Diesel engine emissions and lung cancer: insights from research design to policy

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Comment on: Kim J, Peters CE, Arrandale VH, *et al.* Burden of lung cancer attributable to occupational diesel engine exhaust exposure in Canada. Occup Environ Med 2018;75:617-22.

Received: 19 November 2018; Accepted: 26 December 2018; Published: 30 December 2018.
doi: 10.21037/ace.2018.12.01
View this article at: http://dx.doi.org/10.21037/ace.2018.12.01

Diesel engines are widely used by transportation and equipment in many industry sectors, including mining, construction, and electricity generators. Composition of diesel engine emission (DEE) is very complex and includes carbon monoxide, nitrogen oxides, volatile organic compounds, carbon components, ash, sulfate, and metals. During the past decades, numerous studies provided evidence for adverse health effects of exposure to DEE (1,2). In particular, the issue of long-term exposure to DEE and lung health has attracted extensive attention worldwide. For example, a large cohort study of workers in non-metal mining facilities in the U.S. stated exposure to diesel exhaust increased risk of mortality from lung cancer (3). Another large retrospective cohort study of trucking company workers in the U.S. reported a dose-response relationship between exposure to particles from diesel exhaust and lung cancer mortality (4). Moreover, increased incidence of lung cancer due to exposure to diesel engine exhaust was also observed in animal studies (5). Currently, lung cancer is the most commonly diagnosed cancer and the leading cause of cancer death globally (6). Quantifying the impact of DEE on lung cancer will provide valuable information and scientific basis for reduction of cancer burden. Kim *et al.* estimated the population attributable fraction (PAF) and number of lung cancer cases due to exposure to DEE occupationally in Canada (7).

Kim *et al.* (7) conveys important messages to the public and policymakers. In brief, 2.4% of lung cancer in Canada could be attributed to occupational exposure to diesel exhaust, leading to 560 incident cases and 460 deaths in 2011. The majority of the burden was due to exposure to low concentration rather than high concentration of DEE. An estimated 1.6 million Canadians were occupationally exposed to DEE in 2011, and 97% of whom were male. These results highlight the public health benefits of preventing occupational exposure to DEE, and also convey that low concentration exposure especially among males should be the focus of such preventive strategies (7).

In this study, instead of only examining association between exposure factors and outcome with risk estimates [e.g., odds ratio, relative risk (RR)], Kim *et al.* also provided important evidence relevant to public health policy. Study designs which range from time-series, case-crossover, cross-sectional, case-control, cohort to RCTs, will all lead to similar implications: whether and how strong the outcome is associated with certain exposure factors. The proportion of population exposed (PrE) to a certain factor is an additional key indicator. The PAF can be calculated from the estimates of both the RR and PrE, using Levin's equation. PAF, interpreted as the proportion of the outcome (e.g., lung cancer in Kim *et al.* study) attributed to specific risk factor (e.g., DEE in Kim *et al.* study), can be readily understood by the public and policy makers. However, PAF is only a proportion and the quantity of outcome such as the number of lung cancer cases or deaths as a result of the exposure factor is not known.

The quality of evidence is largely determined by the method of evaluation (8). Although a randomized controlled trial is the ideal study design and meta-analysis or systematic review of RCTs is the most reliable analysis of available evidence, such method cannot be used for assessment of environmental hazards due to ethical reasons. An observational prospective cohort study is the best accessible study design for hazardous risk factors such as diesel engine exhaust. By analyzing results from multiple cohorts through meta-analysis, a rather robust estimation of RR can be obtained. In this study, Kim *et al.* used the dose-response relationship (RRs at different DEE levels) as calculated from three cohorts in America (9). However, two main methodological issues should be mentioned (10). The first one is the generalizability of the epidemiologic evidence to the target population. In Kim *et al.* study, the target population was Canadian from all types of occupations that could be exposed to DEE, while the RRs only came from truck drivers and miners in America. The results were based on the assumption that the RRs from the American cohorts also apply to Canadian occupational population. This assumption is hardly testified and may not be valid, given that the distribution of confounders and covariates in these two populations could be quite different. Another important issue is the confounding effect of other factors such as smoking and asbestos. Kim *et al.* were unable to use the confounder adjusted RR nor to stratify the analyses by confounders to evaluate PAF, and as a result it is likely to have bias.

Kim *et al.* has well utilized the rich data sources in Canada, namely the Canadian National Enhanced Cancer Surveillance System, the Canadian Census with labour data from 1991 to 2001, Labour Force Survey, Canadian life tables, and Canadian Cancer Registry (7). Admittedly, exposure assessment was still based on many assumptions and approximations, but it has been the optimal and acceptable estimation. Most developing countries do not have the capacity to do this because their lack of well-developed public datasets like census, labour statistics and health registry systems.

As millions of workers around the world have been exposed to DEE, this type of studies should be extended to other countries (11). For low- and middle-income countries experiencing rapid industrialization, diesel engines are used more widely and with less strict control on the emission than high-income countries. In addition, these countries also have larger occupational population, so their disease burden attributed to occupational DEE exposure would be expected to be much higher (11). Unfortunately, it is much more difficult to do similar studies in low- and middle-income countries due to the methodological issues discussed above: (I) the unavailability of epidemiologic evidence based on local population; (II) the unsatisfactory population-based data for exposure assessment and disease burden statistics. As a result, almost all current studies on PAF of occupational DEE have been conducted in developed countries, including UK (12), USA (13), Canada (7), Finland (14) and France (15).

In light of the association of DEE and lung cancer risk, occupational health deserves greater attention in many countries. Looking into the future, more prospective studies, particularly multi-center cohorts with large sample size, are necessary to provide reliable and robust risk estimates (RR) with strong study power. Also, low- and middle-income countries like China, given their large population and rapid industrialization and urbanization, need to set high priority for policies and strategies to support more research on occupational health as one of the means to improve population health.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned and reviewed by the Section Editor Elvin Cheng, MBBS, BScMed, MPH (Cancer Research Division, Cancer Council NSW, the University of Sydney, Sydney, Australia).

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/ace.2018.12.01). YMG serves as an unpaid editorial board member of *Annals of Cancer Epidemiology* from Jan 2018 to Jan 2020. The other authors have no conflicts of inerest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/ace.2018.12.01
Cite this article as: Xu R, Chen G, Guo Y, Li S. Diesel engine emissions and lung cancer: insights from research design to policy. Ann Cancer Epidemiol 2018;2:4.