

Cardiovascular disease burden from ambient air pollution in Europe reassessed using novel hazard ratio functions

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Aims

Ambient air pollution is a major health risk, leading to respiratory and cardiovascular mortality. A recent Global Exposure Mortality Model, based on an unmatched number of cohort studies in many countries, provides new hazard ratio functions, calling for re-evaluation of the disease burden. Accordingly, we estimated excess cardiovascular mortality attributed to air pollution in Europe.

Methods and results

The new hazard ratio functions have been combined with ambient air pollution exposure data to estimate the impacts in Europe and the 28 countries of the European Union (EU-28). The annual excess mortality rate from ambient air pollution in Europe is 790 000 [95% confidence interval (95% CI) 645 000–934 000], and 659 000 (95% CI 537 000–775 000) in the EU-28. Between 40% and 80% are due to cardiovascular events, which dominate health outcomes. The upper limit includes events attributed to other non-communicable diseases, which are currently not specified. These estimates exceed recent analyses, such as the Global Burden of Disease for 2015, by more than a factor of two. We estimate that air pollution reduces the mean life expectancy in Europe by about 2.2 years with an annual, attributable per capita mortality rate in Europe of 133/100 000 per year.

Conclusion

We provide new data based on novel hazard ratio functions suggesting that the health impacts attributable to ambient air pollution in Europe are substantially higher than previously assumed, though subject to considerable uncertainty. Our results imply that replacing fossil fuels by clean, renewable energy sources could substantially reduce the loss of life expectancy from air pollution.

Keywords

Air pollution • Fine particulate matter • Excess mortality rate • Loss of life expectancy • Cardiovascular risk • Health promotion intervention

Introduction

According to the World Health Organization (WHO), non-communicable diseases (NCD) are the globally leading cause of mortality.¹ About 71% of 56 million deaths that occurred worldwide in

2015 are attributed to NCD, mainly cardiovascular diseases (CVD, 31%), cancers, diabetes, and chronic lung diseases. In Europe, CVD account for 45% of the mortality rate, and within the 28 countries of the European Union (EU-28) it is 37%.^{1,2} This amounts to 2.14 million and 1.85 million deaths per year, respectively.¹ Well-known risk

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factors include tobacco smoking, unhealthy diets, lack of physical activity, overweight, raised blood pressure, blood sugar, and cholesterol, which can be either avoided or substantially reduced. It is estimated that 80% of premature heart disease, stroke, and diabetes can be prevented.¹ Environmental factors, in particular air pollution, pose additional risks with health implications that have been underestimated in the Global Burden of Disease (GBD).³ Chronic exposure to enhanced levels of fine particle matter impairs vascular function, which can lead to myocardial infarction, arterial hypertension, stroke, and heart failure.^{4,5} Predominant sources of fine particulates are fossil fuel and biomass combustion, industry, agriculture, and wind-blown dust.⁶

While air pollution is often ignored as a health risk factor,² the *Lancet Commission on pollution and health* recommends air quality action plans for the prevention and control of NCD.³ The commission estimated that about nine million excess deaths worldwide are attributable to degraded environmental conditions, of which about half to ambient (outdoor) air pollution, being the main environmental health risk. Previously we estimated that the excess mortality rate from air pollution, related to CVD, amounts to 2.4 million per year, of which 269 000 in Europe.⁷ These estimates combine exposure of the population to fine ambient particulates with disease-specific hazard ratios from epidemiological cohort studies.⁸ The underlying biomedical and chemical mechanisms are not fully resolved, but there is mounting evidence of a causal relationship between the exposure to fine particulate matter with a diameter below 2.5 μm ($\text{PM}_{2.5}$) and cardiovascular morbidity and mortality.^{3,9–12} Mechanistic factors include $\text{PM}_{2.5}$ -induced inflammation, oxidative stress, and vascular (endothelial) dysfunction, which can facilitate the development of hypertension, diabetes, and atherosclerosis, with a possibly much larger health impact than expected.¹¹

To update the estimates of CVD mortality attributable to $\text{PM}_{2.5}$, we applied recent hazard ratio functions in a new Global Exposure Mortality Model (GEMM), based on a large number of cohort studies,¹³ employing a much extended database and range of exposures than the recent GBD assessment for 2015.^{8,14} The new hazard functions complement those of the GBD for 2015, including new information on NCDs.¹³ Five disease categories, i.e. lower respiratory tract illness (LRI), chronic obstructive pulmonary disease (COPD), lung cancer (LC), ischaemic heart disease (IHD), and cerebrovascular disease (CEV) leading to stroke, have been identified, similar to earlier assessments.^{8,14} The new GEMM also identifies a category non-accidental diseases, defined as NCD + LRI, and by subtracting the above categories, we derive one that is referred to as 'other NCD'. Here, we show that air pollution is a much larger mortality factor than previously assumed, especially from CVD, associated with a mean loss of life expectancy (LLE) of more than two years in Europe. We discuss the mechanistic factors that may explain the large impact of air pollution on CVD.

Methods

Model calculated exposure

The global exposure of the population to air pollution in the year 2015 has been computed through data-informed modelling (for details, see [Supplementary material online](#)). We used the EMAC atmospheric

chemistry–climate model, which comprehensively simulates atmospheric chemical and meteorological processes and interactions with the land, oceans, and biosphere.^{15,16} The model computes exposure by accounting for the atmospheric chemistry of natural and anthropogenic emissions, leading to $\text{PM}_{2.5}$ and gaseous oxidants such as ozone (O_3).^{6,7} The EMAC model development is pursued by an international consortium (<https://www.messy-interface.org>). This website offers additional model description, references, and model output. The software is publicly available through a community end-user license agreement. The model is continually evaluated through comparison to measurement data from ground-based networks, field campaigns, and satellite remote sensing. We applied the model configuration described by Lelieveld *et al.*⁷ Emission categories were defined according to Lelieveld *et al.*,⁶ updated for the year 2015, with fossil sources from power generation, industry and traffic, and additional anthropogenic sources from residential energy use (biofuels), agriculture, and biomass burning.⁷

Global Exposure Mortality Model

While we applied the same model calculations of air pollution, baseline mortality and population data of the WHO for the year 2015 used previously,⁷ we revised our results by using the new hazard ratio functions given by the GEMM of Burnett *et al.*,¹³ which is based on 41 cohort studies in 16 countries. These functions relate hazard ratios to air pollution concentrations, being dependent on age and geographical location (usually country level). Applying them to model calculated pollution concentrations, in combination with population data and baseline mortality rates of the WHO,¹ yields excess mortality rates in the five defined disease categories (LRI, COPD, IHD, CEV, and LC), plus the difference between NCD + LRI and the former five, yielding the 'other NCD'. While the latter cannot be specified, below we argue that it is significantly associated with CVD mortality.

The GEMM accounts for a much larger range of air pollution concentrations than the GBD of 2015, by including new cohort data from China, where air quality tends to be poorer than in Europe and North America from where epidemiological data have dominated former GBD assessments.^{8,14} *Figure 1* illustrates the consequences of using the expanded database in the GEMM, and the large differences in hazard ratios compared with the GBD 2015. For additional examples, we refer to *Supplementary material online, Figure S1* of Burnett *et al.*¹³ While for GBD 2015 the available $\text{PM}_{2.5}$ observations extended from a few $\mu\text{g}/\text{m}^3$ to about 35 $\mu\text{g}/\text{m}^3$, the new data include much higher concentrations up to 84 $\mu\text{g}/\text{m}^3$, encompassing 97% of all relevant cases.¹³ The limited information at high $\text{PM}_{2.5}$ concentrations was hitherto made up for by using data from second-hand and active smoking studies, which apparently lead to an underestimate of hazard ratios, for example by allowing the number of IHD and CEV events to increase only marginally at high $\text{PM}_{2.5}$ concentrations.⁸

Results

Burden of disease

Previously we estimated a global mortality rate attributable to ambient air pollution by $\text{PM}_{2.5}$ and O_3 of 4.55 [95% confidence interval (95% CI) 3.41–5.56] million in 2015,⁷ in close agreement with the GBD 2015.^{8,14} The 95% CIs express uncertainty in epidemiological data.^{8,13} With the new GEMM we estimate 8.79 (95% CI 7.11–10.41) million in 2015. This agrees well with the global estimate of 8.9 (95% CI 7.5–10.3) of Burnett *et al.*¹³ To put this into perspective, the WHO estimates that the excess death rate from tobacco smoking is

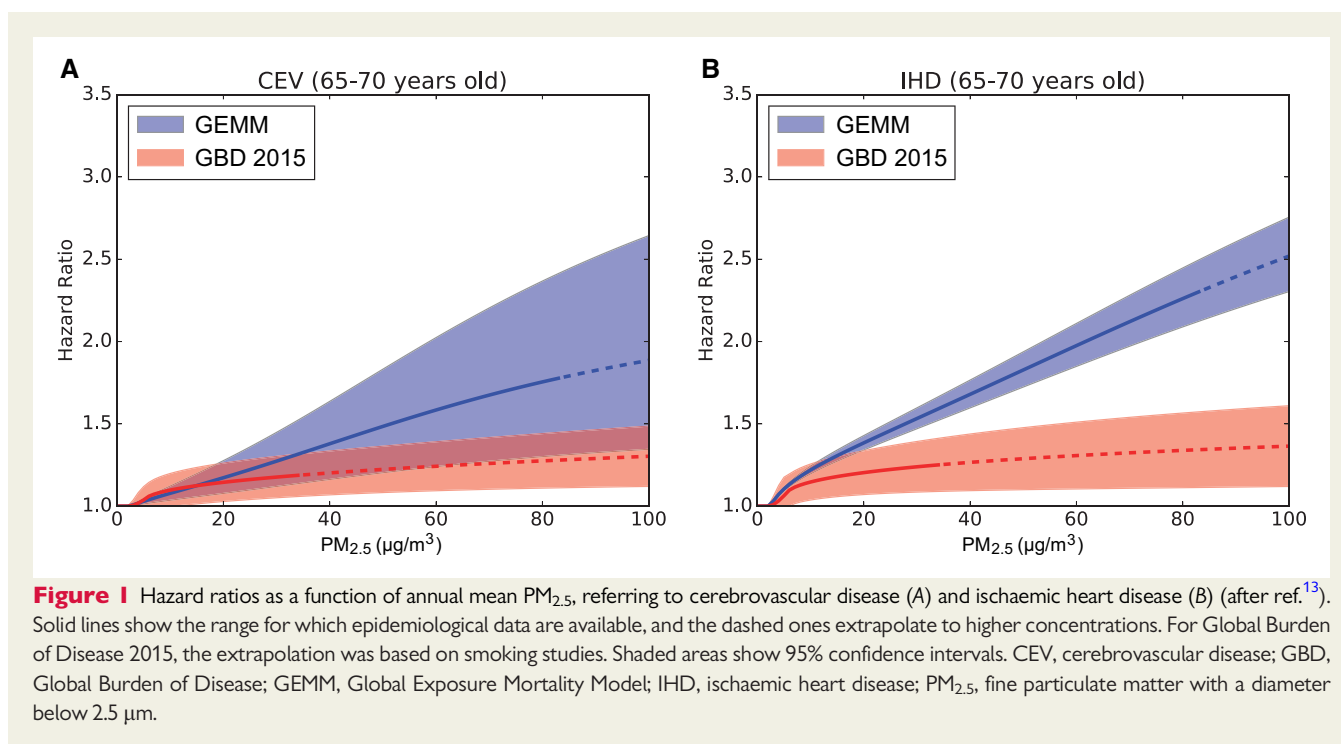


Figure 1 Hazard ratios as a function of annual mean PM_{2.5}, referring to cerebrovascular disease (A) and ischaemic heart disease (B) (after ref.¹³). Solid lines show the range for which epidemiological data are available, and the dashed ones extrapolate to higher concentrations. For Global Burden of Disease 2015, the extrapolation was based on smoking studies. Shaded areas show 95% confidence intervals. CEV, cerebrovascular disease; GBD, Global Burden of Disease; GEMM, Global Exposure Mortality Model; IHD, ischaemic heart disease; PM_{2.5}, fine particulate matter with a diameter below 2.5 µm.

7.2 million per year¹⁷; hence air pollution is now rated as the larger risk factor. The new GEMM leads to a doubling of the air pollution attributable mortality. It corresponds to a global mean per capita mortality rate of 120/year per 100 000 inhabitants. In Europe, the per capita rate exceeds the global mean with 133/year per 100 000, and 129/year per 100 000 in the EU-28 (Table 1). We find that especially in eastern Europe per capita mortality rates are very high, for example in Bulgaria, Croatia, Romania, and the Ukraine, where they exceed 200/year per 100 000. Table 1 also presents the years of life lost (YLL) and the LLE. In Europe, the number of YLL is 14 (95% CI 12–17) million/year, and the mean LLE is 2.2 (95% CI 1.8–2.6) years. The LLE in Europe from air pollution attributable CVD alone is 1.0 (95% CI 0.9–1.2) year, and 1.8 (95% CI 1.2–2.5) years if we also include the other NCD.

Large health impact through cardiovascular disease

Table 1 and Supplementary material online, Table S1 list disease categories that contribute to excess mortality from air pollution. It presents results for Europe, the EU-28, and the five countries that are leading in terms of total CVD mortality as well as attributable CVD deaths. Cerebrovascular events in Europe contribute 64 000 (95% CI 31 000–95 000) per year. This includes ischaemic and haemorrhagic strokes, with about 38 000 and 26 000 per year, respectively. The attributable IHD mortality rate in Europe is 313 000 (95% CI 286 000–339 000) per year. Note that the uncertainty range for CEV is larger than for IHD, which is illustrated by the 95% CIs in Figure 1. Supplementary material online, Table S1 provides disease-itemized

and country-level results, including the minimum and maximum values defined by the CIs.

Figure 2 presents a map of attributable CVD mortality, showing relatively high incidence in the south-eastern UK, the Benelux, Germany, northern Italy, and eastern European countries. The total excess CVD mortality rate in Europe is 377 000 (95% CI 317 000–434 000) per year, and in the EU-28 it is 264 000 (95% CI 221 000–304 000) per year. This represents 48% and 40%, respectively, of the total excess mortality rate related to all disease categories. Figure 3 shows the allocation to different diseases in the EU-28, which corroborates the major role of CVD mortality. It also emphasizes the significant increase between the GBD 2015 and the new estimates, especially for IHD events. The total mortality rate from air pollution in the EU-28 has more than doubled with the new GEMM, from about 263 000 to 659 000 per year. To a large extent this is explained by the category 'other NCD', previously not accounted for.

The WHO states that CVD make the relatively largest contribution to NCD deaths (by 41%), followed by cancers, respiratory diseases, and diabetes. Since the categories LRI, COPD, and LC, included in the GEMM, account for the known respiratory and LC events, it appears that at least part of the mortality rate from air pollution by other NCD, being 1.74 (95% CI 0.96–3.29) million/year globally, must be credited to CVD events, which encompass a wide range of diseases. We find that in Europe other NCD contribute 255 000 (95% CI 115 000–394 000) per year to excess mortality, and in the EU-28 it is 249 000 (95% CI 132 000–365 000) per year. The total attributable CVD mortality rate in the EU-28 of 1.85 million/year is made up by 633 000 from IHD (34%), 426 000 from CEV (stroke) (23%) and 790 000 per year by other CVD (43%).² In view of this considerable fraction of 'other CVD' we hypothesize that a

Table 1 Estimated annual excess mortality attributed to air pollution^a

	All risks	From air pollution ^b				All diseases ^d (×10 ³)	Deaths per 100 000	YLL (×10 ⁶)	LLE (years)
	Total CVD mortality (×10 ³)	CEV (×10 ³)	IHD (×10 ³)	CVD ^c (×10 ³)	Other NCD ^c (×10 ³)				
Europe	2138	64	313	377 (48%)	255 (32%)	790	133	14	2.2
EU-28	1849	48	216	264 (40%)	249 (38%)	659	129	11.5	2.1
Germany	330	7	42	49 (40%)	48 (39%)	124	154	2.1	2.4
Italy	221	6	23	29 (36%)	35 (43%)	81	136	1.2	1.9
Poland	180	6	27	33 (57%)	13 (22%)	58	150	1.1	2.8
United Kingdom	147	3	14	17 (27%)	29 (45%)	64	98	1.1	1.5
France	144	3	13	16 (24%)	38 (57%)	67	105	1.1	1.6

^aData for all EU countries, including 95% CI, are given in the [Supplementary material online](#) (overall uncertainty about ±50%).

^bCEV is cerebrovascular disease, IHD is ischaemic heart disease, CVD are total cardiovascular diseases (CEV + IHD), NCD are non-communicable diseases. YLL are years of life lost. LLE is loss of life expectancy.

^cPercentages refer to fractional contributions of CVD and other NCD to attributable mortality from all diseases.

^dAll diseases refer to NCD + LRI according to Burnett *et al.*¹³

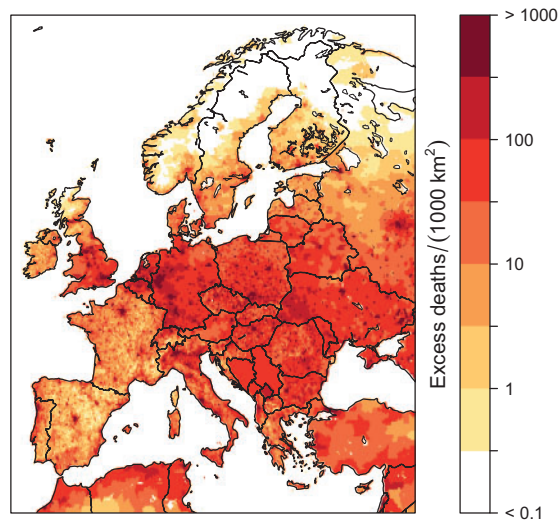


Figure 2 Regional distribution of estimated annual excess mortality rates from cardiovascular diseases (CVD = IHD + CEV) attributed to air pollution. These rates are lower limits as other non-communicable diseases are not included.

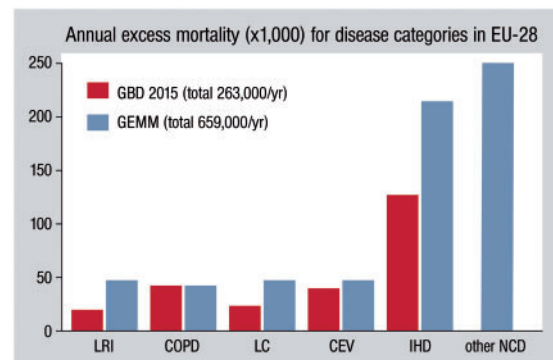


Figure 3 Estimated annual excess mortality rates attributed to air pollution in the EU-28 for lower respiratory tract infections, chronic obstructive pulmonary disease, lung cancer, cerebrovascular disease, ischaemic heart disease, and other non-communicable diseases. Bars compare results from the Global Burden of Disease (2015) and the new GEMM. CEV, cerebrovascular disease; COPD, chronic obstructive pulmonary disease; EU-28, 28 countries of the European Union; GBD, Global Burden of Disease; GEMM, Global Exposure Mortality Model; IHD, ischaemic heart disease; LC, lung cancer; LRI, lower respiratory tract infections; NCD, non-communicable diseases.

large fraction of the air pollution related mortality from other NCD coincides with other CVD.

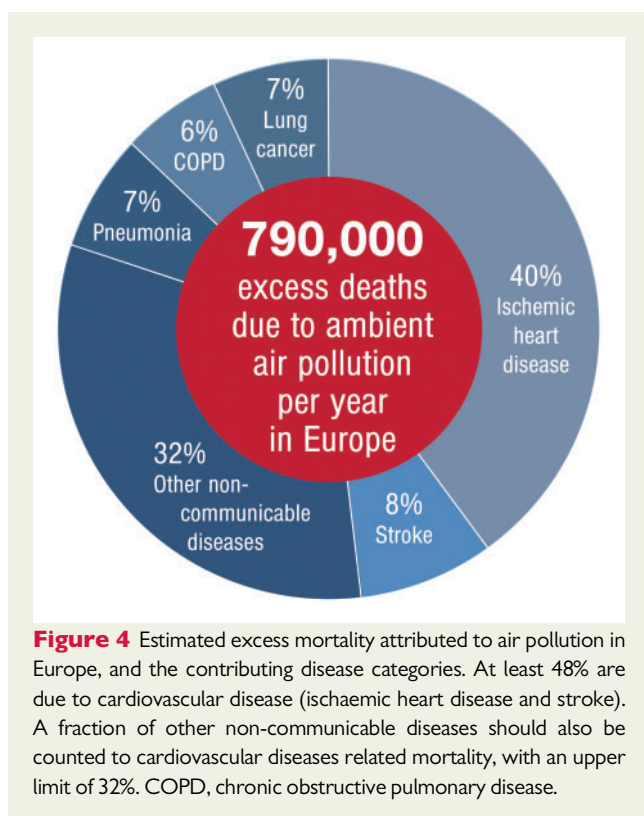
Air pollutants such as PM_{2.5}, as well as the gaseous compounds O₃ and nitrogen dioxide (NO₂), may aggravate atherosclerosis through yet non-explicitly identified risk factors that cause CVD mortality, which may include diabetes and hypertension. Below we argue that general pathways of health impacts by particulate and gaseous pollutants impair vascular function, which may explain their remarkably large influence on excess mortality rates through the combined IHD, CEV, and other NCD events. In the upper limit, i.e. by assuming that all other NCD deaths occur through cardiovascular events, the

mortality rate from air pollution by CVD in Europe would account for about 80% of the total (and about 78% within the EU-28).

Discussion

Air pollution mortality in Europe

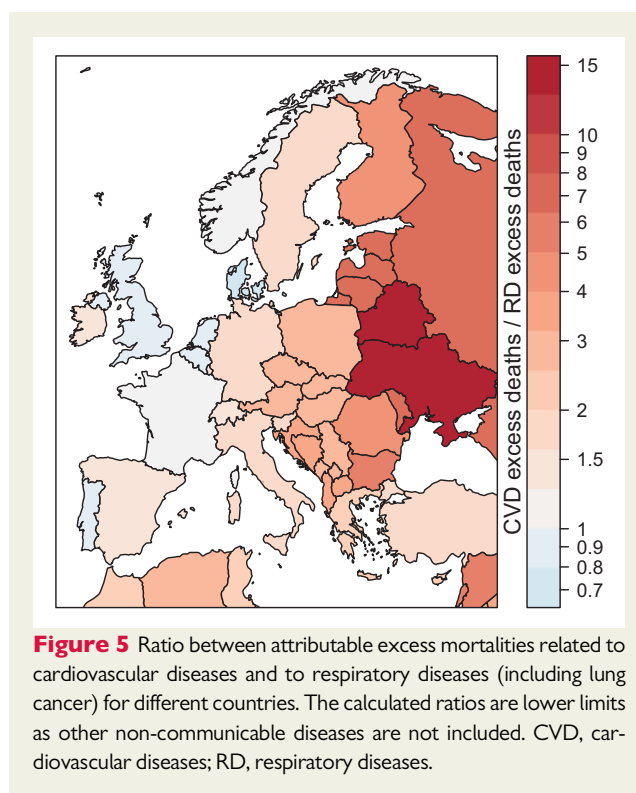
The relatively high attributable per capita mortality rate in Europe of about 133/year (and 129/year in the EU-28) per 100 000 is explained by the combination of poor air quality and dense population, leading to exposure that is among the highest in the world. We reiterate that



the total estimated excess mortality rate is 790 000 (95% CI 645 000–934 000) per year in Europe (Figure 4), and 659 000 (95% CI 537 000–775 000) per year in the EU-28. The European Environment Agency¹⁸ acknowledges about 400 000/year for the EU-28, which thus needs to be revised substantially upward. Our results indicate that the contribution by CVD alone in the EU-28 is 264 000 per year, and potentially up to 513 000 per year if we include the other NCD, albeit with substantial uncertainty. This adds weight to the special report of the European Court of Auditors, which affirms that health within the EU-28 is insufficiently protected.¹⁹ The report states that ‘European citizens still breathe harmful air, mostly due to weak legislation and poor policy implementation’.

The major impact of air pollution on CVD is illustrated by Figure 5, showing the ratio between the attributable excess mortalities related to CVD (IHD + CEV) and respiratory diseases (RD = LRI + COPD + LC). On average, this ratio is close to two in Europe and the EU-28; and it would be about twice as high if the other NCD would be included. While the respiratory system acts as ‘gatekeeper’ between polluted air and the human body, being directly affected through RD, even greater harm is done through CVD. Figure 5 also shows a remarkable west-east gradient in the CVD/RD ratio, being an order of magnitude higher in eastern than in western Europe. Since this gradient does not correspond to a similar gradient in air pollution exposure, it may be explained by more advanced health care in western Europe, where life expectancy is generally higher. Obviously, both health care and air quality can be limiting factors.

The EU applies an annual mean air quality limit of 25 µg/m³ for PM_{2.5} since 2015, which is 2.5 times higher than the guideline concentration of 10 µg/m³ of the WHO. Figure 1 shows that even at 10 µg/



m³ hazard ratios significantly exceed 1.0, both for the GEMM and the GBD 2015, while especially for IHD they increased substantially with the GEMM. Clearly, hazard ratios are high at 25 µg/m³, e.g. about 1.5 for IHD (Figure 1), indicating that the EU-28 air quality standard is insufficient. For comparison, in the USA, the annual mean limit is 12 µg/m³ (since 2012), and in Canada 10 µg/m³ since 2015, to be reduced to 8.8 µg/m³ in 2020. In Australia, the annual PM_{2.5} limit is 8 µg/m³ with the goal to further reduce to 7 µg/m³ in 2025. The EU has formulated exposure reduction targets for 2020, associated with an annual PM_{2.5} level of 20 µg/m³. However, even the current limit is exceeded in several parts of Europe.²⁰ Clearly, additional efforts are needed to warrant clean air.

Cardiovascular disease associated with PM_{2.5}

It is generally accepted that chronic effects of air pollution on cardiovascular events are larger than acute effects, and that elderly and individuals with prior CVD or associated factors are at higher risk.¹¹ An increase of 10 µg/m³ in annual mean PM_{2.5} is associated with a significantly enhanced risk for hospitalizations and heart failure mortality.²¹ There is ample evidence of adverse health effects from PM_{2.5} at concentrations below current standards in the USA.²² Numerous studies have established a strong association between air pollution and cardiovascular events, such as myocardial infarction, stroke, heart failure (including hospitalization for acute left heart decompensation), arrhythmia, and venous thromboembolism (for reviews, see refs^{5,11,23}). The ESCAPE project established a 13% increase in non-fatal acute coronary events from the long-term exposure to PM_{2.5} at 5 µg/m³ elevation.²⁴ Recent evidence indicates an excess risk of acute

coronary syndrome in response to PM_{2.5} exposure in subjects with angiographically diagnosed coronary artery disease.²⁰

We find that the number of CVD deaths attributable to air pollution is higher than expected, which may be explained by adverse effects on other NCD such as diabetes and hypertension. This is supported by two recent meta-analyses, which calculated a substantially increased risk for diabetes mellitus Type 2 per 10 µg/m³ increase of PM_{2.5}.^{23,25} Further, the enhanced exposure to PM_{2.5} by 10 µg/m³ leads to an increase of systolic and diastolic blood pressure by 1–3 mmHg and is associated with a hazard ratio of 1.13 for the development of arterial hypertension.^{26,27} Fine particulate matter has been shown to cause vascular (endothelial) dysfunction by activating molecular pathways leading to increased oxidative stress¹¹ through mechanisms that are strikingly similar to those underlying vascular dysfunction established in the setting of diabetes²⁸ and hypertension.²⁹ Therefore, it appears that air pollution triggers and/or aggravates other NCD, such as diabetes and hypertension, which may significantly contribute to CVD outcomes.

Emission control—an effective intervention

While it is desirable to reduce annual mean PM_{2.5} pollution well below 10 µg/m³ (the safe threshold is around 2–3 µg/m³), in reality there are limitations to what is achievable, in part because some PM_{2.5} is natural. We performed sensitivity calculations by assuming a phase-out of fossil fuel related emissions (needed to achieve the 2°C climate change goal under the Paris Agreement). The calculations indicate that in Europe an excess mortality rate of 434 000 (95% CI 355 000–509 000) per year could be avoided by removing fossil fuel related emissions. About 80% of the avoided European mortality is within the EU-28. The increase in mean life expectancy in Europe would be 1.2 (95% CI 1.0–1.4) years. It follows that the switch from fossil to clean, renewable energy sources is a highly effective health promotion intervention. The European attributable mortality rate would decrease by about 55%. This is a tremendous health co-benefit from the phase-out of carbon dioxide emissions.

Limitations

Figure 1 illustrates the higher hazard ratios of the GEMM compared with the last GBD estimates, especially for IHD, including uncertainty ranges (95% CI).^{8,13} It should be emphasized that the 95% CI refers to statistical uncertainty associated with the epidemiological data, and not methodological uncertainty, including unaccounted confounding factors, assumptions about counterfactuals or limited representativeness of the hazard ratio functions (for details, see [Supplementary material online](#)). The confounder problem can work in two directions, either by over-attributing air pollution deaths to disease categories, or by unaccounted air pollution impacts, e.g. on birth weight and neonatal deaths, and diseases that may not be captured under the other NCD.^{3,7} Since the contribution by other NCD has been derived from the difference between the total and the known NCD the 95% CI is relatively large, about ±55%, while for the other disease categories ±10–40% (for Europe). Because it is not possible to unambiguously determine the total uncertainty from epidemiological data alone, we estimate the overall uncertainty to be larger than the

indicated 95% CI, i.e. about ±50% of the calculated mean values.⁷ In the presentation of our results, however, we follow the GBD convention by reporting the 95% CI.

Future directions

Newby *et al.*¹² emphasized the abundance of evidence that air pollution contributes to CVD and associated mortality. Our results indicate a much higher disease burden than previously assumed. It will be important to reconcile the air pollution-induced mechanisms responsible for relatively well-established causes of CVD and mortality (e.g. IHD and stroke) and potentially newly identified ones that contribute to other NCD (e.g. hypertension and diabetes). Furthermore, there is still little mention of air pollution as a risk factor in the European and American guidelines on health care and disease prevention. While the clinical practice guidelines of the European Society of Cardiology indicate that air pollution can adversely affect cardiovascular health, we propose to additionally include recommendations on the mitigation of risks by individuals, organizations or governments.³⁰

Conclusions

By combining the new GEMM of Burnett *et al.*,¹³ which is based on an unmatched large number of cohort studies, with global air pollution exposure data,⁷ we estimate that the attributable excess mortality rate is about 8.79 million per year with an overall uncertainty of about ±50%. It is associated with a mean LLE of 2.2 years in Europe. In the EU-28 alone, between 15% and 28% of the total CVD mortality of 1.85 million/year is attributable to air pollution, the upper limit being associated with ‘other NCD’, though with substantial uncertainty. By considering the general pathways of how air pollution causes vascular impairment, the actual percentage may be closer to the upper than the lower limit, indicating that it may be higher than 20%, and suggesting that air pollution is a health risk factor that may exceed that of tobacco smoking. We conclude that improving European air quality is an achievable, highly effective, and therefore imperative health promotion intervention. By replacing fossil energy sources with clean, renewable fuels, needed to meet the goals of the Paris Agreement on climate change, the attributable mortality rate in Europe could be reduced by 55%. Further reductions are feasible by additionally controlling other industrial and agricultural pollution sources.

Supplementary material

[Supplementary material](#) is available at *European Heart Journal* online.

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Conflict of interest: none declared.

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