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

Vladimir M. Shkolnikov[1], Dmitri A Jdanov[1], Azeem Majeed[2], Nazrul Islam[3]

[1] Laboratory of Demographic Data, Max Planck Institute for Demographic Research, Rostock, Germany

[2] Department of Primary Care and Public Health, Imperial College London, London, UK

[3] Faculty of Medicine, University of Southampton, Southampton, UK

ORCID IDs
Vladimir M. Shkolnikov: 0000-0003-2259-5423
Dmitri A Jdanov: 10000-0003-4633-2011
Azeem Majeed: 0000-0002-2357-9858
Nazrul Islam: 0000-0003-3982-4325

Correspondence to: Nazrul Islam; Nazrul.Islam@soton.ac.uk

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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 flu, data on the COVID-19 pandemic has 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 to 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** is the newest publication by the **I**nternational Consortium on COVID-19 Mortality (C-MOR).[36] 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 five weekly and annual measures of excess mortality (weekly Z-scores, annual crude and age-standardised mortality rates, 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 indices.

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 multi-level model, the authors emphasize 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 and colleagues 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 age-standardized mortality rates (ASMRs), as acknowledged by the authors. For this reason, they could not carry out quantitative comparisons of ASMRs across countries. In this study, the incomparability is explained by 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.

References

1 Jdanov DA, Galarza AA, Shkolnikov VM, *et al.* The short-term mortality fluctuation data series, monitoring mortality shocks across time and space. *Sci Data*. 2021;8:235.

2 Karlinsky A, Kobak D. Tracking excess mortality across countries during the COVID-19 pandemic with the World Mortality Dataset. *eLife*. 2021;10:e69336.

3 Vestergaard LS, Nielsen J, Richter L, *et al.* Excess all-cause mortality during the COVID-19 pandemic in Europe – preliminary pooled estimates from the EuroMOMO network, March to April 2020. *Eurosurveillance*. 2020;25. doi: 10.2807/1560-7917.ES.2020.25.26.2001214

4 Riffe T, Acosta E, the COVerAGE-DB team. Data Resource Profile: COVerAGE-DB: a global demographic database of COVID-19 cases and deaths. *Int J Epidemiol*. 2021;50:390–390f.

5 Leon DA, Shkolnikov VM, Smeeth L, *et al.* COVID-19: a need for real-time monitoring of weekly excess deaths. *The Lancet*. 2020;395:e81.

6 Beaney T, Clarke JM, Jain V, *et al.* Excess mortality: the gold standard in measuring the impact of COVID-19 worldwide? *J R Soc Med*. 2020;113:329–34.

7 Islam N. “Excess deaths” is the best metric for tracking the pandemic. *BMJ*. 2022;376:o285.

8 Kontis V, Bennett JE, Rashid T, *et al.* Magnitude, demographics and dynamics of the effect of the first wave of the COVID-19 pandemic on all-cause mortality in 21 industrialized countries. *Nat Med*. 2020;26:1919–28. doi: 10.1038/s41591-020-1112-0

9 Islam N, Shkolnikov VM, Acosta RJ, *et al.* Excess deaths associated with covid-19 pandemic in 2020: age and sex disaggregated time series analysis in 29 high income countries. *BMJ*. 2021;373:n1137.

10 Eickhoff TC, Sherman IL, Serfling RE. Observations on Excess Mortality Associated with Epidemic Influenza. *JAMA*. 1961;176:776–82.

11 Msemburi W, Karlinsky A, Knutson V, *et al.* The WHO estimates of excess mortality associated with the COVID-19 pandemic. *Nature*. 2023;613:130–7. doi: 10.1038/s41586-022-05522-2

12 Wang H, Paulson KR, Pease SA, *et al.* Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020–21. *The Lancet*. 2022;399:1513–36.

13 Levitt M, Zonta F, Ioannidis JPA. Comparison of pandemic excess mortality in 2020–2021 across different empirical calculations. *Environ Res*. 2022;213:113754.

14 Ioannidis JPA, Zonta F, Levitt M. Variability in excess deaths across countries with different vulnerability during 2020–2023. *Proc Natl Acad Sci*. 2023;120:e2309557120.

15 Kepp KP, Björk J, Kontis V, *et al.* Estimates of excess mortality for the five Nordic countries during the COVID-19 pandemic 2020−2021. *Int J Epidemiol*. 2022;51:1722–32.

16 Aburto JM, Schöley J, Kashnitsky I, *et al.* Quantifying impacts of the COVID-19 pandemic through life expectancy losses: a population-level study of 29 countries. *Int J Epidemiol*. 2021;dyab207.

17 Schöley J, Aburto JM, Kashnitsky I, *et al.* Life expectancy changes since COVID-19. *Nat Hum Behav*. 2022;6:1649–59. doi: 10.1038/s41562-022-01450-3

18 Islam N, Jdanov DA, Shkolnikov VM, *et al.* Effects of covid-19 pandemic on life expectancy and premature mortality in 2020: time series analysis in 37 countries. *BMJ*. 2021;375:e066768.

19 Alicandro G, La Vecchia C, Islam N, *et al.* A comprehensive analysis of all-cause and cause-specific excess deaths in 30 countries during 2020. *Eur J Epidemiol*. 2023;38:1153–64.

20 Islam N, Sharp SJ, Chowell G, *et al.* Physical distancing interventions and incidence of coronavirus disease 2019: natural experiment in 149 countries. *BMJ*. 2020;370:m2743.

21 Mendoza-Cano O, Trujillo X, Huerta M, *et al.* Assessing the Influence of COVID-19 Vaccination Coverage on Excess Mortality across 178 Countries: A Cross-Sectional Study. *Vaccines*. 2023;11:1294.

22 Rovetta A. Annual Excess Crude Mortality in Europe during the COVID-19 Pandemic: A Longitudinal Joinpoint Regression Analysis of Historical Trends from 2000 to 2021. *COVID*. 2022;2:1778–86.

23 Watson OJ, Barnsley G, Toor J, *et al.* Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. *Lancet Infect Dis*. 2022;22:1293–302.

24 Kapitsinis N. The underlying factors of excess mortality in 2020: a cross-country analysis of pre-pandemic healthcare conditions and strategies to cope with Covid-19. *BMC Health Serv Res*. 2021;21:1197.

25 Pilkington H, Feuillet T, Rican S, *et al.* Spatial determinants of excess all-cause mortality during the first wave of the COVID-19 epidemic in France. *BMC Public Health*. 2021;21:2157.

26 The White House. Excess Mortality during the Pandemic: The Role of Health Insurance | CEA. White House. 2022. https://www.whitehouse.gov/cea/written-materials/2022/07/12/excess-mortality-during-the-pandemic-the-role-of-health-insurance/ (accessed 26 January 2024)

27 Ylli A, Burazeri G, Wu YY, *et al.* COVID-19 excess deaths in Eastern European countries associated with weaker regulation implementation and lower vaccination coverage. *East Mediterr Health J*. 2022;28:776–80.

28 Bănică A, Muntele I. Local and regional factors of spatial differentiation of the excess mortality related to the COVID-19 pandemic in Romania. *Lett Spat Resour Sci*. 2023;16:23.

29 Rossen LM. Disparities in Excess Mortality Associated with COVID-19 — United States, 2020. *MMWR Morb Mortal Wkly Rep*. 2021;70:1114–9.

30 Cronin CJ, Evans WN. Excess mortality from COVID and non-COVID causes in minority populations. *Proc Natl Acad Sci*. 2021;118:e2101386118.

31 Woolf SH, Masters RK, Aron LY. Effect of the covid-19 pandemic in 2020 on life expectancy across populations in the USA and other high income countries: simulations of provisional mortality data. *BMJ*. 2021;n1343.

32 Aburto JM, Tilstra AM, Floridi G, *et al.* Significant impacts of the COVID-19 pandemic on race/ethnic differences in US mortality. *Proc Natl Acad Sci*. 2022;119:e2205813119.

33 Andrasfay T, Goldman N. Reductions in 2020 US life expectancy due to COVID-19 and the disproportionate impact on the Black and Latino populations. *Proc Natl Acad Sci*. 2021;118. doi: 10.1073/pnas.2014746118

34 Nafilyan V, Islam N, Mathur R, *et al.* Ethnic differences in COVID-19 mortality during the first two waves of the Coronavirus Pandemic: a nationwide cohort study of 29 million adults in England. *Eur J Epidemiol*. 2021;36:605–17.

35 Bosworth ML, Ahmed T, Larsen T, *et al.* Ethnic differences in COVID-19 mortality in the second and third waves of the pandemic in England during the vaccine rollout: a retrospective, population-based cohort study. *BMC Med*. 2023;21:13.

36 Pallari CT, Achilleos S, Quattrocchi A, *et al.* Magnitude and determinants of excess total, age-specific and sex-specific all-cause mortality in 24 countries worldwide during 2020 and 2021: results on the impact of the COVID-19 pandemic from the C-MOR project. *BMJ Glob Health*. 2024;9:e013018.

37 Office for National Statistics (ONS). COVID-19 vaccine effectiveness estimated using Census 2021 variables, England - Office for National Statistics. 2023. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/bulletins/covid19vaccineeffectivenessestimatedusingcensus2021variablesengland/31march2021to20march2022 (accessed 26 January 2024)

38 Johnson AG, Linde L, Ali AR, *et al.* COVID-19 Incidence and Mortality Among Unvaccinated and Vaccinated Persons Aged ≥12 Years by Receipt of Bivalent Booster Doses and Time Since Vaccination — 24 U.S. Jurisdictions, October 3, 2021–December 24, 2022. *MMWR Morb Mortal Wkly Rep*. 2023;72:145–52.

39 Haas EJ, Angulo FJ, McLaughlin JM, *et al.* Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. *The Lancet*. 2021;397:1819–29.

40 Hernández Bautista PF, Grajales Muñiz C, Cabrera Gaytán DA, *et al.* Impact of vaccination on infection or death from COVID-19 in individuals with laboratory-confirmed cases: Case-control study. *PLOS ONE*. 2023;18:e0265698.