ESC European Society of Cardiology
Cardiovascular Research
doi:10.1093/cvr/cvaa288

Regional and global contributions of air pollution to risk of death from COVID-19

Andrea Pozzer [1,2], Francesca Dominici[3], Andy Haines[4], Christian Witt [5], Thomas Münzel [6,7]*, and Jos Lelieveld [2,8]*

[1]International Center for Theoretical Physics, Trieste, Italy; [2]Max Planck Institute for Chemistry, Atmospheric Chemistry Department, Mainz, Germany; [3]Harvard T.H. Chan School of Public Health, Department of Biostatistics, Boston, MA, USA; [4]Centre for Climate Change and Planetary Health, London School of Hygiene and Tropical Medicine, London, UK; [5]Charité University Medicine, Pneumological Oncology and Transplantology, Berlin, Germany; [6]University Medical Center of the Johannes Gutenberg University, Mainz, Germany; [7]German Center for Cardiovascular Research, Mainz, Germany; and [8]The Cyprus Institute, Climate and Atmosphere Research Center, Nicosia, Cyprus

Received 24 June 2020; revised 3 October 2020; editorial decision 23 September 2020; accepted 30 September 2020

Time for primary review: 6 days

Aims The risk of mortality from the coronavirus disease that emerged in 2019 (COVID-19) is increased by comorbidity from cardiovascular and pulmonary diseases. Air pollution also causes excess mortality from these conditions. Analysis of the first severe acute respiratory syndrome coronavirus (SARS-CoV-1) outcomes in 2003, and preliminary investigations of those for SARS-CoV-2 since 2019, provide evidence that the incidence and severity are related to ambient air pollution. We estimated the fraction of COVID-19 mortality that is attributable to the long-term exposure to ambient fine particulate air pollution.

Methods and results We characterized global exposure to fine particulates based on satellite data, and calculated the anthropogenic fraction with an atmospheric chemistry model. The degree to which air pollution influences COVID-19 mortality was derived from epidemiological data in the USA and China. We estimate that particulate air pollution contributed ~15% (95% confidence interval 7–33%) to COVID-19 mortality worldwide, 27% (13 – 46%) in East Asia, 19% (8–41%) in Europe, and 17% (6–39%) in North America. Globally, ~50–60% of the attributable, anthropogenic fraction is related to fossil fuel use, up to 70–80% in Europe, West Asia, and North America.

Conclusion Our results suggest that air pollution is an important cofactor increasing the risk of mortality from COVID-19. This provides extra motivation for combining ambitious policies to reduce air pollution with measures to control the transmission of COVID-19.

Keywords COVID-19 • Air pollution • Fine particulate matter • comorbidity • mortality

1. Introduction

Poor air quality, especially from fine particulate matter with a diameter <2.5 μm ($PM_{2.5}$), is one of the leading risk factors, and responsible for many excess deaths.[1,2] The global loss of life expectancy from long-term exposure to ambient air pollution exceeds that of infectious diseases, and is comparable with that of tobacco smoking.[1–3] The mortality from COVID-19 depends on comorbidities, including conditions that increase cardiovascular risks such as arterial hypertension, diabetes mellitus, obesity, and established coronary artery disease, as well as respiratory conditions such as asthma and chronic obstructive pulmonary disease (COPD), being similar to those that are influenced by air pollution.[3–6] The risk of death is strongly related to age, being particularly high in those aged >70. It is also higher amongst males, economically disadvantaged populations, and in some ethnic groups. In assessing the relationships between exposures to risk factors and outcomes, potential confounders therefore need to be accounted for in the design of studies and in data analysis. These include the age distribution of the population, availability of hospital beds (and intensive care capacity), and the proportion of the population living in poverty.

* Corresponding authors. Jos Lelieveld: Tel: +49 6131 305 4000, Fax: +49 6131 305 4019, Email: jos.lelieveld@mpic.de or Thomas Münzel: Tel: +49 6131 17 7250, Fax: +49 6131 17 6615, Email: tmuenzel@uni-mainz.de

A recent study, using an ecological design, assessed how environmental influences modify the severity of COVID-19 outcomes in the USA.[7] Potential confounders were identified, and statistical models were used to relate long-term exposure to ambient $PM_{2.5}$ to COVID-19 deaths. The computed mortality rate ratios (MRRs) express the relative increase in COVID-19 deaths for each microgram per cubic meter increment of $PM_{2.5}$ in ambient air. The $PM_{2.5}$ data were derived from satellite and ground-based measurements combined with atmospheric modelling,[8] and the confounders were determined from county-level censuses, homeland infrastructure, and meteorological data. Here we test the assumption that the derived MRRs are representative for the populations of other countries (China) and consider the global impact. In the present study, we apply the MRRs to estimate the excess mortality, i.e. the fraction of COVID-19 deaths that could be avoided if the population were exposed to lower counterfactual air pollution levels without fossil fuel-related and other anthropogenic emissions. We emphasize that our results are provisional, based on epidemiological data collected up to the third week of June 2020, and a comprehensive evaluation will need to follow after the COVID-19 pandemic.

1.1 SARS and air pollution

In the early 2000s, the first severe acute respiratory syndrome coronavirus (SARS-CoV-1) appeared in China (Guangdong Province). The virus was zoonotic, as it originally developed in bats.[9] The World Health Organization (WHO) reported that it resulted in a SARS epidemic with >8000 cases in 26 countries, mostly in south-east Asia and in Canada.[8] The disease emerged in November 2002 and was contained in July 2003. SARS-CoV-1 and SARS-CoV-2 have many similarities, as their RNA genomes are closely related and the viruses enter the host cells by binding to the same entry receptor angiotensin-converting enzyme 2 (ACE2).[10–12] About 2–14 days after infection, the systemic symptoms of both diseases are alike, and a similar fraction of patients develops severe symptoms with a mortality rate that increases strongly with advanced age.[13–16] In China alone, >5000 cases of SARS-CoV-1 were reported, leading to nearly 350 fatalities. Since the exposure to ambient air pollution is associated with respiratory and cardiovascular diseases, it was hypothesized that health outcomes of SARS were aggravated by poor air quality. A study in 2003 corroborated that in parts of China with moderate levels of air pollution, the risk of dying from the disease was >80% higher compared with areas with relatively clean air, while in heavily polluted regions the risk was twice as high.[17]

1.2 COVID-19 and air pollution

In 2019, the related second virus strain appeared (SARS-CoV-2) in China (Hubei Province), which also developed in bats,[4] causing COVID-19, which grew from an epidemic into a pandemic in the early part of 2020. A Chinese analysis indicated that the risk of symptomatic infection typically increases by ∼4% for each year of age between 30 and 60, and that the lethality is highest for individuals >60 years.[15]COVID-19 is associated with a combination of respiratory and cardiovascular complications, which may comprise myocardial infarction, heart failure, venous thrombo-embolisms, and increases in biomarkers,[18] which are also found in connection with high levels of air pollutants.[5] In a recent analysis of 5700 patients hospitalized with COVID-19 in the New York City area, the most common comorbidities were hypertension (57%), obesity (42%), and diabetes (34%),[19] representing cardiovascular risk factors that are also observed in relation to elevated $PM_{2.5}$ concentrations,[5,20] suggesting additive or synergistic effects on the cardiovascular system. In addition, advanced age is a strong risk factor for cardiovascular disease, and the effects on immune function may be equally important for COVID-19 susceptibility. The age dependency coincides with that of excess mortality from $PM_{2.5}$.[3,15] The COVID-19 mortality rate has been estimated to be ∼4% in symptomatic cases, in part because pre-existing conditions such as cardiovascular and respiratory disorders increase the risk.[21]

Considering the cardiovascular and respiratory health impacts of air pollution, the relationship to COVID-19 mortality is not unexpected. Preliminary studies addressed the influence of air pollution on COVID-19 in different regions. In China, the incidence of COVID-19 was found to be significantly enhanced by $PM_{2.5}$,[22] while a correlation between ambient $PM_{2.5}$ and the mortality rate was also established.[23] In Italy, it was found that the high pollution concentrations that are typical for the Po valley, especially in the Lombardy region of which Milan is the capital, were associated with a high mortality rate.[24] As mentioned above, in the USA the severity of COVID-19 outcomes was linked to $PM_{2.5}$ exposure, making use of Medicare data for >60 million people and nationwide air quality measurements.[7] Data were collected for 98% of the population in 3087 of the total number of 3142 counties, of which ∼42% had reported COVID-19 deaths up to the third week of April 2020. The death counts relied on data from the Coronavirus Resource Center of the Johns Hopkins University.[25] The study accounted for 20 potential confounding factors including population size, age distribution, population density, time period since the beginning of the outbreak, time elapsed since the home confinements, hospital beds, number of individuals tested, meteorological conditions, and socioeconomic and risk factors such as obesity and smoking.[7] The results showed significant overlap between the causes of death in COVID-19 patients and those that lead to mortality from $PM_{2.5}$. The MRR, i.e. the percentage increase of COVID-19 mortality risk per $\mu g/m^3$ increase of exposure to $PM_{2.5}$, was found to be 8%, with a 95% confidence interval of 2–15%.[7] The calculations are continually updated based on the most recent data (up to 18 June at the time of writing), showing no significant changes in the MRR in the preceding 4 months.

2. Methods

2.1 Global model and data

We applied a global atmospheric chemistry general circulation model (EMAC) which comprehensively simulates atmospheric chemical and meteorological processes and interactions with the oceans and the biosphere, in the same set-up as in recent studies on climate change, air pollution, and public health.[3,26] In addition to the standard simulation, we performed two sensitivity calculations: (i) with fossil fuel-related emissions removed and (ii) with all anthropogenic emissions removed. The model results were used to estimate the ratio of fine particulates in simulation (i) and (ii) and the standard simulation. The annual atmospheric near-surface $PM_{2.5}$ concentrations were taken from model-integrated satellite data, for the year 2019.[8,27] The horizontal resolution is 0.01 by 0.01 degrees, corresponding to a grid size of ∼1 km × 1 km. The near-surface concentrations of $PM_{2.5}$ for fossil fuel-related and all anthropogenic emissions are estimated by scaling this data set to the ratios (i) and (ii) obtained with the EMAC model simulations.

2.2 Relative risk

To estimate the relative risk (RR or hazard ratio) of excess COVID-19 mortality from the long-term exposure to air pollution, we used the exposure–response function of the WHO,[28]

$$RR = \left(\frac{X+1}{X_0+1}\right)^{\beta},$$

RR is a function of the concentration of air pollutants, which specifies annual average exposure dependent on location (grid cell) derived from the data mentioned above. X is the pollutant ($PM_{2.5}$) and X_0 is the pollutant threshold concentration below which exposure does not have implications for public health. Both β and X_0 are estimated by fitting to data from the literature with a least square method (*Figure 1*). We adopted the threshold $PM_{2.5}$ concentration (X_0) from Burnett *et al.*[2] (i.e. < 2.4 $\mu g/m^3$ $PM_{2.5}$), forcing the curve fitting into this range. We tested different exposure–response functions, e.g. of Burnett *et al.*,[2] and values for X_0, and find that the results are not sensitive to these assumptions.

Because the COVID-19 mortality rate ratio due to air pollution, based on data in the USA alone,[7] may not represent countries with very high fine particle concentrations (associated with a lack of observations in such regions), we investigated the effect of including data from the enhanced mortality rate derived for the Chinese SARS epidemic in 2003.[17] We make the assumption that SARS and COVID-19 mortality are similarly affected by long-term exposure to air pollution. Since the analysis for SARS was based on the Chinese Air Pollution Index (API), we converted the API to $PM_{2.5}$ concentrations following empirical relationships from the literature.[29,30] The large uncertainty range in the fitting function to a large degree derives from those in these relationships (black squares and ranges in *Figure 1*). In spite of uncertainties, the curves for the USA only and those that include the Chinese results are almost identical, providing confidence in the function derived for conditions in the USA only.

2.3 Attributable fraction

We calculated RR globally using $PM_{2.5}$ distributions calculated under the standard scenario. The attributable fraction (AF) of COVID-19 mortality to air pollution is calculated from the RR by AF = 1 – 1/RR. From the globally distributed, gridded AFs, we aggregated into regional and country-level AFs, weighted according to the population density, in order to account for the varying population distributions within regions and countries. The population data for the year 2020 were obtained from the NASA Socioeconomic Data and Applications Center (SEDAC), hosted by the Columbia University Center for International Earth Science Information Network (CIESIN).[31] Our definition of AF does not imply a direct cause–effect relationship between air pollution and COVID-19 mortality (although it is possible). Instead it refers to relationships between the two, direct and indirect, i.e. by aggravating comorbidities that could lead to fatal health outcomes of the virus infection.

3. Results

3.1 Attribution of COVID-19 mortality

To estimate the AF from exposure to ambient $PM_{2.5}$ to COVID-19 mortality, we used the epidemiological data from the USA (red curve in *Figure 1*). The chronic exposure to $PM_{2.5}$ in the years prior to the COVID-19 outbreak was estimated on the basis of satellite observations over the year 2019. The anthropogenic and fossil fuel-related fractions were calculated with the global EMAC model. Here we focus on anthropogenic and fossil fuel-related $PM_{2.5}$ to determine the impact of potentially avoidable air pollution on COVID-19 mortality. *Figure 2* and *Table 1* present the average fractions of COVID-19 mortality attributed to the exposure to $PM_{2.5}$ pollution, both globally and regionally. *Table S1* (available as Supplementary material online) lists the results for all countries. To account for the different population distributions within countries, e.g. between rural and urban areas, the averages have been weighted accordingly.

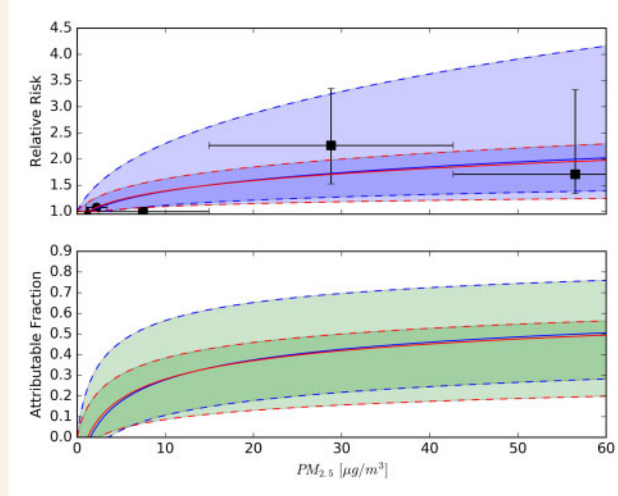

Figure 1 Exposure-response dependencies, based on a log-normal relationship[28]. The relative risk (or hazard ratio), from which the attributable fraction has been derived, is based on mortality rate ratios attributed to air pollution in the COVID-19 pandemic[7] and the SARS epidemic[17], indicated by the black bullet and squares, respectively. The triangle represents the threshold concentration below which $PM_{2.5}$does not have health implications[2]. The red curves depict the function fitted to the data from COVID-19 in the USA only[7], plus the threshold[2] (triangle and bullet). The blue curves depict the function fitted to all data[2,7,17]. The colored ranges show the 95% confidence intervals, which are wider after including the SARS-related results (blue), mostly due to uncertainty from converting Chinese API's into $PM_{2.5}$concentrations (black squares).

In regions with strict air quality standards and relatively low levels of air pollution, such as Australia, the attributable fraction by human-made air pollution to COVID-19 mortality is found to be a few percent only. Relatively high fractions occur in parts of east Asia (~35%), central Europe (~25%), and eastern USA (~25%). The country-level contribution to COVID-19 that we find for China, i.e. 27% (95% confidence interval 13 – 47%), agrees well with that found for the SARS epidemic in 2003.[17] The largest country-average fractions are found in the Czech Republic, Poland, China, North Korea, Slovakia, Austria, Belarus, and Germany, all above 25% (Supplementary material, *Table S1*). Globally, anthropogenic air pollution contributes ~15% (7 – 33%) to COVID-19 mortality, which could have been largely prevented, for example by adopting the air quality regulations applied in Australia (annual $PM_{2.5}$ limit of 8 $\mu g/m^3$). The global mean contribution of fossil fuel use to the anthropogenic fraction is ~56%, being highest in North America (83%), West Asia (75%), and Europe (68%) (*Table 1*).

4. Discussion

4.1 Pathophysiological aspects

Both the air pollutant $PM_{2.5}$ and the SARS-CoV-2 virus enter the lungs via the bronchial system (portal organ), with potential systemic health impacts through the blood circulation. Both $PM_{2.5}$ and SARS-CoV-2 cause vascular endothelial dysfunction, oxidative stress, inflammatory responses, thrombosis, and an increase in immune cells.[32–36] The SARS-CoV-2 infection facilitates the induction of endothelial inflammation in

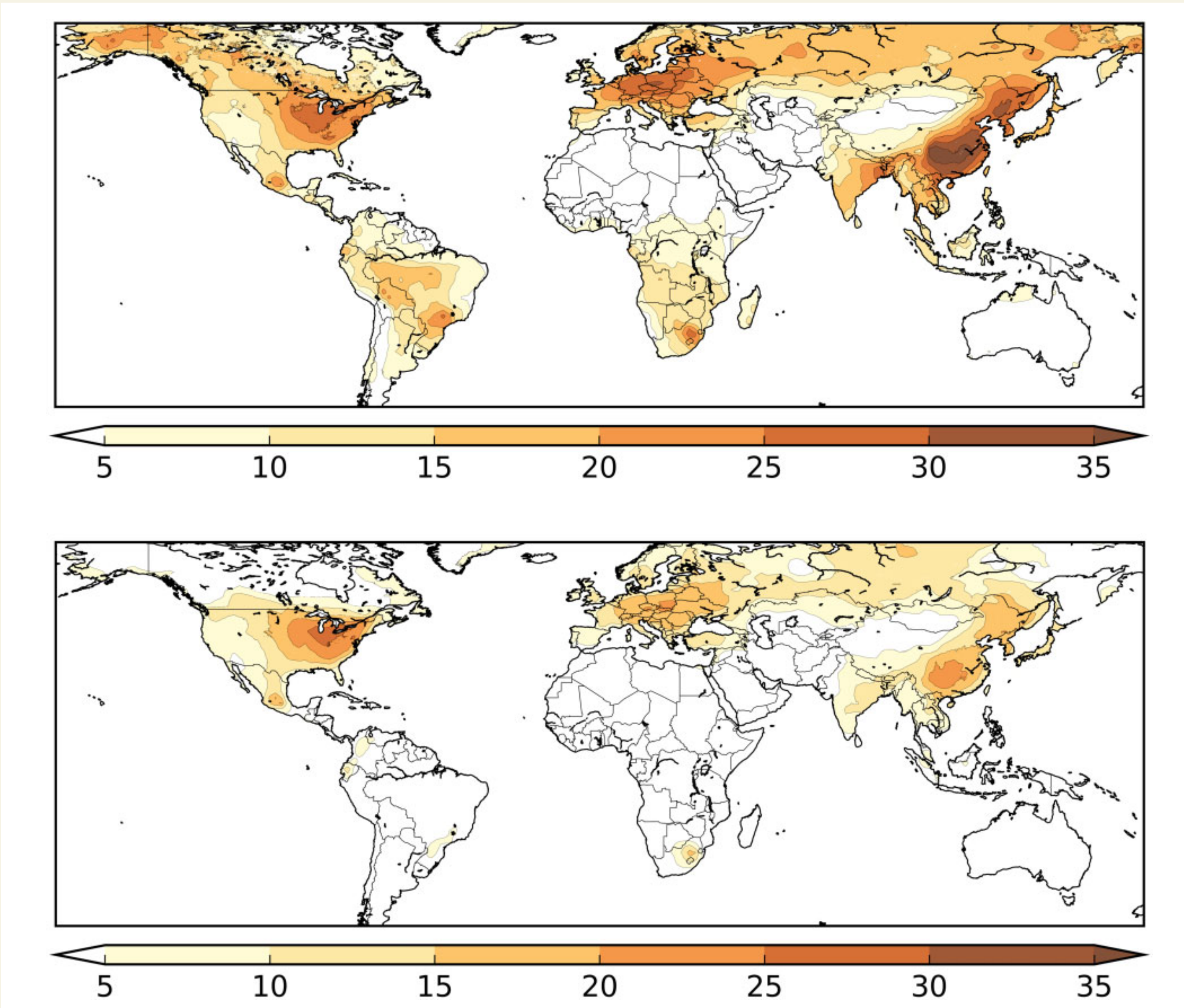

Figure 2 Estimated percentages of COVID-19 mortality attributed to air pollution from all anthropogenic sources (top), and from fossil fuel use only (bottom). The regions with high attributable fractions coincide with high levels of air pollution. The mapped results account for population density, thus reflecting population weighted exposure to $PM_{2.5}$.

several organs as a direct consequence of viral cytotoxic effects and the host inflammatory response, which can aggravate pre-existing chronic respiratory and vascular (coronary) dysfunction, and cause lung injury by alveolar damage, as well as stroke and myocardial infarction by inducing plaque rupture.[37] Potential common pathophysiological mechanisms of increased risk thus relate to endothelial injury[33,38] and pathways that regulate immune function.[39,40] Further, there are strong indications of increased susceptibility to viral infections from exposure to air pollution.[41–46]

Lung injuries, including the life-threatening acute respiratory distress syndrome and respiratory failure, as well as acute coronary syndrome, arrhythmia, myocarditis, and heart failure, were shown to be clinically dominant, leading to critical complications of COVID-19.[47,48] Recent studies in China, the USA, as well as Europe indicate that patients with cardiovascular risk factors or established cardiovascular disease and other comorbid conditions are predisposed to myocardial injury during the course of COVID-19.[19,46,49–52] From the available information, it thus follows that air pollution-induced inflammation leads to greater vulnerability and less resiliency, and the pre-conditions increase the host vulnerability. Air pollution causes adverse events through myocardial infarction and stroke, and it is an additional factor capable of increasing blood pressure, while there is emerging evidence for a link with type 2 diabetes and a possible contribution to obesity and enhanced insulin resistance.[36] Bronchopulmonary and cardiovascular pre-conditions, including hypertension, diabetes, coronary artery disease, cardiomyopathy, asthma, COPD, and acute lower respiratory illness, all negatively influenced by air pollution, lead to a substantially higher mortality risk in COVID-19. Furthermore, it seems likely that fine particulates prolong the atmospheric lifetime of infectious viruses, thus favouring transmission.[53] It is possible that future research will reveal additional pathways that mediate the relationship between air pollution and the risk of death from COVID-19.

Table 1 Regional percentages of COVID-19 mortality attributed to fossil fuel-related and all anthropogenic sources of air pollution

Region	Population (million)	COVID-19 mortality fraction attributed to air pollution (%)	
		Fossil fuel-related emissions	All anthropogenic emissions
Europe	628	13 (6–33)	19 (8–41)
Africa	1345	2 (1–19)	7 (3–25)
West Asia	627	6 (3–25)	8 (4–27)
South Asia	2565	7 (3–22)	15 (8–31)
East Asia	1685	15 (8–32)	27 (13–46)
North America	525	14 (6–36)	17 (6–39)
South America	547	3 (1–23)	9 (4–30)
Oceania	28	1 (0–20)	3 (1–23)
World	7950	8 (4–25)	15 (7–33)

The 95% confidence levels are given in parentheses.

4.2 Limitations

Our results indicate that the long-term exposure to high levels of fine particulate matter is a significant cofactor that influences the severity of COVID-19 outcomes. Since $PM_{2.5}$ in China and the USA, from which epidemiological data have been used, is dominated by anthropogenic sources that are potentially preventable, we focus our analysis on this fraction of $PM_{2.5}$. The good agreement of our results for the USA and China is in line with recent studies, showing that the association between air pollution and excess mortality is valid for many different countries.[2,55] Nevertheless, the calculations of RRs (hazard ratios) and the AF to mortality rely on the use of data from an ecological study design that has limitations, even though 19 county-level variables and one state-level variable, some of which are more important than air pollution, were considered as potential confounders in the analysis—and the $PM_{2.5}$ exposure data have been extensively cross-validated.[7] However, we acknowledge that residual confounding cannot be excluded. While cross-sectional ecological studies do not allow conclusions about cause–effect relationships, the biological mechanisms of air pollution-related disorders, acting as comorbidities in COVID-19, are well documented.[56,57] Recent studies in England and The Netherlands corroborate the positive relationships between air pollution and the number of COVID-19 cases, hospital admissions, and mortality.[58–60] The reported MRRs for $PM_{2.5}$ range from 1–7% to 13–21% (we applied 2–15%), which confirms the significant role of air pollution but emphasizes the large uncertainty ranges. Furthermore, our approach is likely to realistically approximate the contribution of fossil fuels and other anthropogenic sources to the total excess deaths through long-term ambient $PM_{2.5}$ air pollution exposure.

We reiterate that the data used for China are associated with substantial uncertainty, and underly the assumption that comorbidity and mortality from air pollution in COVID-19 are the same as in SARS. Nonetheless, using these data does not change the results, providing confidence in the robustness of our findings. We emphasize that the data relevant to the present study are from upper-middle and high-income countries, and the representativeness of our results for low-income countries may be limited, and uncertainties are likely to exceed the 95% confidence intervals. It is expected that in countries with high levels of aeolian dust, e.g. in Africa and West Asia, $PM_{2.5}$ pollution is also a cofactor but with less contribution from human activities. Household air pollution is also likely to be important, being of particular relevance in low-income countries.[61] It will be critical to collect epidemiological evidence from many regions with different socio-economic and environmental conditions, to support analyses of the COVID-19 pandemic and investigate the role of environmental factors. The uncertainty ranges that accompany our results are considerable but, taking into account the biological plausibility of the relationship and the strong evidence of the impact of air pollution on conditions that are known to increase COVID-19 mortality, they can nevertheless inform policy decisions.

4.3 Short- and long-term health impacts

A new, though preliminary, finding of the present study is that a significant fraction of worldwide COVID-19 mortality is attributable to anthropogenic air pollution, of which ∼50 – 60% is related to fossil fuel use (∼70 – 80% in Europe, West Asia, and North America). This represents potentially avoidable, excess mortality. The links between economic activity, traffic, energy use, and public health have been illustrated by the strong reduction of air pollution in many locations during the lockdown measures.[62,63] There is ample evidence for a relationship between short-term exposure to $PM_{2.5}$ and adverse health effects, including excess mortality from cardiovascular and respiratory diseases.[55] While it is in principle possible to disentangle the acute from the chronic outcomes from short- and long-term exposure to air pollution,[64] at this stage it is difficult to make that distinction for $PM_{2.5}$-induced comorbidity and mortality from COVID-19. Generally, short-term associations between air pollution and mortality are substantially less than those from long-term exposure, due to the more persistent, cumulative effects from the latter.[65] By relating air pollution anomalies to short-term health outcomes during the COVID-19-induced societal lockdown, it was found that in China alone >4600 excess deaths may have been avoided.[62] This can be viewed as a health co-benefit from the containment measures, which may reduce air pollution-induced COVID-19 mortality. Such benefits could also be achieved after the COVID-19 lockdown. Both perspectives of air pollution during the pandemic underscore the important role of fossil fuel-related and other anthropogenic emissions.

4.3 Future directions

Our results suggest the potential for substantial benefits from reducing air pollution exposure even at relatively low $PM_{2.5}$ levels. Refinement of the exposure–response relationship and reducing uncertainties will require additional data analyses, including from large cohort studies as the COVID-19 pandemic evolves, but may appear too late to guide decision-making. A lesson from our environmental perspective of the COVID-19 pandemic is that the quest for effective policies to reduce anthropogenic emissions, which cause both air pollution and climate change, needs to be accelerated. The pandemic ends with the vaccination of the population or with herd immunity through extensive infection of the population. However, there are no vaccines against poor air quality and climate change. The remedy is to mitigate emissions. The transition to a green economy with clean, renewable energy sources will further both environmental and public health locally through improved air quality and globally by limiting climate change.

Supplementary material

Supplementary material is available at *Cardiovascular Reseach* online.

Funding

We thank the Mainz Heart Foundation for continuous support. T.M. is the principal investigator of the DZHK (German Center for Cardiovascular Research), Partner Site Rhine-Main, Mainz, Germany.

Conflict of interest: none declared.

Data availability

The data underlying this article will be shared upon reasonable request to the corresponding author.

References

1. Cohen AJ, Brauer M, Burnett R, Anderson HR, Frostad J, Estep K, Balakrishnan K, Brunekreef B, Dandona L, Dandona R, Feigin V, Freedman G, Hubbell B, Jobling A, Kan H, Knibbs L, Liu Y, Martin R, Morawska L, Pope CA 3rd, Shin H, Straif K, Shaddick G, Thomas M, van Dingenen R, van Donkelaar A, Vos T, Murray CJL, Forouzanfar MH. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: an analysis of data from the Global Burden of Diseases Study 2015. *Lancet* 2017;**389**:1907–1918.
2. Burnett R, Chen H, Szyszkowicz M, Fann N, Hubbell B, Pope CA, Apte JS, Brauer M, Cohen A, Weichenthal S, Coggins J, Di Q, Brunekreef B, Frostad J, Lim SS, Kan H, Walker KD, Thurston GD, Hayes RB, Lim CC, Turner MC, Jerrett M, Krewski D, Gapstur SM, Diver WR, Ostro B, Goldberg D, Crouse DL, Martin RV, Peters P, Pinault L, Tjepkema M, van Donkelaar A, Villeneuve PJ, Miller AB, Yin P, Zhou M, Wang L, Janssen NAH, Marra M, Atkinson RW, Tsang H, Quoc Thach T, Cannon JB, Allen RT, Hart JE, Laden F, Cesaroni G, Forastiere F, Weinmayr G, Jaensch A, Nagel G, Concin H, Spadaro JV. Global estimates of mortality associated with long-term exposure to outdoor fine particulate matter. *Proc Natl Acad Sci USA* 2018;**115**: 9592–9597.
3. Lelieveld J, Pozzer A, Pöschl U, Fnais M, Haines A, Münzel, T. Comparison of mortality from ambient air pollution with other risk factors: a worldwide perspective. *Cardiov Res* 2020;doi: 10.1093/cvr/cvaa025.
4. World Health Organization. *Report of the WHO–China Joint Mission on Coronavirus Disease 2019 (COVID-19)*. Geneva: WHO; 2020.
5. Miller MR. Oxidative stress and the cardiovascular effects of air pollution. *Free Radic Biol Med* 2020;**151**:69–87.
6. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, Curtis HJ, Mehrkar A, Evans D, Inglesby, P, Cockburn J, McDonald HI, MacKenna B, Tomlinson L, Douglas IJ, Rentsch RT, Mathur R, Wong AYS, Grieve R, Harrison D, Forbes H, Schultze, A, Croker R, Parry J, Hester F, Harper S, Perera R, Evans SJW, Smeeth L, Goldacre B. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 2020;**584**:430–436.
7. Wu X, Nethery RC, Sabath MB, Braun D, Dominici F. Exposure to air pollution and COVID-19 mortality in the United States. *MedRxiv* 2020; doi: 10.1101/2020.04.05.20054502.
8. van Donkelaar A, Martin RV, Li C., Burnett RT. Regional estimates of chemical composition of fine particulate matter using a combined geoscience-statistical method with information from satellites, models, and monitors. *Environ Sci Technol* 2019;**53**: 2595-2611.
9. World Health Organization. SARS (Severe Acute Respiratory Syndrome) Disease Information. Geneva: WHO; 2020. https://www.who.int/ith/diseases/sars/en/
10. Shang J, Wan Y, Luo C, Ye G, Geng Q, Auerbach A, Li F. Cell entry mechanisms of SARS-CoV-2. *Proc Natl Acad Sci USA* 2020;**117**:11727–11734.
11. Li Y, Liu B, Cui J, Wang Z, Shen Y, Xu Y, Yao K, Guan Y. Similarities and evolutionary relationships of COVID-19 and related viruses. *arXiv* 2020;2020030316 (doi: 10.20944/preprints202003.0316.v1).
12. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, Si HR, Zhu Y, Li B, Huang CL, Chen HD, Chen J, Luo Y, Guo H, Jiang RD, Liu MQ, Chen Y, Shen XR, Wang X, Zheng XS, Zhao K, Chen QJ, Deng F, Liu LL, Yan B, Zhan FX, Wang YY, Xiao GF, Shi ZL. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020;**579**:270–273.
13. Chan-Yeun M, Xu R-H. SARS: epidemiology. *Respiration* 2003;**8**:S9–S14.
14. Yang M, Li CK, Li K, Hon KLE, Ng MHL, Chan PKS, Fok TF. Hematological findings in SARS patients and possible mechanisms (Review). *Int J Mol Med* 2004;**14**:311–315
15. Wu JT, Leung K, Bushman M, Kishore N, Niehus R, de Salazar PM, Cowling BJ, Lipsitch M, Leung GM, Estimating clinical severity of COVID-19 from the transmission dynamics in Wuhan, China. *Nat Med* 2020;**26**:506–510.
16. Tian S, Hu N, Lou J, Chen K, Kang X, Xiang Z, Chen H, Wang D, Liu N, Liu D, Chen G, Zhang Y, Li D, Li J, Lian H, Niu S, Zhang L, Zhang J. Characteristics of COVID-19 infection in Beijing. *J Infect* 2020;**80**:401–406.
17. Cui Y, Zhang Z-F, Froines J, Zhao J, Wang H, Yu S-Z, Detels R. Air pollution and case fatality of SARS in the People's Republic of China: an ecologic study. *Environ Health* 2003;**2**:15.
18. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, Brown TS, Nigoghossian CD, Zidar DA, Haythe J, Brodie D, Beckman JA, Kirtane AJ, Stone GW, Krumholz HM, Parikh SA. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. *J Am Coll Cardiol* 2020;**75**: 2352–2371.
19. Richardson S, Hirsch JS, Narasimhan M, Crawford JM, McGinn T, Davidson KW, and the Northwell C-RC, Barnaby DP, Becker LB, Chelico JD, Cohen SL, Cookingham J, Coppa K, Diefenbach MA, Dominello AJ, Duer-Hefele J, Falzon L, Gitlin J, Hajizadeh N, Harvin TG, Hirschwerk DA, Kim EJ, Kozel ZM, Marrast LM, Mogavero JN, Osorio GA, Qiu M, Zanos TP. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City area. *JAMA* 2020;**323**:2052–2059.
20. Münzel T, Sorensen M, Gori T, Schmidt FP, Rao X, Brook J, Chen LC, Brook RD, Rajagopalan S. Environmental stressors and cardio-metabolic disease: part I—epidemiologic evidence supporting a role for noise and air pollution and effects of mitigation strategies. *Eur Heart J* 2017;**38**:550–556.
21. Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. *Lancet* 2020;**395**:470–473.
22. Wang B, Liu J, Fu S, Xu X, Li L, Ma Y, Zhou J, Yao J, Liu X, Zhang X, He X, Yan H, Shi Y, Ren X, Niu J, Luo B, Zhang K. An effect assessment of airborne particulate matter pollution on COVID-19: a multi-city study in China. *MedRxiv* 2020;https://doi.org/10.1101/2020.04.09.20060137.
23. Yao Y, Pan J., Wang W, Liu X, Kan H., Meng X, Wang W. Spatial correlation of particulate matter pollution and death rate of COVID-19. *MedRxiv* 2020;https://doi.org/10.1101/2020.04.07.20052142.
24. Conticini E, Frediani B, Caro D. Can atmospheric pollution be considered a co-factor in extremely high level of SARS-CoV-2 lethality in Northern Italy? *Environ Poll* 2020; **261**:114465.
25. Coronavirus Resource Center. Johns Hopkins University and Medicine, Baltimore, MD, USA, 2020; https://coronavirus.jhu.edu.
26. Lelieveld J, Klingmüller K, Pozzer A, Burnett RT, Haines A, Ramanathan V. Effects of fossil fuel and total anthropogenic emission removal on public health and climate. *Proc Natl Acad Sci USA* 2019;**116**:7192–7197.
27. van Donkelaar A, Martin RV, Brauer M, Hsu NC, Kahn RA, Levy RC, Lyapustin A, Sayer AM, Winker D.M. Global estimates of fine particulate matter using a combined geophysical–statistical method with information from satellites, models, and monitors. *Environ Sci Technol* 2016;**50**:3762–3772.
28. Ostro B. *Outdoor Air Pollution: Assessing the Environmental Burden of Disease at National and Local Levels. World Health Organization Protection of the Human Environment*. Geneva: WHO; 2004.
29. Guo JP, Zhang X-Y, Che H-Z, Gong S-L, An X, Cao C-X, Guang J, Zhang H, Wang Y-Q, Zhang XC, Xue M, Li X-W. Correlation between PM concentrations and aerosol optical depth in eastern China. *Atmos Environ* 2009;**43**:5876–5886.
30. Zheng S, Cao CX, Singh RP. Comparison of ground based indices (API and AQI) with satellite based aerosol products. *Sci Total Environ* 2014;**488**:398–412.
31. Center for International Earth Science Information Network, CIESIN, Columbia University. *Gridded Population of the World, Version 4 (GPWv4): Population Count, Revision 11. Palisades, NY.* NASA Socioeconomic Data and Applications Center (SEDAC) 2020; https://doi.org/10.7927/H4JW8BX5.
32. Pope CA III, Bhatnagar A, McCracken JP, Abplanalp W, Conklin DJ, O'Tool T. Exposure to fine particulate air pollution is associated with endothelial injury and systemic inflammation. *Circ Res* 2016;**119**:1204–1214.
33. Münzel T, Gori, T, Al-Kindi S, Deanfield J, Lelieveld J, Daiber A, Rajagopalan S. Effects of gaseous and solid constituents of air pollution on endothelial function. *Eur Heart J* 2018;**39**:3543–3550.

34. Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, Mehra MR, Schuepbach RA, Ruschitzka F, Moch H. Endothelial cell infection and endotheliitis in COVID-19. *Lancet* 2020;**395**:1417–1418.
35. Tsai D-H, Riediker M, Berchet A, Paccaud F, Waeber G, Vollenweider P, Bochud M. Effects of short- and long-term exposures to particulate matter on inflammatory marker levels in the general population. *Environ Sci Poll Res* 2019;**26**:19697–19704.
36. Thurston GD, Kipen H, Annesi-Maesano I, Balmes J, Brook RD, Cromar K, De Matteis S, Forastiere F, Forsberg B, Frampton MW, Grigg J, Heederik D, Kelly FJ, Kuenzli N, Laumbach R, Peters A, Rajagopalan ST, Rich D, Ritz B, Samet JM, Sandstrom T, Sigsgaard T, Sunyer J, Brunekreef B. A joint ERS/ATS policy statement: what constitutes an adverse health effect of air pollution? An analytical framework. *Eur Respir J* 2017;**49**:1600419.
37. Wenzel P, Kopp S, Göbel S, Jansen T, Geyer M, Hahn F, Kreitner K-F, Escher F, Schultheiss H-P, Münzel T. Evidence of SARS-CoV-2 mRNA in endomyocardial biopsies of patients with clinically suspected myocarditis tested negative for COVID-19 in nasopharyngeal swab. *Cardiovasc Res* 2020;**116**:1661–1663.
38. Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, Vanstapel A, Werlein C, Stark H, Tzankov A, Li WW, Li VW, Mentzer SJ, Jonigk D. Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. *N Engl J Med* 2020; **383**:120–128.
39. Kelly FJ, Fussell JC. Linking ambient particulate matter pollution effects with oxidative biology and immune responses. *Ann N Y Acad Sci* 2015;**1340**:84–94.
40. O'Driscoll CA, Owens LA, Gallo ME, Hoffmann EJ, Afrazi A, Han M, Fechner JH, Schauer JJ, Bradfield CA, Mezrich JD. Differential effects of diesel exhaust particles on T cell differentiation and autoimmune disease. *Part Fibre Toxicol* 2018;**15**: 35.
41. Becker S, Soukup JM Exposure to urban air particulates alters the macrophage-mediated inflammatory response to respiratory viral infection. *J Toxicol Environ Health A* 1999;**57**:445–457.
42. Harrod KS, Jaramillo RJ, Rosenberger CL, Wang S-Z, Berger JA, McDonald JD, Reed MD. Increased susceptibility to RSV infection by exposure to inhaled diesel engine emissions. *Am J Respir Cell Mol Biol* 2003;**28**:451–463.
43. Kaan PM, Hegele RG. Interaction between respiratory syncytial virus and particulate matter in guinea pig alveolar macrophages. *Am J Respir Cell Mol Biol* 2003;**28**:697–704.
44. Lambert AL, Mangum JB, DeLorme MP, Everitt JI. Ultrafine carbon black particles enhance respiratory syncytial virus-induced airway reactivity, pulmonary inflammation, and chemokine expression. *Toxicol Sci* 2003;**72**:339–346.
45. Ye Q, Fu J, Mao J, Shang S. Haze is a risk factor contributing to the rapid spread of respiratory syncytial virus in children. *Environ Sci Poll Res* 2016;**23**:20178–20185.
46. Liang Y, Fang L, Pan H, Zhang K, Kan H, Brook JR, Sun Q. PM2.5 in Beijing—temporal pattern and its association with influenza. *Environ Health* 2014;**13**:102.
47. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, Ma K, Xu D, Yu H, Wang H, Wang T, Guo W, Chen J, Ding C, Zhang X, Huang J, Han M, Li S, Luo X, Zhao J, Ning Q. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ* 2020;**368**:m1091.
48. Guzik TJ, Mohiddin SA, Dimarco A, Patel V, Savvatis K, Marelli-Berg FM, Madhur MS, Tomaszewski M, Maffia P, D'Acquisto F, Nicklin SA, Marian AJ, Nosalski R, Murray EC, Guzik B, Berry C, Touyz RM, Kreutz R, Wang DW, Bhella D, Sagliocco O, Crea F, Thomson EC, McInnes IB. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. *Cardiovasc Res* 2020;**116**: 1666–1687.
49. Guo T, Fan J, Chen M, Wu X, Zhang L, He T, Wang H, Wan J, Wang X, Lu Z. Cardiovascular implications of fatal outcomes of patients with Coronavirus Disease 2019 (COVID-19). *JAMA Cardiol* 2020;**5**:811–818.
50. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, Gong W, Liu X, Liang J, Zhao Q, Huang H, Yang B, Huang C. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol* 2020;**5**:802–810.
51. Inciardi RM, Adamo M, Lupi L, Cani DS, Di Pasquale M, Tomasoni D, Italia L, Zaccone G, Tedino C, Fabbricatore D, Curnis A, Faggiano P, Gorga E, Lombardi CM, Milesi G, Vizzardi E, Volpini M, Nodari S, Specchia C, Maroldi R, Bezzi M, Metra M. Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy. *Eur Heart J* 2020;**41**:1821–1829.
52. European Society of Cardiology (ESC). ESC guidance for the diagnosis and management of CV disease during the COVID-19 pandemic; https://www.escardio.org/Education/COVID-19-and-Cardiology/ESC-COVID-19-Guidance.
53. Frontera A, Martin C, Vlachos K, Sgubin G. Regional air pollution persistence links to COVID-19 infection zoning. *J Infect* 2020;**81**:318–356.
54. Yan J, Grantham M, Pantelic M, Bueno de Mesquita PJ, Albert B, Liu F, Ehrman S, Milton DK, EMIT Consortium. Infectious virus in exhaled breath of symptomatic seasonal influenza cases from a college community. *Proc Natl Acad Sci USA* 2018;**115**: 1081–1086.
55. Liu C, Chen R, Sera F, Vicedo-Cabrera AM, Guo Y, Tong S, Coelho MSZS, Saldiva PHN, Lavigne E, Matus P, Valdes Ortega N, Osorio Garcia S, Pascal M, Stafoggia M, Scortichini M, Hashizume M, Honda Y, Hurtado-Díaz M, Cruz J, Nunes B, Teixeira JP, Kim H, Tobias A, Íñiguez C, Forsberg B, Åström C, Ragettli MS, Guo Y-L, Chen B-Y, Bell ML, Wright CY, Scovronick N, Garland RM, Milojevic A, Kyselý J, Urban A, Orru H, Indermitte E, Jaakkola JJK, Ryti NRI, Katsouyanni K, Analitis A, Zanobetti A, Schwartz J, Chen J, Wu T, Cohen A, Gasparrini A, Kan H. Ambient particulate air pollution and daily mortality in 652 cities. *N Engl J Med* 2019;**381**:705–715.
56. Brook RD, Rajagopalan S, Pope CA III, Brook JR, Bhatnagar A, Diez-Roux AV, Holguin F, Hong Y, Luepker RV, Mittleman MA, Peters A, Siscovick D, Smith SCJrWhitsel, L Kaufman, JD; on behalf of the American Heart Association Council on Epidemiology and Prevention, Council on the Kidney in Cardiovascular Disease, and Council on Nutrition, Physical Activity and Metabolism. Particulate matter air pollution and cardiovascular disease. An update to the scientific statement from the American Heart Association. *Circulation* 2010;**121**:2331–2378.
57. Landrigan PJ, Fuller R, Acosta NJR, Adeyi O, Arnold R, Basu N, Baldé AB, Bertollini R, Bose-O'Reilly S, Boufford JI, Breysse PN, Chiles T, Mahidol C, Coll-Seck AM, Cropper ML, Fobil J, Fuster V, Greenstone M, Haines A, Hanrahan D, Hunter D, Khare M, Krupnick A, Lanphear B, Lohani B, Martin K, Mathiasen KV, McTeer MA, Murray CJL, Ndahimananjara JD, Perera F, Potočnik J, Preker AS, Ramesh J, Rockström J, Salinas C, Samson LD, Sandilya K, Sly PD, Smith KR, Steiner A, Stewart RB, Suk WA, van Schayck OCP, Yadama GN, Yumkella K, Zhong M. *The Lancet Commission on pollution and health. Lancet* 2018;**391**:464–512.
58. Office for National Statistics. *Coronavirus (COVID-19) Related Mortality Rates and the Effects of Air Pollution in England*. 2020; https://www.ons.gov.uk/economy/environmentalaccounts/methodologies/coronaviruscovid19relatedmortalityratesandtheeffectsofairpollutioninengland.
59. Cole MA, Ozgen C, Strobl E. *Air Pollution Exposure and COVID-19*. IZA Institute of Labor Economics 2020; IZA DP No. 13367: https://www.iza.org/publications/dp/13367/air-pollution-exposure-and-covid-19.
60. Travaglio M, Yu Y, Popovic R, Selley L, Santos Leal N, Martins LM. Links between air pollution and COVID-19 in England. https://www.medrxiv.org/content/10.1101/2020.04.16.20067405v5.
61. Smith KR, Bruce N, Balakrishnan K, Adair-Rohani H, Balmes J, Chafe Z, Dherani M, Hosgood HD, Mehta S, Pope D, Rehfuess E, and others in the HAP CRA Risk Expert Group. Millions dead: how do we know and what does it mean? Methods used in the Comparative Risk Assess of Household Air Pollution. *Ann Rev Pub Health* 2014;**35**: 185–206.
62. Chen K, Wang M, Huang C, Kinney PL, Anastas PT. Air pollution reduction and mortality benefit during the COVID-19 outbreak in China. *Lancet Planet Health* 2020; 10.1016/S2542-5196(20)30107-8.
63. Venter ZS, Aunan K, Chowdhury S, Lelieveld J. COVID-19 lockdowns cause global air pollution declines. *Proc Natl Acad Sci USA* 2020;**117**:18984–18990.
64. Eftim S, Dominici F. Multisite time-series studies versus cohort studies: methods, findings, and policy implications. *J Toxicol Environ Health A* 2005;**68**;1191–1205.
65. Beverland IJ, Cohen GR, Heal MR, Carder M, Yap C, Robertson C, Hart CL, Agius RM. A comparison of short-term and long-term air pollution exposure associations with mortality in two cohorts in Scotland. *Environ Health Perspect* 2012; **120**,1280–1285.

Translational perspective

COVID-19 infections and air pollution cause excess mortality from cardiovascular and pulmonary diseases. We estimated the fraction of COVID-19 mortality attributable to the long-term exposure to ambient fine particulate air pollution ($PM_{2.5}$). Global exposure to $PM_{2.5}$ was characterized based on satellite data, and the anthropogenic fraction was calculated with an atmospheric chemistry model. $PM_{2.5}$ contributed ~15% to COVID-19 mortality worldwide, 27% in East Asia, 19% in Europe, and 17% in North America. Globally ~50–60% of the attributable, anthropogenic fraction is related to fossil fuel use, and 70–80% in Europe/West Asia/North America, indicating the potential for substantial health benefits from reducing air pollution exposure.