation of the strength of the association between environmental tobacco smoke and disease.[2]

A second approach to evaluating the risks of passive smoking is to assess the exposure to known carcinogens produced by environmental tobacco smoke. Tobacco industry consultants have repeatedly said that levels of such exposures are too low to be of concern and that even a heavily exposed passive smoker inhales much less than the equivalent of one cigarette a day.[2] However, the amount of exposure to the over 4000 compounds within cigarette smoke differs between passive and active smokers, since sidestream and mainstream smoke have different compositions. Metabolites of the tobacco specific nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone are excreted in urine, and concentrations in non-smoking women married to smokers are about 6% of those of their spouses.[8] Given the strength of relation between active smoking and lung cancer, exposure to 6% of the dose that is received by an active smoker could easily produce the level of risk

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associated with passive smoking.[9] However, the exact factors in cigarette smoke responsible for its detrimental health consequences are not fully understood, and such calculations are approximate.

The considerable problems with measurement imprecision, confounding, and the small predicted excess risks limit the degree to which conventional observational epidemiology can address the effects of exposure to environmental tobacco smoke. Randomised controlled trials of exposure to environmental tobacco smoke will clearly not be carried out, but understanding could be improved through Mendelian randomisation.[10]

Genetic polymorphisms that are associated with poor detoxification of carcinogens in tobacco smoke have been identified. The distribution of these polymorphisms in the population will not be associated with the behavioural and socioeconomic confounders that exposure to environmental tobacco smoke is. Among people unexposed to the carcinogens in environmental tobacco smoke there is no reason to believe that the detoxification polymorphisms should be related to risk of lung cancer. However, among those exposed to environmental tobacco smoke a decrease in the ability to detoxify such carcinogens should be related to risk of lung cancer, if exposure to environmental tobacco smoke is indeed responsible for increased risk of lung cancer. One study showed that a null (non-functional) variant of one such detoxification enzyme, glutathione S-transferase M1, was associated with an increased risk of lung cancer in non-smoking women exposed to environmental tobacco smoke, but not in non-exposed non-smoking women.[11] A later study failed to confirm this finding,[12] reflecting one limitation of Mendelian randomisation, which is that large sample sizes are required to produce robust results. However, this is a promising strategy if we really want to know whether passive smoking increases the risk of various diseases.

George Davey Smith *professor of clinical epidemiology*

Department of Social Medicine, University of Bristol, Bristol BS8 2PR

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The therapeutic effects of meditation

The conditions treated are stress related, and the evidence is weak

Meditation includes techniques such as listening to the breath, repeating a mantra, or detaching from the thought process, to focus the attention and bring about a state of self awareness and inner calm. There are both cultic and non-cultic forms, the latter developed for clinical or research use. The relaxation and reduction of stress that are claimed to result from meditation may have prophylactic and therapeutic health benefits, and a plethora of research papers purport to show this. However, this research is fraught with methodological problems, which I outline here, along with a short summary of the best evidence for the therapeutic effects of meditation in clinical populations. There is no Cochrane review on meditation.

Showing that certain physiological effects such as a slowed heart rate or a particular electroencephalographic pattern occur during meditation and characterise a "relaxed state" may give insight into how meditation works but does not prove its therapeutic value. Most trials of the cumulative effects of meditation have had weak designs. Trials of transcendental meditation (a popular form of mantra meditation), when controlled at all, often compared self selected meditators with non-meditators or long term meditators with novices. These trials did not control for systematic differences between people who elect to learn the technique and those who do not, and between people who persist with the practice and those who abandon it. Randomised trials have often recruited favourably predisposed subjects so that expectations of benefit differ from control subjects. In trials of transcendental meditation for cognitive effects I found that positive outcome was confined to trials with subjects so recruited and to trials with passive controls such as "eyes closed rest." Trials with naive subjects and plausible controls (for example, pseudo-meditation) were negative. A similar association was previously found in a meta-analysis of cognitive behavioural techniques (including meditation) for hypertension.[1] Other weaknesses have been use of multiple co-interventions, high attrition, and inadequate statistical analysis. Recent trials in clinical

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