



Correspondence



Letter in response to Cole-Hunter et al., 2023: What does “Parkinson’s disease mortality” mean?

We read with interest the recent multi-country study by Cole-Hunter et al. (2023), that evaluated the association between air pollution and Parkinson’s disease (PD) mortality in the ELAPSE cohorts. As noted by the authors of that paper, and by the World Health Organization previously, (World Health Organization, 2013) more evidence on the role of air pollution in neurodegenerative disorders is needed. However, when these studies are conducted, more attention needs to be paid on the outcome definition. Thus, our main concern is that the results may simply reflect air pollution related all-cause mortality rather than PD specific effects. While this study is an impressive international collaboration utilizing existing cohorts to study the adverse health effects of air pollution at lower levels, the study design is not ideal to study PD as an outcome. PD is a challenging outcome as the diagnosis is complex, and the prodromal phase is long. Consequently, atypical, secondary and undetermined parkinsonisms are often included in PD outcome cohorts, although these are distinct disorders, with very different aetiologies and prognoses. (Keener and Bordelon, 2016) To their merit, although Cole-Hunter et al. included secondary parkinsonism in their outcome, they report that only one of the “PD deaths” was due to secondary parkinsonism, although it was not clear if those with other non-PD parkinsonism were included in the remaining 380 deaths.

Furthermore, it is difficult to interpret what the increased risk of PD mortality means because the study is not restricted to persons with PD, and no information on the overall mortality or other cause-specific mortality is given. As ambient air pollution is robustly associated with higher risk of death also in the ELAPSE cohorts, (Strak et al., 2021) the results can simply be due to this. It appears that the group who did not experience the outcome in the present ELAPSE study also includes the survivors, increasing the survival in this group. To exclude the overall increase in mortality among those with higher exposure to ambient air pollution as the explanation for the findings by Cole-Hunter et al., it would have been helpful to reflect these findings to overall survival in the ELAPSE cohort and to provide more detailed information on the censoring distribution.

The number of inception cohort studies assessing the mortality and life expectancy of persons with PD in recent years is limited, but it seems that although the relative risk of death is increased (mortality ratio 1.52), (Macleod et al., 2014) the life expectancy varies significantly depending on the stage of PD, or type of parkinsonian disorder. For example, the life expectancy of those with PD and normal cognition was not different to the general population, while those with atypical parkinsonism had significantly increased mortality. (Bäckström et al., 2018) A Norwegian cohort study of patients with clinical diagnosis of PD reported a median survival of 15 years, and highest mortality rate among those with young age of onset (20–39 years). (Hustad et al., 2021)

The average age at the end of follow-up in the study by Cole-Hunter et al. was 67 years, which is somewhat younger than the average age of

PD diagnosis (70 years). (Macleod et al., 2018) This suggests that even if the results did not reflect the overall increase in mortality among those with the higher exposure to ambient air pollution, the results are more affected by patients with younger onset PD. Based on the supplementary material (Table S8), the associations are indeed driven by the data from VHM&PP cohort, as excluding them significantly affected the point estimates. This cohort had the youngest participants (mean age at baseline and the end of follow-up were 42 and 65 years, respectively), but one of the highest PD mortality rates based on Table S2. This raises the question on whether these persons truly had early-onset PD, or rather atypical parkinsonisms or other disorders, and how this affects the interpretation of the results. Further, as the results are not interpreted in the context of overall increase in mortality, and there is no information on the total number of persons with PD in ELAPSE, the meaning of the results is unclear.

As ambient air pollution is an important risk factor for health and its significance for many outcomes is still poorly understood, high-quality environmental epidemiological studies are needed. Cole-Hunter et al. describe their exposure assessment very clearly and provide an excellent discussion on possible explanation for the findings as well as the role of individual pollutants. However, it would have been equally important to provide more information on what the outcome actually represents.

Declaration of Competing Interest

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Data availability

No data was used for the research described in the article.

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