Weekly Journal Scan

Weekly journal scan: every breath you take, air pollution impacts your cardiovascular health

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Comment on ‘Exposure-response associations between chronic exposure to fine particulate matter and risks of hospital admission for major cardiovascular diseases: population-based cohort study’ which was published in The British Medical Journal, https://doi.org/10.1136/bmj-2023-076939.

Key Points
- In this population-based cohort study, the authors estimated exposure–response associations between chronic exposure to fine particulate matter (<2.5 µm in diameter (PM2.5)), a critical component of air pollution, and the risks of a first hospital admission for seven major cardiovascular disease (CVD) subtypes [ischaemic heart disease (IHD), cerebrovascular disease, heart failure (HF), cardiomyopathy (CMP), arrhythmias (AR), valvular heart disease (VHD), and thoracic and abdominal aortic aneurysms (AA)] or a composite of these CVD. Subgroup analyses were performed based on individual- and neighbourhood-level factors to identify susceptible groups.
- The study included nearly 60 million Medicare beneficiaries aged ≥65 years (most aged 65–74 years at study entry; 84% white; 55% female) who resided in the contiguous USA and had enrolled in the fee-for-service programme during 2000–16. Drawing from a variety of air pollution data sources (such as satellite data, meteorology, land use variables, and chemical transport model simulations), calibrated predictive maps of PM2.5 levels were linked to each participant’s residential zip code as a proxy for exposure measurements. The researchers followed the individuals annually until their first hospitalization for any subtype of CVD. For exposure–response estimations, a causal framework was developed against confounding bias and bias resulting from errors in exposure measurements. Both relative and absolute effects were assessed.
- Three-year average exposure to PM2.5 was associated with increased relative risk (RR) of first hospital admissions for IHD, cerebrovascular disease, HF, CMP, AR, and AA. Ischaemic heart disease was the most prevalent CVD resulting in hospitalization (8.8%) followed by cerebrovascular disease (7.7%), HF (6.6%), and AR (6.5%). Notably, the curve for HF showed the steepest slope, with the RR for a first hospitalization ranging from 1.19 (95% confidence interval (CI), 1.17–1.22) for the exposure interval 5–6 µg/m³ to 2.31 (95% CI, 2.28–2.35) for the highest exposure interval (>14 µg/m³).
- Overall, 22% of subjects had a composite CVD-related hospital admission. No safe threshold for chronic exposure to PM2.5 was identified. The exposure–response curve showed a monotonic increase in risk associated with PM2.5. Compared with the lowest exposure interval ≤5 µg/m³ [World Health Organization (WHO) air quality guidelines], the RR of hospital admission was already raised for exposures between 5 and 6 µg/m³. The RR for exposures between 9 and 10 µg/m³, which included the US national average of 9.7 µg/m³ during the study period, was 1.29 (95% CI, 1.28–1.30). On an absolute scale, the risk of hospitalization for composite CVD increased from 2.6% with exposures ≤5 µg/m³ to 3.4% for exposures ranging between 9 and 10 µg/m³ and then up to 4.7% for the highest levels of exposure (>14 µg/m³). The effects persisted for at least 3 years after exposure to PM2.5. Age, education, accessibility to healthcare facilities, and the level of neighbourhood-related deprivation appeared to have an impact on susceptibility to PM2.5.

Comment
Air pollution is contamination of the outdoor or indoor environment by any chemical, physical, or biological agent that modifies the natural characteristics of the air that we breathe. Environmental air pollution is mainly caused by fossil fuel combustion, while household air pollution is caused by the combustion of biomass fuels, smoking, and gas stoves. Air pollution is nearly ubiquitous as the WHO estimates that >90% of the world’s population live in areas with annual average levels of air pollutants that exceed the limits of WHO global air quality guidelines. Among the different components of air pollution, PM2.5 has demonstrated the strongest association with CVD. Multiple lines of evidence...
link PM$_{2.5}$ exposure to a greater susceptibility to the development of coronary atherosclerosis and the progression to high-risk plaques prone to rupture. PM$_{2.5}$ can promote the generation of reactive oxygen species and reactive nitrogen species by interfering with many cellular mechanisms. PM$_{2.5}$ exposure has been associated with systemic inflammation, direct activation of circulating leukocytes and vascular endothelium, and leukocyte adhesion and migration. PM$_{2.5}$ promotes autonomic and neuroendocrine dysfunction, metabolic alterations, increased thrombosis, and hypercoagulability. Therefore, PM$_{2.5}$ is emerging as a major determinant of atherosclerotic CV risk worldwide. However, its specific impact on different CVD subtypes, as well as exposure–response associations, have remained largely unquantified. Furthermore, results of studies adjusted for exposure measurement errors and reporting estimates of absolute effects are limited. In this context, the paper of Wei et al. deserves great consideration.

The recently released WHO air quality guidelines have reinforced setting the annual average level of PM$_{2.5}$ to no more than 5 µg/m$^3$, i.e. substantially lower than the previous limit of 10 µg/m$^3$ and much lower than the new standard of 9 µg/m$^3$ for the USA and the threshold of 20 µg/m$^3$ set by the UK and Europe. During the period analysed in this study, the annual level of PM$_{2.5}$ in the USA averaged 9.7 µg/m$^3$. The authors estimated that a 23% decrease in overall hospital admissions for CVD could be achieved by reducing PM$_{2.5}$ exposure to <5 µg/m$^3$. This benefit would be even more marked for HF, with an estimated 38% reduction. For people living in the most polluted regions with annual PM$_{2.5}$ levels > 14 µg/m$^3$, reducing these levels to <5 µg/m$^3$ could lead to a 45% decrease in overall hospital admissions for CVD.

The results of the present study are in line with a recent meta-analysis, which reported highly comparable associations between long-term exposure to PM$_{2.5}$ and mortality from IHD and cerebrovascular diseases (23% and 24% increased risk, respectively, for each 10 µg/m$^3$ increase in long-term exposure to PM$_{2.5}$), as well as with previous studies reporting associations between chronic exposure to PM$_{2.5}$ and the risks of HF and AR (a specific sub-analysis was conducted for atrial fibrillation).

Susceptibility varied in relation to age, gender (women and younger people had a higher risk of hospitalization for composite CVD and for most individual CVD), level of education, access to healthcare services, and level of general deprivation related to the neighbourhood. All social and individual variables acted on susceptibility in a predictable way, with the exception of age, since the older group was less susceptible to PM$_{2.5}$ exposure than the younger group. The authors discuss some possible reasons for this, but a simple explanation could be that the most susceptible individuals may have died before reaching the older age. A non-uniform association between PM$_{2.5}$ and VHD was found, since a larger influence was reported for the aortic and the right-sided valves.

Perhaps, the most important and unsettling finding of the present study is represented by the monotonic increase of the exposure–response curve for composite CVD, suggesting that there is no risk threshold of PM$_{2.5}$ for CV health. Therefore, adherence to the WHO air quality guidelines of <5 µg/m$^3$ does not seem to guarantee a completely safe environment. Overall, the effect of PM$_{2.5}$ persisted for at least 3 years after exposure, suggesting a long-lasting impact of PM$_{2.5}$ on CV health. It also implies that the benefits of policies to reduce PM$_{2.5}$ may be realized immediately after implementation and continue to accumulate over time.

The current study has several strengths. A large-scale analysis, using spatially and temporally resolved air pollution predictions of PM$_{2.5}$ effects on CVD outcomes, addressed a major concern related to the exposure measurement error observed in previous studies. The analysis used also reduced confounding bias. Estimates of the absolute effect of PM$_{2.5}$ on risks of hospitalization for IHD, cerebrovascular disease, HF, and AR could inform targeted interventions to mitigate the adverse impacts of PM$_{2.5}$ on these conditions.

The study has some limitations. First, due to the limited data sources available, relevant individual risk factors (such as body mass index and smoking) were not considered. However, ambient air pollution levels in neighbourhoods are unlikely to be substantially influenced by individual covariates. In support of this theory, the authors performed a sensitivity analysis that excluded all available individual-level covariates (gender, race/ethnicity, age, Medicare enrolment status) and found that the results remained highly consistent with the main analysis. Secondly, the exposure assessment relied on zip code rather than individual residential address to match PM$_{2.5}$ to each subject, thus introducing possible measurement errors. Third, the demographic profile of the Medicare population and the study period from 2000 to 2016 limited the generalizability of these findings.

In conclusion, the study of Wei et al. provides new additional fuel to the recognition of the CVD burden attributable to air pollution, which appears substantially comparable with other major global health issues. Together with the rapidly accumulating evidence in this area, the current findings may contribute to raise awareness of the importance of mitigating environmental contaminants in the prevention of CVD. Stronger and more urgent efforts are needed to improve air quality, not only to reduce the burden of CVD and other disease conditions but also to contribute to fighting climate change on our planet, with expected co-benefits under the umbrella concept of One Health.

**References**