years since cessation, and residential and occupational second-hand smoke exposure) and air pollution exposures, which limits any positive bias in our results. While the potential for response and recall bias exists in all case-control studies, this population-based study has a relatively high response rate for cases (62%) and controls (67%). Furthermore, we found no difference between cases and controls in the completeness of the self-reported residential histories that we used to assign air pollution exposures.

Our long-term exposure assessment approach represents clear improvements over past studies. Specifically, we included complete residential histories over a 20-year period and applied multiple spatiotemporal models of $PM_{2.5}$, NO_2, and O_3. While some degree of exposure misclassification is present, this error is likely nondifferential and thus would produce bias toward (rather than away from) the null. As reported,[2] the increased lung cancer odds ratio for NO_2 exposures derived from fixed-site monitors likely represents contributions from $PM_{2.5}$ due to the high correlation of these two pollutants. Furthermore, all other sensitivity analyses using various spatiotemporal models revealed consistent associations. Thus, our study offers a useful contribution to the epidemiologic evidence regarding air pollution exposure and lung cancer incidence.

While we made no claims of a causal association in our article, we concur with recent commentaries[4] and systematic reviews and meta-analyses[5,6] that the current weight of evidence supports an association of $PM_{2.5}$ and NO_2 exposures with lung cancer incidence. Whether these associations are causal is the focus of the upcoming International Agency for Research on Cancer monograph evaluating the carcinogenicity of ambient air pollution.[7] We do note, however, that the Environmental Protection Agency's Integrated Science Assessment[8] mentioned by Drs. Sax and Goodman concluded that the evidence is "suggestive of a causal relationship between long-term exposures to $PM_{2.5}$ and cancer." We also highlight that NO_2 itself is not likely to be responsible for the increase in lung cancer risk but rather is a marker for other traffic-related carcinogens.

Perry Hystad
School of Population and Public Health
University of British Columbia
Vancouver, BC, Canada
phystad@gmail.com

Paul A. Demers
Occupational Cancer Research Centre
Cancer Care Ontario
Ontario, Canada

Kenneth C. Johnson
Department of Epidemiology and Community Health
University of Ottawa
Ottawa, Ontario, Canada

Richard M. Carpiano
Department of Sociology
University of British Columbia
Vancouver, BC, Canada

Michael Brauer
School of Population and Public Health
University of British Columbia
Vancouver, BC, Canada

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Nonmalignant Respiratory Disease Mortality in Styrene-Exposed Workers

To the Editor:

Collins and colleagues[1] focus on cancer risk in their study of more than 15,000 workers at 30 US reinforced-plastic facilities. Yet their demonstration of excess mortality from nonmalignant respiratory disease warrants further discussion. For this cohort of styrene workers, the standardized mortality ratio (SMR) for "bronchitis, emphysema, and asthma" was elevated at 1.35 (95% confidence interval [CI] = 1.17–1.56).

The authors attribute this excess of deaths to smoking. Certainly, smoking is a recognized contributor to obstructive lung diseases. Furthermore, the observed inverse relationship with employment duration may appear to be inconsistent with an occupational cause of disease. However, previous studies have demonstrated excess mortality from nonmalignant respiratory disease in short-term styrene workers. An earlier examination of this same cohort found excess mortality (SMR = 1.40 [95% CI = 1.04–1.84]) from "other nonmalignant respiratory diseases," with the highest risk (SMR 1.79) in those with less than 1 year of styrene exposure.[2] Similarly, among US fiberglass boat builders employed between 1959 to 1978 and followed to 1998, those with high styrene exposures had elevated mortality (SMR = 2.54 [95% CI = 1.31–4.44]) from "pneumoconioses and other respiratory diseases"; the excess mortality

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was associated with short (<1 year) employment duration.[3]

How could occupational styrene exposure be responsible for an excess of mortality from obstructive lung disease among mostly short-term workers? A recent report of obliterative bronchiolitis in styrene-exposed workers is informative.[4] Obliterative bronchiolitis is a disabling lung disease that follows, with short latency, certain inhalational exposures. Obliterative bronchiolitis is likely under-recognized and confused with other obstructive lung diseases. Hence the excess mortality due to "bronchitis, emphysema, and asthma" described by Collins et al may represent not a consequence of smoking but a burden of misdiagnosed obliterative bronchiolitis in workers who were disabled by styrene exposure early in their tenure and thus left employment.

The authors note a lack of trend between cumulative or peak styrene exposures and nonmalignant respiratory disease. Analytic approaches designed for cancer mortality may be poorly suited, however, to mortality from disease with short latency from exposure to disability. In a study of European reinforced-plastics workers, associations between short duration of exposure and nonmalignant respiratory mortality may have been obscured by an assumption that longer exposures pose greater risk.[5] In future studies of styrene-exposed workers, consideration of obliterative bronchiolitis and its mechanism, so distinct from carcinogenesis, is warranted.

Kristin J. Cummings
Division of Respiratory Disease Studies
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
Morgantown, WV
kcummings@cdc.gov

Anna-Binney McCague
Division of Respiratory Disease Studies
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
Morgantown, WV

Kathleen Kreiss
Division of Respiratory Disease Studies
National Institute for Occupational Safety and Health
Centers for Disease Control and Prevention
Morgantown, WV

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The authors respond:

Dr. Cummings[1] correctly points out that in our study[2] of the US reinforced-plastics industry, there were more deaths from bronchitis, emphysema, and asthma than expected.[1] We surmised that this excess may be due in part to cigarette smoking because several other cancers and diseases related to smoking were also elevated, and the mortality was inversely related to number of days exposed to styrene. We also found that workers with potential workplace asbestos exposure had a higher standardized mortality ratio for bronchitis, emphysema, and asthma (1.42; 95% confidence interval = 1.21–1.65) than workers without asbestos exposure (1.04; 0.69–1.51). Both smoking and asbestos are well-known risk factors for nonmalignant respiratory diseases. In our study, risks for bronchitis alone (not published) were similar to risks for the combination of bronchitis, emphysema, and asthma.

We also found no increasing risk with either cumulative or peak exposure to styrene. This finding is consistent with the large European industry-wide study that found neither an exposure response with styrene nor any excess in workers overall.[3,4] Small excesses were observed in two smaller reinforced-plastics-industry studies for nonmalignant respiratory system diseases, but no excess was observed in a large synthetic-rubber-worker study with styrene exposure.[5–7]

We agree with Dr. Cummings that obliterative bronchiolitis is a rare disease, likely underreported or misclassified on death certificates.[8] That would make it difficult to examine risk factors for this disease in a historical follow-up study, especially where smoking and other potential risk factors are not tracked and pathology reports and medical records are unavailable. Nevertheless, we found no evidence in our study that styrene exposure was a risk factor for deaths from bronchitis, emphysema, and asthma.

James J. Collins
Kenneth M. Bodner
The Dow Chemical Company
Midland, MI
jjcollins@dow.com

James S. Bus
Exponent, Inc.
Alexandria, VA

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