Advancing Understanding of Environmental Contributions to Disparities in Lung Cancer

Lung cancer is the second most commonly diagnosed and leading cause of cancer death in the United States, with an estimated 236,740 new cases and 130,180 deaths in 2022, corresponding to more than 350 lung cancer deaths per day (1). Although lung cancer survival rates are typically poor, recent advances in screening and treatment have resulted in notable declines in advanced-stage diagnoses and corresponding gains in localized-stage diagnoses and improvements in survival, with 3-year survival rates increasing to 31% overall (1). However, there are also established disparities in lung cancer incidence and survival by sex, race/ethnicity, and socioeconomic factors (1, 2).

Although cigarette smoking continues to account for the majority of lung cancer cases, there are a range of other environmental and occupational agents that are established human lung carcinogens, which also contribute substantially to the lung cancer disease burden, including ambient air pollution (3). Ambient air pollution represents a diverse mixture of particulate and gaseous components and compounds. In 2013, the evidence from studies in humans and in experimental animals, in addition to the availability of strong mechanistic evidence, was determined to be sufficient by a working group convened by the International Agency for Research on Cancer to classify outdoor air pollution and particulate matter in outdoor air as carcinogenic to humans (group 1) (4). Results from large-scale epidemiological studies conducted mainly in the United States and in Europe contributed to the classification, as did findings among never smokers. Recent meta-analyses support small but statistically significant increases in lung cancer risk associated with increasing ambient particulate matter with diameter less than 2.5 μm ($PM_{2.5}$) concentrations (5, 6); for nitrogen dioxide (NO_2), the strength of the evidence is somewhat weaker (7, 8).

Although globally cigarette smoking was estimated to contribute to 64.2% (95% uncertainly interval [UI], 61.9–66.4) of the 2.04 (95% UI, 1.88–2.19) million deaths caused by cancer of the trachea, bronchus, and lung in 2019, ambient PM pollution represented the second leading risk factor, contributing to 15.1% (95% UI, 11.3–18.9) of such deaths (3). Findings differed somewhat by sex and by country sociodemographic index (SDI). There were also differential trends in age-standardized tracheal, bronchial, and lung cancer death rates attributable to ambient PM pollution, with a 130% increase observed in countries of lower SDI over recent decades, where air quality management efforts have largely been limited, compared with a 50% decrease in countries in the highest SDI quintile (*see also* Figure 1). Occupational asbestos was the third leading risk factor (9.7%; 95% UI, 6.9–12.5) overall. Among females in the lowest SDI quintile, household air pollution from solid fuels was the leading risk factor.

Despite the established link of ambient air pollution and lung cancer, there remain outstanding research needs, including, for example, epidemiological studies in areas of higher ambient air pollution and in more diverse or susceptible populations, understanding of the toxicity of different sources and components of the air pollution mixture, and associations with specific lung cancer histologic cell types (6). There are also few studies of the impact of ambient air pollution on lung cancer survival. In one study, ambient PM and NO_2 exposures were related to poorer lung cancer survival, particularly among patients with early-stage non–small cell disease (9).

The analysis by Cheng and colleagues in this issue of the *Journal* (pp. 1008–1018) of traffic-related air pollution in the California Multiethnic Cohort provides useful findings for characterizing associations of lung cancer incidence in a racially/ethnically and socioeconomically diverse population (10). The study, motivated at least in part by findings of greater smoking-related lung cancer incidence among African American and Native Hawaiian cohort participants at lower smoking intensity (characterized as less than 10 cigarettes per day) than that in White, Japanese American, or Latino participants, which were not fully explained by self-reported or urinary biomarker smoking intensity, sought to further examine racial/ethnic differences in lung cancer risk (11).

Included cohort participants consisted of over 97,000 California (largely Los Angeles County) residents and monthly time-varying estimates of traffic-related air pollutants (nitrogen oxide [NO_x], NO_2, particulate matter with a diameter less than 10 μm, $PM_{2.5}$, carbon monoxide, ozone, benzene) at the participant residence were assessed together with detailed information on other relevant demographic, lifestyle, and personal factors, including cigarette smoking. Latino (41%) and African American (32%) participants represented the majority of the included study population and more often lived in neighborhoods characterized by lower socioeconomic status (SES) and higher average ambient air pollution concentrations. A total of 2,796 incident lung cancer cases were observed over an average 17-year follow-up period between 1993 and 2013. There were positive associations of most ambient air pollutants and lung cancer incidence overall and some suggestive findings of stronger associations of NO_x and NO_2 among participants residing in lower SES neighborhoods, with no association in higher SES neighborhoods. Findings were generally similar across histologic cell types. Results from multipollutant models indicated some stronger associations with benzene exposure overall.

Potential limitations of the study include a modest sample size in subgroup analysis, personal covariates assessed at baseline, estimated

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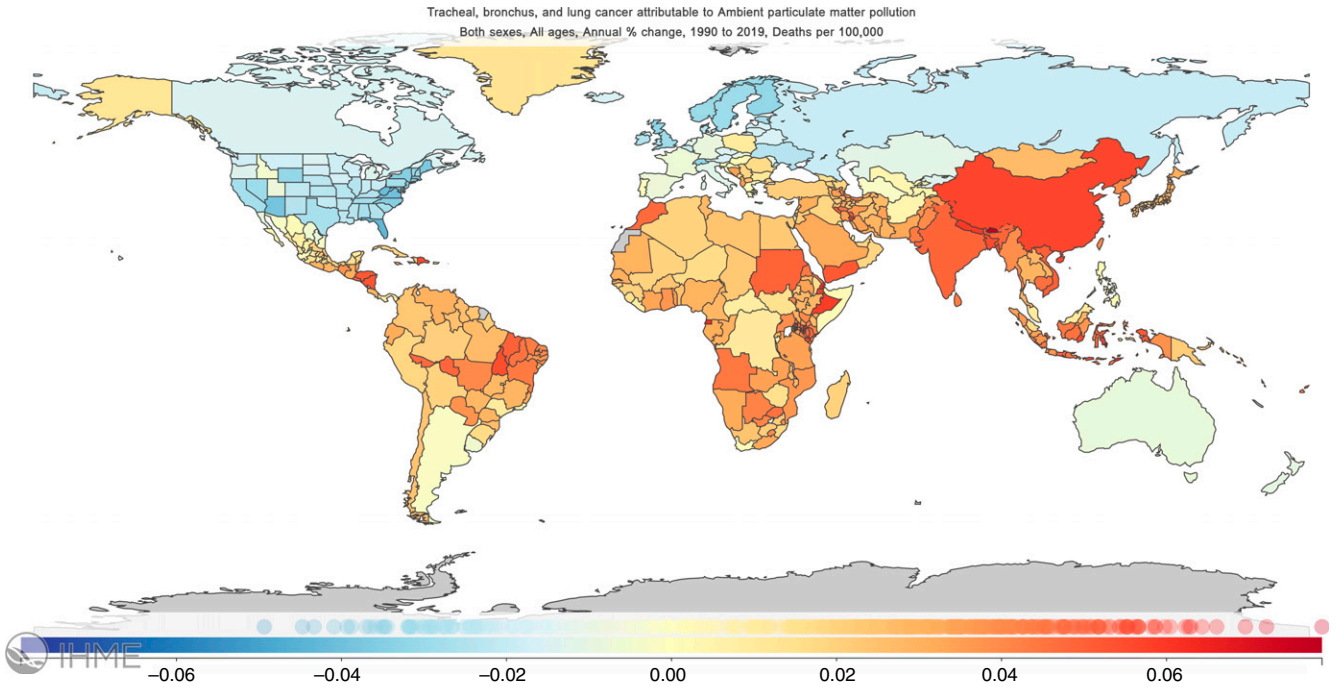

Figure 1. Tracheal, bronchus, and lung cancer attributable to ambient particulate matter pollution, both sexes, all ages, annual percentage change, 1990–2019, deaths per 100,000. *Source:* Institute for Health Metrics and Evaluation (IHME). GBD Compare Data Visualization. Seattle, WA: IHME, University of Washington; 2020 [accessed 2022 Jun 11]. Available from: https://www.healthdata.org/data-visualization/gbd-compare.

smoking quitting probabilities, and limited or lack of data on occupational or environmental tobacco smoke exposures. Nevertheless, the findings in a diverse cohort population contribute substantially to the existing literature, suggesting stronger ambient air pollution associations for lung cancer in lower SES neighborhoods. Results of other studies of ambient air pollution and lung cancer by race/ethnicity are limited and mixed (12–14). In another previous study, conducted in a less racially/ethnically diverse cohort, there was some evidence for an interaction between ambient $PM_{2.5}$ and cigarette smoking on the additive scale, suggesting greater lung cancer mortality risk for both exposures combined beyond that expected on the basis of the sum of their individual effects (15). Findings further suggest that the potential impact of both tobacco control and air quality management efforts may result in greater than expected reductions in lung cancer; however, the population impacts of implementation of such types of efforts are often differentially experienced according to a range of personal and neighborhood sociodemographic factors over time. Further efforts to examine and address multifactorial contributions to disparities in lung cancer, both in the United States and globally, are warranted. ■

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