have yet to show progression of hypothesis given the presence of widespread availability of the potent treatment, none of these five patients had in common clinical presentation undocumented. We reported five natural history of specific AIDS-related opportunistic infections such as CMV retinitis who began only after retinitis was diagnosed. Third, the nadir CD4 counts reported, ranging from 14 to 82 cells/μL, were obtained 1–17 weeks before HAART was initiated. And last, of the patients enrolled in ACTG 1995; 349: 1443-45.

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and mortality, particularly in patients with impaired autonomic thermoregulation. Depending on environmental conditions and other risk factors, failure of autonomic or behavioural thermoregulation can cause fluctuations of core temperature or overt hypothermia or hyperthermia with potentially lethal consequences. Even small decreases in core temperature can induce striking changes in cardiovascular, (neuro)physiological, and immunological responses; hence, core temperature should be taken into account in the analysis of cold-related disorders. Since core temperature and underlying medical disorders were not evaluated in the Eurowinter study, the relation between these variables and cold-related mortality remains uncertain.

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1 The Eurowinter Groups. Cold exposure and winter mortality from ischaemic heart disease, cerebrovascular disease, respiratory disease, and all causes in warm and cold regions of Europe. Lancet 1997; 349: 1341–46.

SIR—The Eurowinter Group's report on cold exposure and winter mortality, presents important findings, but the investigators draw inferences beyond the limits of the data and study design. First, in an ecological study of this sort individual risk factors are not related to individual outcomes; thus, causality cannot be proved. To demonstrate associations in an ecological study, it is essential that the populations used should be as similar as possible with respect to time and population characteristics. We assume that quota sampling was used to obtain the survey sample in this study, although the methods are not made explicit. This method is likely to have resulted in an unrepresentative population. For example, population groups unavailable at the time of survey, (eg, shift workers, and those without permanent residence) may not have been included. Such potential sources of bias have not been assessed in this study.

Second, the study is limited in its approach to the explanation of potential protective and risk factors for cold-related deaths. For example, it would have been helpful to take into account race, family history, diet, and other cultural factors. Genetic variation in both risk factors for cardiovascular disease and adaptation to cold may affect mortality outcomes. In addition, although the wearing of hats may be an important protective measure, it is likely that hat wearing is determined by other cultural factors as well as outdoor temperatures.

This is an important research study that has highlighted significant associations between mortality and cold exposure, but the data and study design do not support conclusions about causality. The logical next step should be prospective studies of the relation between cold exposure and mortality. Such studies could also examine the effects of climate on morbidity, which may be equally important.

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SIR—The report by the Eurowinter Group¹ presents fascinating evidence that the association between low temperature and mortality is not constant across Europe. The finding that the slope of the association is steeper in countries with warmer winters may have implications for interpretation of studies of the association between daily mortality and air pollution. Although most of these studies found a positive association, even after statistically controlling for daily mean temperature, there are some inconsistencies with respect to the strength of the association. We suggest that part of this inconsistency between studies may be attributable to residual confounding by temperature. The argument is as follows: (1) daily temperature is inversely correlated with daily concentrations of sulphur dioxide and particulates; (2) temperature is inversely related to mortality; and (3) crude (bivariate) association between pollution and mortality is substantially attenuated by adjustment for temperature, suggesting a confounding role of temperature. It is plausible that the use of a single daily value of temperature may not be sufficient to remove entirely all the effect of temperature. Additionally, any residual confounding by temperature would be stronger in southern countries where the slope of the association between temperature and mortality is steeper.

As a consequence, the effects of pollution would seem stronger in countries with warmer winters.

This is the case in the APHEA project which analysed daily mortality and air pollution in several European countries. In this project, the effect of air pollution was apparent in centres in western and south Europe, but was weak or absent in central Europe.² Explanation for this inconsistency is not clear. We speculate that the difference in the effects of pollution between the regions can be caused by differences in winter temperatures, since average winter temperatures in central Europe were substantially lower than in the west or south (table). Unfortunately, the effects of daily concentration of pollutants on deaths were not presented in identical units in the APHEA reports, and this speculation cannot be directly examined in published data. However, this is a testable suggestion that may also be relevant for studies outside Europe.

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1 The Eurowinter Group. Cold exposure and winter mortality from ischaemic heart disease, cerebrovascular disease, respiratory mortality, and all causes in warm and cold regions of Europe. Lancet 1997; 349: 1341–46.
2 The APHEA Project. Short term effects of air pollution on health: a European approach using epidemiological time series data. 3 Epidemiol Comm Health 1995; 50 (suppl 1): S1–S80.

Authors' reply
SIR—Marius Mackenzie asks whether the large differences in winter mortality that we reported between different regions of western Europe were attributable to the concomitant differences that we reported in cold exposure.

Our study did deal with the main alternative possibilities that he suggests. Variations in age structure were avoided