

- 29 Lehnert G, Garfinkel L, Hirayama T, *et al.* Round table discussion from symposium on medical perspectives on passive smoking (Vienna, April 1984). *Prev Med* 1984;13:732-3.
- 30 Russell MAH, Jarvis MJ, West RJ. Use of urinary nicotine concentrations to estimate exposure and mortality from passive smoking in non-smokers. *British Journal of Addiction* 1986;81: 275-81.
- 31 Doll R, Peto R. Mortality in relation to smoking: 20 years' observation on male British doctors. *Br Med J* 1976;iii:1525-30.

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## Appendix

Let the number of subjects in each of the epidemiological studies be classified by disease status and exposure in this way:

	With lung cancer	Without lung cancer	Total
Living with a smoker	a	b	m <sub>1</sub>
Living with a non-smoker	c	d	m <sub>2</sub>
Total	m <sub>3</sub>	m <sub>4</sub>	T

The relative risk of lung cancer in association with living with a smoker (and its confidence limits) were then calculated as follows:

*For each of the case-control studies*—In the absence of a risk from exposure to environmental tobacco smoke the expected number of people (E) who live with a smoker and have lung cancer is  $m_1 m_3 / T$ . The difference (O-E) between observed (O) and expected (E) numbers of people with lung cancer who live with a smoker was calculated, the variance of this difference being

$$\text{Var}(O-E) = \frac{m_1 \times m_2 \times m_3 \times m_4}{T \times T \times (T-1)}$$

The natural logarithm of the relative risk (RR) was estimated for each study using<sup>19</sup>

$$\ln \text{RR} = \frac{O-E}{\text{Var}(O-E)}$$

Confidence limits for  $\ln \text{RR}$  were calculated using the variance

$$\text{Var}(\ln \text{RR}) = 1/\text{Var}(O-E)$$

and the estimate of RR and its confidence limits were estimated from the calculations on a logarithmic scale by exponentiation.

*For each of the prospective studies*—For prospective studies the

published relative risk values were used in the following calculations as in all of the articles the authors had estimated the relative risk, adjusting for variables such as age. For those studies in which relative risk estimates were given separately for different levels of smoking by the spouse<sup>12,14</sup> a combined estimate of relative risk was calculated as an average of the individual estimates, each weighted inversely proportional to its variance. (See method below for combining the prospective studies.) The variance of the natural logarithm of the relative risk was derived from the published confidence limits for the estimate of relative risk in all studies except one<sup>13</sup> (where adjustment for age seemed of little importance and no confidence limits had been published), in which the method given above for the case-control studies was used.

*For combining the results from the studies*—The method used for combining the results from the case-control studies is based on that of Yusuf *et al.*<sup>19</sup> The overall estimate of RR was calculated by adding the values of (O-E) and their variances for all the studies and using

$$\ln \text{RR} = \frac{\Sigma(O-E)}{\Sigma \text{Var}(O-E)}$$

and for the variance

$$\text{Var}(\ln \text{RR}) = \frac{1}{\Sigma \text{Var}(O-E)}$$

The method used for combining the results from the prospective studies is based on a pooled value for the  $\ln \text{RR}$  calculated as an average of the individual  $\ln \text{RR}$ s, each inversely weighted according to its variance.<sup>20</sup>

$$\ln \text{RR} = \frac{\Sigma \frac{(\ln \text{RR})}{\text{Var}(\ln \text{RR})}}{\Sigma \frac{1}{\text{Var}(\ln \text{RR})}}$$

and for the variance

$$\text{Var}(\ln \text{RR}) = \frac{1}{\Sigma \frac{1}{\text{Var}(\ln \text{RR})}}$$

The overall value for the  $\ln \text{RR}$  in all of the studies combined was obtained using the same method that was used to pool results from the prospective studies, using the overall values for the case-control and prospective studies.

### Can Fybogel sachets (*Ispaghula husk*) be taken indefinitely?

I know of no documented or anecdotal evidence of long term ill effects from taking ispaghula over many years. The only theoretical problem is of reduced calcium absorption which might lead to an increased risk of osteoporosis. Faecal calcium excretion is increased by any form of extra fibre; a short term study showed such an increase during the ingestion of ispaghula and of bran but the changes did not reach statistical significance.<sup>1</sup> It is unlikely that this would be an adverse effect of any practical importance.—JOHN R BENNETT, consultant physician, Kingston upon Hull.

1 Smith RG, Rowe MJ, Smith AN, *et al.* A study of bulking agents in elderly patients. *Age and Ageing* 1980;9:267-71.

### Can non-steroidal anti-inflammatory drugs cause tinnitus?

Tinnitus has been reported as a side effect of treatment with most, if not all, non-steroidal anti-inflammatory drugs. Most of the reports have been on clinical trials rather than as well documented case reports. The Committee On Safety Of Medicines has had a few reports with most non-steroidal anti-inflammatory drugs. The incidence appears to be low, and there is no good evidence that one non-steroidal anti-inflammatory drug is more likely to have this effect than another. In some cases tinnitus has been accompanied

by sensorineural deafness which is usually reversible though one case of irreversible deafness has been reported with piroxicam.<sup>1</sup> I was unable to find any studies of the mechanism of this effect, but aspirin produces dose related cochlear toxicity characterised by depolarisation of the cochlear apparatus with reduced hearing over the whole frequency range.<sup>2</sup>—LINDA BEELEY, consultant clinical pharmacologist, Birmingham.

1 Vernick DM, Kelly JH. Sudden hearing loss associated with piroxicam. *Am J Otol* 1986;7:97-8.

2 Dukes MNG, ed. *Meyler's side effects of drugs*. 10th ed. Amsterdam-New York-Oxford: Elsevier, 1984:143.

## Correction

### Severe hypermagnesaemia due to magnesium sulphate enemas in patients with hepatic coma

We regret that an error occurred in this paper by Dr P O Collinson and Dr A K Burroughs (18 October, p 1013). In figure 2 it is stated that calcium is represented by blocked circles and magnesium by blocked squares. It should have said that calcium is represented by blocked squares and magnesium by blocked circles.