



Premature deaths attributed to ambient air pollutants: let us interpret the Robins–Greenland theorem correctly

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Dear Editor,

Héroux and colleagues (Héroux et al. 2016) replied to our Letter to the Editor (Morfeld and Erren 2016). They stated after “close reading of Greenland (1999)” the following: “So, contrary to what Morfeld and Erren write, the calculation as performed in our paper estimates etiologic cases (if we follow Greenland’s notation)” and the authors concluded “As is well known, the GBD [Global Burden of Disease] estimates are also expressed as numbers of deaths attributed to certain risk factors, and these are typically denoted as ‘premature’ deaths precisely because there is no such thing as avoidable or excess deaths when it comes to total mortality. Therefore, in contrast to Morfeld’s and Erren’s assertion, our project recommendations do properly take into account methodological considerations with respect to quantification of mortality impacts of air pollution”.

Héroux and colleagues are mistaken. Greenland’s paper and other publications (Beyea and Greenland 1999; Greenland 2012, 2015; Robins and Greenland 1989, Greenland and Robins 2000) conveyed as a main message that the hazard fraction $(RR - 1)/RR$ does not estimate the etiologic fraction.

Thus, the following and typical statement on premature deaths is unjustified: “Modelled trends in pollutant levels show that under a business-as-usual scenario (baseline projection) the impacts of air pollution will continue to decrease by 2020, where they will amount to an estimated 340,000 premature deaths” (Héroux et al. 2015, p. 625).

Given circumstances as described in Greenland (1999) (person-years almost unaffected by exposure) one may use $(RR - 1)/RR$ to estimate the excess fraction. We agree that this metric is vacuous if total mortality is the endpoint of interest because excess deaths do not exist. Thus, the interest is in premature deaths, indeed. Unfortunately, the number of premature deaths given in Héroux et al. (2015) is a *non-sequitur*.

We like to explain in more detail why the statement about premature deaths cited from Héroux et al. (2015) is unjustified. Robins and Greenland (1989) proved that transformations of RRs into numbers of premature deaths (‘etiologic deaths’) based on the hazard fraction $(RR - 1)/RR$ are potentially biased. Indeed, $(RR - 1)/RR$ has to be replaced by a factor F in such a calculation. Robins and Greenland showed that F cannot be estimated from epidemiological data alone and that F is bounded by $(RR - 1)/[RR^{RR/(RR-1)}]$ and 100 % assuming proportional hazards [see Eq. (11) in Robins and Greenland 1989]. Table 1 in Héroux et al. (2015) reported $RR = 1.064$ per $10 \mu\text{g}/\text{m}^3$ $\text{PM}_{2.5}$ (annual mean) for all-cause mortality (natural), age 30+ years. Given $RR = 1.064$ the bounds for F are 0.028 and 1, whereas $(RR - 1)/RR = 0.060$. It follows that the point estimates of number of premature deaths based on $(RR - 1)/RR = 0.060$ suffer from a potential relative bias between -94 and $+164$ %. We note that F may vary in this wide range across regions or with covariates. Imprecision as estimated by confidence

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intervals is an independent source of uncertainty that has to be considered additionally.

We like to emphasize that we agree with the following statement in Héroux et al. (2016) reply to our Letter: “The RRs used in our project, therefore, essentially estimate the ratio of life expectancies in exposed vs. unexposed over the observation period, as the period of observation is censored at time of death and thus shorter among the exposed (who die sooner) than among the unexposed”. We think that “years of life lost due to exposure” is a better metric to be used in public health issues than the potentially biased “number of premature deaths due to exposure” (although it may seem easier and more effective—*prima facie*—to communicate the latter to politicians and stakeholders). However, we noted in our Letter that there are problems related to this preferable metric, too, if, for instance, years of life lost due to exposure are broken down by age or calculated for specific causes of death and then used to calculate DALYs (Disability Adjusted Life Years lost due to exposure) with weights that reflect specific ages or specific causes of death (Robins and Greenland 1991; Morfeld 2004). For more details, see the discussion on metrics in Greenland and Robins (2000).

Taken together, the response by Héroux and colleagues (Héroux et al. 2016) to our Letter to the Editor (Morfeld and Erren 2016) hinges on the misreading of Greenland (1999) to mean the opposite of what it actually meant. The key statement to which we pointed in Héroux et al. (2015) continues to conflict—as a *non-sequitur*—with a mathematically proven theorem.

Unfortunately, this methodological error in calculating numbers of premature deaths due to exposure is widespread (e.g., Turner et al. 2015; Lelieveld et al. 2015). We hope that this letter exchange may contribute to clarifications so that future burden-of-disease analyses will no longer apply the unjustified method: “Mistakes in peer-reviewed papers are easy to find but hard to fix” (Allison et al. 2016). We also hope that Héroux and colleagues can provide a correction and revise their inferences as needed.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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