available both before and during N-acetylcysteine treatment.

In conclusion, we still find that most of the observed effect on prothrombin index in our study is due to N-acetylcysteine.

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Mortality and indicators of traffic-related air pollution

Sir—Gerard Hoek and colleagues (Oct 19, p 1203)[1] relate mortality to small-scale variability in air pollution. However, a methodological factor might have resulted in underestimation of the CIs about the point estimates of the pollutant effects.

Study participants were recruited from 204 municipalities in the Netherlands. Hoek and colleagues adjusted for various confounding variables, but they did not account for geographical clustering of the participants. Individuals from the same, or neighbouring, municipalities might share characteristics not captured by the variables used for confounder adjustment. Such potential clustering should therefore have been accounted for in the statistical analysis.[2]

Another intriguing issue is the number of participants influencing the results. We are informed that 5% of participants lived close to a major road, 3% within 100 m of a freeway, and 2% within 50 m of a major urban road. If we assume that the distribution of residence locations was roughly similar among deceased individuals, then among the 185 who died from cardiopulmonary causes, ten would have lived close to a major road, six within 100 m of a freeway, and four within 50 m of a major road. Table 4 presents the results of regression models in which living near a major road was included as an independent variable. For black smoke and nitrogen dioxide, the point estimates are close to 2, and the 95% CIs range from 1·1 to 3·5. If, in fact, these estimates are derived from the experience of only ten deceased individuals who lived near these roads, then one must wonder about the generalisability of the results and the width of the CIs. In the same table, the CIs for the estimates of the effect of background concentrations of the pollutants range from about 0·7 to 2·6, on the basis of 185 deaths. I am surprised that the CI on ten deaths should, in comparison, be so narrow.

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Authors' reply

Sir—The first issue that Murray Finkelstein raises was discussed on page 1208 of our paper, where we referred to the more recently developed methods of adjustment for spatial autocorrelation in air pollution epidemiology. We mentioned that non-use of these methods might result in underestimation of SEs, although we admit that the actual sentence in the paper could be interpreted differently. We adjusted for area-level confounders in addition to individual-level confounders to account for part of the clustering. Since we also assessed exposure to air pollution on a detailed spatial scale, we expect that the lack of adjustment for spatial autocorrelation will not have led to substantial underestimation of the SEs. More importantly, the effect estimates themselves would not be affected. In fact, in a US cohort study, adjustment for spatial clustering had very little effect on effect estimates or CIs.[1]

The second issue of generalisability is important. Contrary to what Finkelstein suggests, the number of cardiopulmonary deaths seen among those living near main roads was in the order of 20, not ten (the relative risk was close to 2). Comparison of CIs of a categorical variable (living near a major road) and a continuous variable (background air pollution) is not informative, since the CI for a continuous variable depends on the selected range used for presenting relative risks. We selected an increment that was about the difference between the 5th and 95th percentile—ie, a large increment. The confidence limits depend not only on the number of deaths of those living near a major road, but also on the number of deaths of those not living near a major road and the person-time in the cohort of about 5000 individuals who were followed up for 8 years.

Nevertheless, expansion of the analysis to the full cohort—which is now in progress—and repetition of the study in other populations is important.

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1 Pope CA III, Burnett RT, Thun MJ, et al. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *JAMA* 2002; **287:** 1132–41.

The ISAT trial

Sir—We agree with the International Subarachnoid Aneurysm Trial (ISAT) collaborative group (Oct 26, p 1267)[1] that endovascular coiling is safe compared with surgical clipping in the first year after aneurysm treatment. However, we do not think that the report answered the question of efficacy.

In the treatment of ruptured intracranial aneurysm, the primary objective is the prevention of rebleeding. The most important predictive factor for rebleeding after aneurysm treatment is post-treatment residual aneurysm. According to the ISAT protocol, every patient who underwent endovascular coiling had a 6-month follow-up cerebral angiography. Since this interim report was based on the 1-year follow-up data, we were surprised that the authors did not report on the rate of complete occlusion of aneurysm based on the 6-month angiography results in the endovascular coiling group. Endovascular coiling is known to be associated with a substantial rate of incomplete obliteration of intracranial aneurysms (15–46%).[2,3] A substantial proportion of post-treatment residual aneurysms will have further growth if left without definitive treatment such as surgical clipping or second endovascular coiling.[4,5]

If there were a significant proportion of patients with residual aneurysm after