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Making sense of national and international disparities in excess mortality from the COVID-19 pandemic

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The COVID-19 pandemic is one of the biggest health challenges faced by humanity in over a century. Unlike the 1918 Spanish influenza, data on the COVID-19 pandemic have been extensively collected, analysed, documented and monitored in real time by numerous organisations.[1–4] Due to the scale of the pandemic and the variable success in tackling it in different countries, it is important to identify factors and policies affecting mortality, to retrospectively assess their effectiveness, and to help inform the response to any future pandemic. Although a large volume of work has been already done, this work will continue for many more years.

Early in the pandemic, testing limitations often led to undercounting of COVID-19 deaths, particularly in countries with weaker health systems. This undercount varied across countries and changed over time as testing became more widespread. Therefore, the straightforward counting of the officially registered deaths from COVID-19 is problematic. Fortunately, in 2020, epidemiologists and demographers reached a consensus regarding the use of the excess mortality approach for the estimation of mortality due to COVID-19.[5–7] This method, based on a comparison of expected (from historical trends) and observed mortalities, produces the most reliable estimates that are not biased by differences in testing and reporting practices. Excess mortality also helps to capture the full impact of the pandemic, including its wider effects on health systems, and allows assessment of the effectiveness of public health, economic and medical interventions.[8 9] Despite a long history of estimating 'excess deaths' during wars and pandemic,[10] and numerous methodological advances based on mathematical modelling in more recent decades, the main obstacle for accuracy of estimations before the COVID-19 pandemic was the limited availability of high-quality data.

Estimates of excess deaths and death rates for the years 2020 and 2021 have been produced by the UN, WHO and other organisations.[2 11 12] Although estimates by different research groups are highly correlated, significant differences between them were identified even in countries with fully reliable mortality data.[13–15] More precise and granular estimates of excess mortality rates and life expectancy losses were produced for 29–37 (depending on the study) high- and middle-income countries with fully reliable vital statistics.[8 9 16–18] Cause-specific excess mortality has also been reported.[19]

Studying mortality differences between countries and population groups as well as ecological associations between excess mortality and characteristics of countries and groups allowed researchers to identify potential determinants of inequality in excess mortality. So far, the results reported associations with excess mortality for vaccination, timeliness of non-pharmaceutical interventions,[17 20–24] primary healthcare supply, healthcare funding, health insurance coverage (for the USA),[24–26] ability for regulatory enforcement,[27] urbanisation, population density and mobility,[25 28] deprivation, and racial minorities (for the USA).[25 29–35]

The *BMJ Global Health* article by Pallari *et al*[36] is the newest publication by the International Consortium on COVID-19 Mortality. The study covers 24 countries from Africa (1), Asia (2), Australia (1), Europe (17), North America (1) and South America (2). The countries include Georgia, Kazakhstan, Mauritius and Ukraine, which rarely appear in excess mortality studies. The study shows how excess mortality varies across countries and across time within each country and identifies factors potentially underlying this

variation. Pallari *et al* used 5 weekly and annual measures of excess mortality (weekly Z-scores, annual crude and age-standardised mortality rates (ASMRs) and P-scores) and estimated country-level cross-sectional and within-country longitudinal associations linking excess mortality Z-scores with explanatory variables.

They found that at the country level, the annual excess mortality is positively associated with income inequality and with the prevalence of diabetes, hypertension and obesity; negatively associated with healthcare access and quality index and the human development index.

The results of the within-countries longitudinal analysis are controversial. No correlation across weeks was found for the vaccination coverage. For the stringency index, there is a positive association with excess mortality during 2020 and a negative association during 2021.

The absence of an expected negative relationship between excess mortality and vaccination is a worrying public health message but also a counterintuitive finding that is inconsistent with individual-level evidence,[37–40] and the negative cross-country correlation found by Pallari *et al* themselves and other studies.[17 21–24]

Finally, Pallari *et al* examined longitudinal time-varying effects within each country. It showed large within-year fluctuations in the impacts of vaccination and stringency and a variety of country-specific patterns that differed from each other. Due to the latter finding and the high impacts of the random country effects in the multilevel model, the authors emphasise the importance of country-specific contexts. The country-specific decision-making and country-specific ways for implementation and enforcement of anti-COVID policies matter.

Although the study by Pallari *et al* is an important contribution to the literature, some research opportunities for strengthening the case were not realised. Choosing the Z-score as a central mortality measure may be suboptimal. Z-score is a reasonable measure for identifying short-term mortality elevations but does not directly express mortality losses. It makes it difficult to evaluate the absolute level of excess mortality and complicates comparisons with numerous studies looking at the excess mortality rates.

Comparative analyses of annual mortality across countries by Pallari *et al* suffer from quantitative incomparability between the ASMRs, as acknowledged by the authors. For this reason, they could not carry out quantitative comparisons of ASMRs across countries. The incomparability is a consequence of differences between age groupings of mortality data in different countries which could potentially distort ASMR estimates. Various methods may address this issue in future studies. For example, by using the annual UN life tables as models to redistribute the mortality estimates from broad age groups into uniform 5-year age intervals in each country.

The puzzling findings concerning the excess mortality impacts of vaccination and stringency were not supplemented by a detailed mathematical specification of the multilevel model and discussion of underlying assumptions and possible biases. There is also no discussion on possible measurement errors of the stringency index or the vaccination coverage. The stringency index does not reflect its real implementations, compliance and adherence. Countries with the same level of stringency index could have a substantially different degree of implementation of pandemic measures. For vaccination, its impact on excess mortality will be influenced by the timing of the programme and how participants were prioritised for vaccination. Countries that started their vaccination programme earlier in the pandemic would be expected to see a larger impact on excess mortality. Countries that started later, in contrast, would be expected to see a lower impact on excess mortality as more people would be exposed to COVID-19 before they could benefit from the protective effects of vaccination. Likewise, given the very strong association between age and risk of death from COVID-19, countries that prioritised the elderly for vaccination before other population groups—and also achieved high coverage in this group, including with booster doses—would also expect to see a greater impact on excess mortality. In contrast, achieving high vaccine uptake among younger people would have much less impact on excess mortality. Simple measure of vaccine uptake may not capture all these subtleties in the analysis.

Considering the importance of country-specific contexts highlighted by Pallari *et al*, future studies on this topic could focus on historical and contemporary vulnerabilities of excess mortality. For example, in Europe, attention could focus on the historical vulnerability and sociopolitical evolution since the era of communism in Eastern Europe. In this regard, future studies should consider historical contexts and sociopsychological factors such as trust and confidence in science and governments. In the USA and UK, attention should be paid to inequities in excess mortality among ethnic minorities, and other socioeconomically marginalised groups.

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