Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Re: An ecological analysis of long-term exposure to $PM_{2.5}$ and incidence of COVID-19 in Canadian health regions

Dear Editor,

We read with interest this paper on air pollution in Canada (Stieb et al., 2020) and its possible contribution to an increased incidence of COVID-19. In this ecological study, the authors used as the unit of observation very broad geographical regions defined administratively (referred to as "health regions"), which vary dramatically in size and constitution within and between Canadian provinces. They then made use of data on incident cases of COVID-19 in these 111 regions (73,390 cases until the end of May 2020). To these grouped counts, they juxtaposed, in a negative binomial statistical model, past satellite observations of fine particulate matter ($PM_{2.5}$) over a 17-year period (2000–2016) that had a spatial resolution of 1 × 1 km. These were then averaged to produce a summary exposure measure for each region. A number of ecological covariates were included in the model. They found that a 1 $\mu g/m^3$ increase in $PM_{2.5}$ increased the incidence of COVID-19 by 7% that they indicated "was several fold larger per unit $PM_{2.5}$ than hazard ratios typically observed in cohort studies of mortality".

The authors indicated that due to the study design "the findings should be interpreted with caution", and they also discussed some limitations due to the "coarseness" of these regions as well as cross-level bias ("ecological fallacy"). Nevertheless, it is our view that the limitations of their data are so severe that they do not advance public health as their risk estimates are neither credible nor interpretable. The basis for this conclusion is our recent detailed methodological review of mortality studies of both SARS and COVID-19 that we published in October 2020 in Environmental Health Perspectives, where we concluded that all studies of associations between these infectious diseases and environmental factors are seriously biased (Villeneuve and Goldberg, 2020).

Our concerns expressed in our review paper (Villeneuve and Goldberg, 2020) about the validity of the risk estimates apply to this study as well. To briefly summarize some of our arguments, studies that make use of the ecological design suffer from cross-level bias that arise by using groups rather than individuals as the unit of analysis. Heterogeneity of populations within these large areas is a key issue. Differences between and within jurisdictions as to the timing on the pandemic curve, behaviour of populations, the measures taken to reduce infections, and the R_0 value will affect incidence rates. Although the authors attempted to account for some of these essential components of the pandemic, by including a term for days since peak daily incidence of new cases, deaths at the health region level, and date of declaration of emergency, these factors cannot possibly account for infection dynamics within and between these vast regions and through time. Not being able to account for clustering of disease, spatiotemporal variations in the strains of COVID-19 that may affect sequelae differently, and, of course, heterogeneity in spatial-temporal assignment of air pollution within regions, that correlates with socio-economic status, leads to bias.

Use of very large areas in a grouped analysis is a major cause of concern. Because cases were aggregated and assigned to each region, it does not matter where the person lived in the region, where they may have travelled, where they may have worked, what social activities they engaged in, and what levels of air pollution they may have been exposed to. This means that any differences within the region are ignored by design.

To be concrete, consider a specific example of population dynamics from Montreal, in which there are a number of "hot spots" that have varied since the beginning of the pandemic. In the spring of 2020, a religious group living in an affluent area of the city, with low levels of air pollution, had the highest counts in the city because many members were in the United States where they became infected. The virus rampaged through the community until it was controlled. Summer came, cases went down, restrictions were reduced, and the members started congregating again. Now in October incidence rates are skyrocketing again. All in a low air pollution part of the city. A study based on individuals would not ignore these or other types of circumstances, but an ecological design where grouped data across these large regions is contrasted is subject to serious error given the vast differences in case identification, screening and implementation of public health practices its correlation with air pollution, and other factors.

Other deficiencies in the design, over and above the ecological fallacy, include serious misclassification and under-reporting of the incidence of COVID-19. In the United States, the CDC and others have recently estimated that deaths in the United States are underestimated by about 20% (Rossen et al., 2020; Woolf et al., 2020). There is clear evidence of undercounting of cases throughout the world and in Canada, and population-based testing and contact tracing is deficient. In a recent paper (Russell et al., 2020), about 20% of cases have not been identified in Canada. The Institute for Health Metrics and Evaluation modelled the under ascertainment of incident COVID-19 cases in Canada and estimated that during the first peak (march–June 2020) less than one in 5 cases of COVID-19 in the population were identified (Institute for Health Metrics and Evaluation, 2020). Similar estimates of under-ascertainment were produced by a research group at Imperial College (Imperial College, 2020). Canadian data suggests that per capita, a greater number of cases are being identified in urban areas which have higher concentrations of air

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pollution (Government of Alberta, 2020; BC Centre for Disease Control, 2020). The increased numbers of cases in urban areas may be driven by a number of factors other than air pollution, including increased person to person interaction, greater capacity for screening, higher probabilities, and hence greater awareness of being infected, or other potential sources of exposure such as travel, or attending large gatherings.

The pandemic is about between-person spread, which implies clustering in different settings. In Canada, many clusters of COVID-19 have been driven by its spread in vulnerable communities, (e.g., long term care homes, occupational settings (e.g., meat packing plants), and large gatherings (e.g., funerals, sports tournaments, and weddings), and now in schools. And the sources of infection have varied across Canada; for example, in the Maritime region, virtually all recent cases have been attributable to travel. In Quebec in the spring, the beginning of the pandemic coincided with the spring break, with families and students bringing the virus back from southern climates. In contrast, the vast majority of cases in Ontario have been due to spread from close contact (Public Health Ontario, 2020). These patterns of COVID-19 incidence raise two critical points. First, attempts to characterize associations between ambient air pollution and COVID-19 should at a minimum be able to account for sources of infection. Second, occurrences of COVID-19 are not independent, and they are more likely to cluster in areas of high population density, which importantly, tend to be areas with higher concentrations of air pollution. Therefore, statistical methods need to account for clustering of cases. The data in the study by Stieb et al. could not be used to take into account the clustered nature of the data, nor did it allow for sources of infection.

Our critical review focussed on mortality from COVID-19 in which there is plausible mechanism by which underlying conditions may affect the clinical course after infection. It is clear that air pollution does not cause COVID-19 and whether it should be considered as a modifier is possible, but these and other data do not shed light on this because of the inherent biases.

In terms of public health, context is essential. Studies of air pollution and COVID-19 may detract from the needed implementation of public health measures needed to control the spread of COVID-19. Stay in place orders, the use of face masks, hand washing, and physical distancing are the most important policies in reducing the spread in COVID-19. The possible contributions of air pollution on increasing incidence of COVID-19, put in this context, is at best a drop in a very large bucket. South Korea, with ambient levels of air pollution far greater than in Canada, or the United States, has been able to minimize the impact of COVID-19 relative to other countries. Is the success of mitigating COVID-19 in New Zealand due to its lower levels of air pollution? Public health experts would unanimously say otherwise (Baker et al., 2020). For these reasons, and particularly when jurisdictions are lacking the political courage or ability to implement these basic measures, it is critically important that authors of these types of papers make some effort to put their findings into context.

Other authors have also expressed concern over these studies Heederik et al. (2020). As we stated in our review: "In fact, we feel that the public is not served well by these studies, many of which have undergone the scrutiny of peer review, especially because the press are on the lookout for sensational stories. All observational studies are not created equal, and the rush to use a flawed design to investigate the association between air pollution and mortality from COVID-19 jeopardizes the clear and compelling evidence of chronic exposure to air pollution as a threat to human health and deflects from the increased rates of infection and health consequences caused by problems of social and income disparities, overcrowding, and other societal issues."

About the authors

As epidemiologists working for over 20 years in air pollution, we have played a role on the narrative about the health impacts from exposure to air pollution. We have analyzed data from the Harvard Six Cities and American Cancer Society's Cancer Prevention cohorts. These cohorts were among the first to establish links between long-term exposure to air pollution and death from cardiovascular and respiratory disease. In Canada, we have participated in multiple national and local air pollution studies, including those that have used national census data. Our experiences provide the foundation for us to critically review the research, and outline what we consider to be the key weaknesses of this study.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Baker, M.G., Wilson, N., Anglemyer, A., 2020. Successful elimination of covid-19 transmission in New Zealand. N. Engl. J. Med. 383, e56.

BC Centre for Disease Control, 2020. COVID-19 Data. http://www.bccdc.ca/health-info/diseases-conditions/covid-19/data.

Government of Alberta, 2020. COVID-19 Alberta Statistics. https://www.alberta.ca/stats/covid-19-alberta-statistics.htm.

Heederik, D.J.J., Smit, L.A.M., Vermeulen, R.C.H., 2020. Go slow to go fast: a plea for sustained scientific rigour in air pollution research during the covid-19 pandemic. Eur. Respir. J. 56.

Imperial College, 2020. Age-structured SEIR Model Focused on Low- and Middle-Income Countries. https://mrc-ide.github.io/global-lmic-reports/.

Institute for Health Metrics and Evaluation, 2020. Hybrid SEIR Model. https://covid19.healthdata.org/2020.

Public Health Ontario, 2020. Daily Epidemiologic Summary. COVID-19 in Ontario: January 15, 2020 to November 9. https://files.ontario.ca/moh-covid-19-report-en-2020-11-10.pdf.

Rossen, L.M., Branum, A.M., Ahmad, F.B., Sutton, P., Anderson, R.N., 2020. Excess deaths associated with COVID-19, by age and race and ethnicity — United States, january 26–october 3, 2020. MMWR Morb. Mortal. Wkly. Rep. 69, 1522–1527. https://doi.org/10.15585/mmwr.mm6942e2.

Russell, T.W., Golding, N., Hellewell, J., et al., 2020. Reconstructing the early global dynamics of under-ascertained COVID-19 cases and infections. BMC Med. 18, 332. https://doi.org/10.1186/s12916-020-01790-9.

Stieb, D.M., Evans, G.J., To, T.M., Brook, J.R., Burnett, R.T., 2020. An ecological analysis of long-term exposure to PM2.5 and incidence of COVID-19 in Canadian health regions. Environ. Res. 191, 110052. https://doi.org/10.1016/j.envres.2020.110052.

Villeneuve, P.J., Goldberg, M.S., 2020. Methodological considerations for epidemiological studies of air pollution and the SARS and COVID-19 coronavirus outbreaks. Environ. Health Perspect. 128, 95001.

Woolf, S.H., Chapman, D.A., Sabo, R.T., Weinberger, D.M., Hill, L., Taylor, D.D.H., 2020. Excess deaths from COVID-19 and other causes, march-july 2020. J. Am. Med. Assoc. 324. Number 15.

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