association between [chronic PM] air pollution exposure and health [mortality]. In applying these criteria, I have included experimental studies in animals and epidemiologic studies in humans (6). Rodents exposed to high concentrations of diesel exhaust for life did not show early or increased mortality (6). The available epidemiologic studies (3–5) showed only weak associations across a narrow exposure range. The possible role of PM and lung function in the Six Cities Study suggested that there were differences in lung function between cities, but no measurable effect attributable to PM$_{2.5}$. In the Seventh Day Adventist Study (5), there appeared to be a coherent relationship between PM and self-reported symptoms, but not between PM and mortality. However, the analyses required to evaluate fully this PM–symptoms association were not reported. Furthermore, short-term exposures and hospital admissions may have little to no relevance for mortality from chronic exposure (6,11). Finally, individual-level measurements of an analogous surrogate PM$_{2.5}$ exposure from the same populations and same cities provided a test of the internal consistency and biological coherence of the ambient PM$_{2.5}$ associations. I know of no other experimental or clinical human studies that can be used as a more appropriate test.

I did not say or imply that all of Hill’s (1) criteria must be obeyed before accepting cause and effect. The only criteria that must be met is that exposure must precede the effect (6,12). I agree with Loomis et al. that Hill’s (1) guidelines can be “helpful at the margins of epidemiologic interpretations” (as with PM), but also provide a good framework for assessing causality in general. I do not believe that evidence was excluded, as alleged by Loomis et al., although further tests of the plausibility and coherence of these associations with PM may be possible.

Regarding the use of Hertz-Picciotto’s criteria (2), my point was to assess whether the EPA was justified in developing quantitative concentration–response information useful in developing an annual PM$_{2.5}$ standard from these studies. Table 5 in my paper (6) was an attempt to do this; because both studies were of the same design, the criteria were applied to both the design and the two individual studies. I concluded (6) that none of the Hertz-Picciotto criteria for quantification of risk and setting air quality standards using [these] epidemiology studies are met.

I believe these are useful guidelines and that they do “contribute to a firmer scientific foundation for low-dose risk estimates and the ensuing regulatory actions” (2).

I suggest that the tobacco analogy analysis provides evidence “that a given type of bias did ... occur” and that it did “quantify its direction and magnitude,” as stated by Loomis et al., within the limits of the data available. It was only possible to suggest possible sources of bias. The magnitude of the confounding could not be calculated as suggested by Loomis et al. for several reasons. The univariate distributions were not provided in the reports of these studies. The bivariate distributions based on individual-level data cannot be determined (6) because the exposure variable is based on aggregate data. Sensitivity analyses are valuable, but I suggest that the tobacco analogy provides a useful and fundamentally sound method for what Loomis et al. describe as “quantitative exploration of potential biases.”

I suggest that one cannot be sure, with any degree of certainty, that studies using group-level measures of exposure are free from the potential biases affecting completely ecological designs. This is an area where research using individual-level data is needed to improve the quality of information used to guide regulatory decisions.

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“Double Exposure”: How Real Is It?

The Focus article “Double Exposure” (EHP 107:A196–A201 (1999)) is, for the most part, nothing more than the continued complaining of those who don’t realize that living is a hazard. They would place a risk on everything and then ignore those they don’t like. I would like to challenge Manuel to provide a laboratory analysis from any reliable source [the American Cancer Society (ACS), etc.] that can identify even half of the stated 4,500 components he cites. The ACS stated that ≥2,000 components were present in smoke, but when asked to list them, they could not. The California Air Resources Board cites <50 components at current detectable levels. Only the tars and benzo[a]pyrene have even been proven harmful to rats, and this has been in massive doses. As a retired chemical engineer with an extensive background in chromatography and mass spectrometry, I can say with certainty that if 4,500 components exist in tobacco smoke, then the clean air we breathe must contain 6,000 or more. At 66 years of age and a smoker of over two packs of cigarettes a day for 47 years, I was recently rejected for a Veterans’ Administration lung health study because my lungs were “too healthy.” Three guesses what their study results will show.

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Response to Briggs

The figure of more than 4,500 compounds in tobacco smoke was obtained from an article titled “Assessment of Exposure to Environmental Tobacco Smoke” (1). The U.S. Environmental Protection Agency (2) cites a figure of “more than 4,000 compounds” in its 1992 report. A table of many of the constituents is listed on pages 3–5 through 3–9 of that report.

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