Global mortality burden attributable to non-optimal temperatures

Katrin Burkart and colleagues[1] present the results of an ambitious study on the global mortality burden attributable to non-optimal temperatures by the Global Burden of Diseases, Injuries,and Risk Factors Collaborators. They report that 2·98% of deaths globally could be attributed to non-optimal temperatures in 2019; 2·37% of deaths from low temperatures and 0·63% of deaths from high temperatures.

Although estimates of the heat mortality burden are broadly consistent with existing literature, the contribution of cold temperatures to this burden differs substantially to assessments at global and regional scales.[2–4] We believe that these differences are the result of crucial methodological limitations of the study,[1] mainly the failure to adequately address the complexities of temperature–mortality relationships, probably resulting in an underestimation of the effects.

Burkart and colleagues only accounted for the effects on the same day (ie, lag 0), whereas substantial epidemiological data shows the presence of lagged effects of temperature (up to 3 weeks for cold temperatures) or mortality displacement, or both.[5] Additionally, the applied method does not account for seasonality or long-term trends—strong confounders in this analysis.[5] In the appendix, we illustrate how markedly different the results of the two approaches are using data from Greater London, UK.

A critical lens needs to be applied to any analytical framework to ensure its suitability and to increase confidence in the results. Burkart and colleagues' analyses[1] would have benefited from method developments in climate epidemiology from the past 20 years. Robust and reliable estimates of the burden of non-optimal temperatures are increasingly important in a changing climate.

We declare no competing interests.

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1 Burkart KG, Brauer M, Aravkin AY, et al. Estimating the cause-specific relative risks of non-optimal temperature on daily mortality: a two-part modelling approach applied to the Global Burden of Disease Study. *Lancet* 2021; **398:** 685–97.

2 Zhao Q, Guo Y, Ye T, et al. Global, regional, and national burden of mortality associated with non-optimal ambient temperatures from 2000 to 2019: a three-stage modelling study. *Lancet Planet Health* 2021; **5:** e415–25.

3 Chen R, Yin P, Wang L, et al. Association between ambient temperature and mortality risk and burden: time series study in 272 main Chinese cities. *BMJ* 2018; **363:** k4306.

4 Martínez-Solanas È, Quijal-Zamorano M, Achebak H, et al. Projections of temperature attributable mortality in Europe: a time series analysis of 147 contiguous regions in 16 countries. *Lancet Planet Health* 2021; **5**:e446–54.

5 Gasparrini A. Modelling lagged associations in environmental time series data: a simulation study. *Epidemiology* 2016; **27**:835–42.

Authors' reply

We are pleased to respond to Ana Vicedo-Cabrera and colleagues, who suggest we underestimated the mortality burden attributable to cold temperatures.[1] We agree that, in explicitly restricting our analysis to same-day temperature effects, not considering lagged effects, we probably underestimated the temperature-attributable mortality, especially for cold temperatures. In asserting that season is a strong confounder, Vicedo-Cabrera and colleagues cite a simulation study that evaluates the role of season in air pollution assessment, which is fundamentally different because both air pollution and health are affected by season and meteorology.

Although we recognise the tradition of seasonal adjustment in analyses of temperature and health, we question the merits of the inherent assumptions. For season to confound temperature–mortality associations it should first be associated with, and lie upstream in, the causal pathway from both temperature and mortality; and second, the association between season and mortality should not be wholly mediated through temperature. Although the first condition seems reasonable, at least in temperate locations, the second condition demands more thoughtful consideration. We intentionally did not adjust for seasonality because the associations between season and both temperature and mortality vary widely across time and space.

See **Online** for appendix

Seasonal mortality trends are driven by either direct biological effects (in response to temperature), or indirect effects that are mediated through sociobehavioural factors (eg indoor crowding in response to the cold). The unpublished example in the appendix of Vicedo-Cabrera and colleagues' Correspondence that simultaneously accounts for lagged effects, trends, and season from a single mid-latitude location is insufficient to show that seasonal effects are globally generalisable or that seasonal adjustments are epidemiologically sound.

Probably more important than the effect of lags and seasonality, our estimates only included causes of death that were significantly associated with temperature, whereas the previous studies cited by Vicedo-Cabrera and colleagues are either based on all-cause mortality[2,3] or exclude non-accidental causes.[4]

See Online for appendix

Further, our study showed that the shape of the exposure–response relationship varies across different causes, highlighting the importance of the underlying mortality composition. Our focus on cause-specific mortality is relevant for the design of interventions and necessary for accurate global applications, such as our new method framework to estimate the heat-attributable and cold-attributable burden for 204 countries and territories.[5]

The strength of our study lies in estimating the exposure–response relationships along different temperature zones and for a multitude of different mortality causes. Together, these features allow for the estimation of the attributable burden by applying our risk curves to data-sparse regions. Although global applications come with limitations and uncertainties, we consider our study to be an important step towards establishing much-needed estimates for areas without data availability.

We are well aware of the method developments in climate epidemiology over the past 20 years but suggest that future research can also build on our work, especially the importance of cause-specific analyses when developing reliable estimates for regions where daily mortality data are not available. We and others are undertaking ongoing work to estimate future mortality effects for different climate scenarios. Ignoring spatiotemporal changes in cause-specific mortality and exposure–response relationships will probably lead to erroneous projections. In an era of climate change, reliable estimates are needed to inform effective, evidence-based interventions.

We declare no competing interests.

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1 Burkart K, Brauer M, Aravkin AY, et al. Estimating the cause-specific relative risks of non-optimal temperature on daily mortality: a two-part modelling approach applied to the Global Burden of Disease Study. *Lancet* 2021; **398:** 685–97.
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Is stenting equivalent to endarterectomy for asymptomatic carotid stenosis?

We read with interest the findings of the ACST-2 trial.[1] However, some of the observations made us wonder whether it was accurate to conclude that carotid artery stenting (CAS) and carotid endarterectomy (CEA) were comparable.

First, in both the intention-to-treat and per-protocol analyses, the rate of procedural strokes in patients receiving CAS was above 3% and significantly higher than in those randomly assigned to CEA (appendix). Second, the trial was probably underpowered to detect a difference between CAS and CEA for disabling or fatal strokes, non-disabling strokes, and the composite endpoints. CEA was superior to CAS for all comparisons, with a power above 45% (appendix). Additionally, evidence suggests that the safety profile of CEA could be further improved by decreasing serum concentrations of lipoprotein(a).[2,3] Third, as shown in the appendix to the Article,[1] the rates of death or any ipsilateral stroke was significantly higher in the CAS group (5·5%) than in the CEA group (3·6%; p=0·005 in intention-to-treat analysis). This finding is important because strokes occurring later during follow-up are less likely to be related to the intervention or to the index carotid stenosis than are strokes occurring within 30 days of the intervention. Furthermore, the first carotid intervention is not expected to prevent strokes due to other causes identified during follow-up (eg, contralateral carotid stenosis, atrial fibrillation, aortic plaques, infections, uncontrolled hypertension, or subsequent carotid surgery).

We have previously reported that the incidence of stroke in patients with asymptomatic carotid stenosis was 3·2 per 100 person-years overall and