INTRODUCTION
Epidemiologic studies have shown an association between airborne particles and mortality data, but uncertainty persists as to which aspects of the particle mixture are the driving force underlying observed associations. Further, only a small number of studies have investigated the role of ultrafine particles (particles less than 0.1 µm in diameter). Although ultrafine particles contribute little to mass concentration, they are present in urban air in high numbers and may be important in terms of health effects. One hypothesis is that these particles may be particularly toxic because their small size allows them to deposit efficiently deep in the lungs and that the higher number of ultrafine particles, and therefore their greater total particle surface area, may increase their toxicologic effects. However, the few epidemiologic studies that have tried to isolate effects of ultrafine particles have evaluated respiratory disease, not deaths.

APPROACH
Dr H-Erich Wichmann and colleagues at the National Research Center for Environment and Health (GSF) in Neuherberg, Germany, prospectively studied the association of daily mortality data with the number and mass concentrations of ultrafine and fine particles in Erfurt, Germany. Using a time-series approach, they looked at short-term changes in particle concentration and the concurrent deaths due to cardiovascular and respiratory causes. Concentrations were measured at one monitoring site, which was close to a road, and mortality was analyzed for 3.5 years. Because Erfurt had a population of roughly 200,000 people, the number of deaths was small (average 5 to 6 deaths per day). The analytic technique that the investigators developed to gather air pollution data, especially monitoring of the ultrafine fraction, was unique in the sharp detail of the size ranges. The statistical methods were Poisson regression with a generalized additive model to smooth time trends, weather, and other variables.

RESULTS AND INTERPRETATION
The authors evaluated whether human deaths were associated in time with levels of outdoor particles (that is, whether the measured day-to-day changes in air pollution related to the day-to-day changes in deaths). If air pollution and adverse health outcomes are closely linked in time, then a daily average value of air pollution will be associated with a daily measure of health. This relation was estimated in the current study by relative risk, the relative increase in deaths given the range of particulate pollutants.

Timing of effect was evaluated by examining pollutant levels on the current day (lag 0), the prior day (lag 1), 2 days prior to death (lag 2), and so on, up to 5 days prior to death (lag 5). A lag is the assumed time period between exposure and effect and can be represented by the best single day or an average of the effect over multiple days. Currently, no biological evidence supports a particular lag. Although many investigators of time-series studies have used the best lag approach, this method can bias the results toward finding positive or negative statistically significant associations.

This study was the first to show that ultrafine particles are associated with human mortality. The investigators found comparable effects for ultrafine and fine particles and have reported a suggestion of a delayed effect for ultrafine particles versus an immediate effect for fine particles. The HEI Health Review Committee agreed with the investigators’ conclusions that associations between mortality...
and ultrafine and fine particles were observed; however, the Committee did not agree that a consistent pattern indicating either a delayed or an immediate effect existed. This study is a major contribution to our knowledge of actual airborne particle levels, and it has provided the first evidence that ultrafine particles as well as fine particles are associated with mortality. Despite the unique analytic technique developed by the investigators, important limitations to the results remain (specifically regarding interpretations of timing of effect). Although the results associate the ultrafine fraction with human deaths, no clear pattern of associations indicates temporal differences between ultrafine and fine particles.