Excess Mortality since COVID-19: What Data Do We Need and What Questions Should We Ask to Understand its Causes in Portugal?

Excesso de Mortalidade desde a COVID-19: Que Dados São Necessários e que Perguntas Devemos Fazer para Compreender as Causas em Portugal?

Excess mortality is occurring since the beginning of the COVID-19 pandemic across Europe and around the world, and it entails both COVID and non-COVID excess mortality.

Between March 2020 and June 2022, the European Union (EU) recorded four distinct waves of excess mortality, with peaks in April 2020 (25.2%), November 2020 (40%, the highest), April 2021 (20.9%) and November 2021 (26.5%).[1]

However, excess mortality is occurring more frequently in many countries since 2020. Moreover, there are more frequent periods of deviation from the baseline expected mortality even if that excess is still within a defined confidence interval. Different methods can lead to different point estimates of expected mortality for a day or period that can then be compared with the observed mortality to calculate the excess.[2] However, most of the literature points towards a relevant excess mortality in many countries, both due to COVID-19 and other causes, and discusses the importance of using death registries data to understand excess deaths by specific diseases, its causes and collateral implications.[3]

The study of excess mortality is also important because it can shed light on the root causes of excess mortality that may also be leading to a large burden of disease, disability and human suffering.

Routine mortality surveillance can have different objectives. One of them is to give warning signals in periods when mortality is acutely higher than expected and should be investigated by public health services and acted upon. For this purpose, 'adequate' confidence intervals are often chosen by surveillance experts to allow a balance between sensitivity and specificity of the warning signal. That is, unnecessary signals can arise if small variations are considered. However, these confidence intervals should not make us neglect systematic increases that do not extend beyond its boundaries and that will cause large increases in deaths at the end of a given year.

This phenomenon must be included in the analysis of excess deaths by specific causes. There were many periods in which the boundaries of the defined confidence intervals were not exceeded but in which mortality is continuously or very often above the expected value.

In Portugal, the number of observed deaths since November 2021, even after the worst COVID-19 healthcare burden, has been systematically above the expected values and often crosses the upper boundary of the confidence intervals. This can be observed in Direção-Geral da Saúde's (DGS) (Portugal's public health authority) eVM (real time mortality surveillance) website.

There are causes of increased mortality that tend to be more distributed throughout the year and therefore do not cause mortality spikes but lead to higher overall mortality.

As an example, cancer mortality due to changes in screening and delayed healthcare when symptoms are present will not be concentrated in peaks, but will be distributed throughout the years. Mortality due to changes in chronic disease care may also be spread but is possibly higher in periods of higher healthcare burden. There may have also been social and economic changes due to the pandemic that may be increasing the vulnerability, isolation and mortality of the most vulnerable. These phenomena can only be understood by first analyzing excess deaths by specific causes from 2020 to 2022.

In wave peak periods of the pandemic, mortality from non-COVID causes has systematically increased. This may be because chronic care became less effective and may lead to more decompensation. In turn, this could be because emergency care has now more difficulty responding and/or because people are delaying seeking healthcare. COVID-19 has contributed to excess mortality directly through deaths due to infection and increased the risk of death in the following months due to sequelae, and indirectly through pressure in healthcare services and broader behavioral, social and economic changes.

The weight of excess mortality during heatwaves is easier to quantify due to their strong time correlation.

EDITORIAL

The impact of aging should not be seen as a relevant cause for the recent increase in mortality because the overall age structure of the population did not change significantly in two years to justify such magnitude of increased mortality. The persistence of excess mortality is also relevant because even after peak pandemic periods, with excess COVID and non-COVID mortality that caused the death of large segments of the more vulnerable population, we have rarely observed a significantly lower subsequent mortality (mortality displacement/harvesting).

The persistence of excess non COVID-19 mortality raises questions about the long-term health consequences of COVID-19 on health and of other simultaneous social, economic, and healthcare services changes.

In Portugal, an initiative to start an in-depth analysis of excess mortality has been publicly announced by the Ministry of Health in an attempt to understand and tackle this problem. It is an opportunity that society, the academia and research institutes need to address. Quality research is critical for understanding reality, for the quality of public debate and public policy and for the health and wellbeing of societies in a post-COVID-19 world.

In Portugal, we must start by analyzing the time series of specific underlying causes of death registered by doctors on death certificates, which is mandatory by law.

It is possible that in some cases, the quality of medical death certification may be low.[4] However, significant changes in quality may not have occurred in recent years, which makes the analysis of excess mortality and trends legitimate. Researchers could analyze the variation of the percentage of nonspecific coding and the percentage of deaths outside hospitals and discuss the results in the face of possible biases and limitations, as must always be done in science. Another problem is that digital registries are still filled in free text and coded manually afterwards by a central team. However, in a recent preprint study using Portuguese death certification data, an automated coding process using artificial intelligence was shown to be sensitive compared to human coding even in periods of excess mortality, when a loss in text quality could happen due to pressure on healthcare services.[5]

As such, researchers and public health services could analyze the underlying causes of death in almost real time even without the final human coding that is routinely done at the central level in DGS and takes much longer time to be finalized, possibly delaying important knowledge for policy.

This would allow to understand how death from specific causes varied over time and during different periods and age groups, for example by stroke, myocardial infarction, specific cancer types, specific decompensated chronic conditions, sepsis, suicide, car accidents, etc. Then we could aim for more detailed research into the most relevant specific causes, considering the time periods where there were large or continuous deviations.

For this second step of the analysis, access to other types of health data and cross referencing of data from different information systems using unique identifiers is essential. For example, in order to better understand the role of previous COVID-19 infection in excess mortality and disability, large cohort studies linking COVID-19 infection and various health outcomes such as stroke and myocardial infarction from hospital morbidity databases (ICD-10 codes) and data from death certificates is necessary. Linking data with socio-economic changes that occurred in individuals may give insights into its potential impact in different age strata, on mortality by different causes. In Portugal there has been an increase in the percentage of population at risk of poverty or social exclusion.[6]

Data from pre-hospital emergency care may identify changes in time from symptom onset to contact with emergency services by the patient, to first on site clinical evaluation, to arrival at the hospital and finally to intrahospital management. The Intrahospital death rate variation for specific emergency diagnoses should be analyzed. This may be important during periods of increased pressure for healthcare services or reduced availability of healthcare resources for emergencies where a delay or provision or suboptimal acute care is known to impact outcomes negatively. Changes in the workload (analyzing changes in workers by specialty and region/municipality, overtime and patients per healthcare workers per time in different periods), stress, burnout, mental health and work satisfaction of healthcare workers should also be investigated.

In summary, we need data to generate and test hypotheses[6] and understand specific causes of non-COVID-19 excess mortality, as well as inform changes in policy and practice. Some of many important hypotheses are:

1. There may have been increases of deaths by myocardial infarction, stroke and decompensated chronic conditions during peak periods of COVID-19 because they are entities that need people to value symptoms early and be treated early;

2. There may have been an important contribution of COVID-19 infection to increased non-COVID-19 mortality and morbidity due to COVID-19 sequelae. Previous research has shown COVID-19 increases the risk of heart attack, stroke, dementia and other health problems and death six to 12 months after infection[7];

3. There may have been an increase in mortality due to cancer. However, deaths due to delayed screening or treatment (surgical or medical) are only expected to occur after a relatively long period and will be distributed evenly throughout time;

4. We may find increases in various specific causes of death, namely in decompensated chronic conditions (diabetes, heart failure, liver disease, chronic respiratory diseases) throughout the year due to individual behavioral and socioeconomic changes, changes in chronic care and possibly delay in acute care during COVID-19 peak periods;

5. There may have been increased mortality due to various bacterial infections acquired in the community (due to possible delay in care) and due to

hospital acquired infections, namely from multi-resistant bacteria (possibly due to increased length of stay, increase in invasive procedures or other changes in patient profiles, hospital environment and clinical management);

6. There may have been excess mortality in specific non-natural causes of death (e.g., car accidents, suicides, homicides, drowning);

7. Social, economic and behavioral changes may play a role in the risk of death;

8. Excess mortality from heat waves may have had a relevant impact during specific periods but may account for only a small proportion of the number of excess deaths in a year;

9. Healthcare quality and timely access may have deteriorated both in outpatient and acute care due to changes in human resource availability and distribution in the healthcare system (public/private and regional asymmetries), possible shortages of healthcare workers in specific regions and specialties, changes in workload, stress and burnout, or other organizational changes.

Science and societies benefit from having strong and broad research. This allows the production of science to answer a wider range of research questions and can benefit public discussion and health policies, in a constructive, participated and open perspective to promote and protect health and wellbeing for all. The pursuit to identify issues that can be improved should be valued by societies, researchers and decision makers as an essential and valuable endeavor that will lead to faster social and economic development and wellbeing.

We cannot forget that excess mortality is the tip of the iceberg. The negative long term health impact of COVID-19 infections, unaddressed health needs, healthcare service vulnerabilities and socioeconomic changes that arose during the pandemic probably hide a much larger burden of disease in terms of years lived with disability and years lost due to premature death now and in the future with relevant social, economic and financial impacts. We must aim to prevent and decrease that burden while preparing society and healthcare services to respond to those needs. The study of excess mortality is a critical component. Finally, we should not forget that investment in health promotion and protection and disease prevention, health literacy and education, healthy habits, healthy environments as well as in reducing poverty and social exclusion will make our health, our healthcare and our society more resilient in facing any incoming storm.

We cannot turn a blind eye to the problem. We must do our best to understand it and understand what we can and want to do about it.

AUTHORS CONTRIBUTION
VRP: Draft of the manuscript.
AV, PA, AA: Critical review of the manuscript.

PROTECTION OF HUMANS AND ANIMALS
The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the Helsinki Declaration of the World Medical Association updated in 2013.

DATA CONFIDENTIALITY
The authors declare having followed the protocols in use at their working center regarding patients' data publication.

COMPETING INTERESTS
The authors have declared that no competing interests exist.

FUNDING SOURCES
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

REFERENCES
1. Eurostat. Excess mortality - statistics - Statistics Explained. [cited 2022 Sep 08]. Available from: https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Excess_mortality_-_statistics.
2. Shkolnikov VM, Klimkin I, McKee M, Jdanov DA, Alustiza-Galarza A, Németh L, et al. What should be the baseline when calculating excess mortality? New approaches suggest that we have underestimated the impact of the COVID-19 pandemic and previous winter peaks. SSM Popul Health. 2022;18101118.
3. COVID-19 Excess Mortality Collaborators. Estimating excess mortality due to the COVID-19 pandemic: a systematic analysis of COVID-19-related mortality, 2020-21. Lancet. 2022;399:1513-36.
4. Sousa Pinto C, Anderson RN, Martins H, Marques C, Maia C, Borralho MC. Mortality information system in Portugal: transition to e-death certification. Eurohealth. 2016;22:1-53.
5. Pita Ferreira P, Godinho Simões D, Pinto de Carvalho C, Duarte F, Fernandes E, Casaca P, et al. A real-time classification of causes of death using artificial intelligence: sensitivity analysis. JMIR Preprints. 11/07/2022:40965.
6. Eurostat. Persons at risk of poverty or social exclusion by age and sex. [cited 2022 Sep 19]. Available from: https://ec.europa.eu/eurostat/databrowser/view/ilc_peps01n/default/table?lang=en.
7. Uusküla A, Jürgenson T, Pisarev H, Kolde R, Meister T, Tisler A, et al. Long-term mortality following SARS-CoV-2 infection: a national cohort study from Estonia. Lancet Reg Health Eur. 2022;18:100394.