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Measuring the impact of COVID-19 in Italy and a global perspective

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ABSTRACT

Introduction: Different metrics have been used to monitor the impact of the COVID-19 pandemic, including the officially registered COVID-19 deaths. However, this metric has important limitations that can be partly addressed by considering total excess deaths. In this study, we compared trends in COVID-19 deaths in Italy with those observed globally and estimated the total number of excess deaths.
Material and methods: We retrieved the number of COVID-19 deaths from the John Hopkins University and the daily number of deaths from any causes from the Italian National Institute of Statistics archives. We fitted an over-dispersed Poisson regression model on historical data to estimate the expected deaths. The models included terms for age, calendar year, a smooth function of the day of the year and an offset term for the population size to account for demographic changes, temporal trends in mortality and seasonality. The excess deaths were obtained by subtracting the number of observed deaths from the number of expected deaths.
Results: As of March 2023, over 6.2 million COVID-19 deaths were registered globally (around 190,000 in Italy). In 2020, we estimated 99,341 excess deaths in Italy, 60,351 in 2021, and 66,303 in 2022. For the first 4 months of 2023, the number of observed deaths was slightly less than the number of expected deaths. The total excess from the beginning of the pandemic in Italy to the end of 2020 amount to approximately 226,000 deaths, a figure that exceeded COVID-19 deaths by 36,000.
Conclusions: Excess total mortality is a key metric to quantify the overall impact of the pandemic. However, the limited availability of data in some densely populated countries introduces significant uncertainty into any global estimates.

KEY WORDS: COVID-19, excess deaths, mortality.

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INTRODUCTION

The COVID-19 emergency started in China and quickly spread to Europe, with northern Italy serving as the epicentre for its global transmission [1]. The pandemic has caused substantial morbidity and mortality worldwide, with a death toll that exceeds 15 million people [2]. The severity of the pandemic in terms of hospitalizations and fatality varied greatly across countries. Italy experienced a severe first wave in March-April 2020, when the country did not have the resources and medical equipment to provide adequate care for the thousands of patients looking for medical assistance [3, 4].

The number of COVID-19 deaths is an important indicator to monitor the impact of the pandemic. However, it probably underestimates (especially in the first phase and in countries with limited diagnostic capabilities) or even overestimates (in the subsequent phases when tracing and diagnostic capabilities had

improved) the real impact of the pandemic. In this regard, excess total mortality, i.e. mortality from any cause, is a better indicator for assessing the overall impact of the pandemic. This metric takes into account under-reporting of COVID-19 cases or overdiagnosis in cases where SARS-CoV-2 infection was not the primary cause of death, and it also covers the indirect effects of the pandemic on the management of other conditions [5].

In this study, we compared the trend in COVID-19 deaths in Italy with that reported globally and estimated the total excess deaths in Italy until April 2023.

MATERIAL AND METHODS

We obtained the number of COVID-19 deaths in Italy and globally from the John Hopkins University database [6]. This database provides a comprehensive and regularly updated record of COVID-19 deaths worldwide from 20 January 2020, to 9 March 2023. The data were presented graphically using the 7-day rolling mean of daily deaths.

To estimate the number of excess deaths, we compared the number of observed deaths during the pandemic with the number of expected deaths had the pandemic not occurred. Expected deaths were obtained from 2 over-dispersed Poisson regression models fitted separately for men and women on the historical daily number of deaths in a pre-pandemic period starting from 1 January 2011 to 31 December 2019. Daily numbers of deaths were obtained from the archives of the Italian National Institute of Statistics (ISTAT) [7]. The data span from 1 January 2011, to 30 April 2023.

The following model was used to estimate the expected number of deaths for the age group (i), year (j), and day of the week (k):

$$\ln(E(\text{deaths}_{i,j,k})) = \beta_0 + \beta_1(age_i) + \beta_2(year_j) + f(day_k) + \ln(\text{pop}_{i,j,k}),$$

where: β_0 is the intercept, β_1 represents the effect of age on mortality rates, β_2 captures the annual trend in mortality rates, $f(day_k)$ is a natural spline function of the day of the year to model seasonal variations in mortality rates, $ln(pop_{i,j,k})$ serves as an offset term to account for demographic changes in population size and age structure.

The number of knots of the spline function was determined using the quasi-Akaike Information Crite-

rion (QAIC), testing up to 10 knots with equal spacing. The model's coefficients were estimated using daily mortality data from 1 January 2011 through 31 December 2019.

The 95% confidence intervals (CI) were derived using a Monte Carlo simulation. We sampled 10,000 model parameters values from a multivariate normal distribution using the parameter estimates and the variance-covariance matrix. The variance was then calculated by subtracting the number of observed deaths from the expected deaths obtained from each iteration. The 95% confidence interval was then computed based on the quantiles of the standard normal distribution.

RESULTS

Figure 1 illustrates the trends in the daily number of COVID 19 deaths globally (Panel A) and in Italy (Panel B). Globally, COVID-19 deaths reached their peaks at the beginning of 2021, in the spring of the same year, and in the initial months of 2022, followed by a gradual decrease. In Italy, the trend was characterized by a huge peak in the months of March 2020 and subsequent peaks in October–November 2020, in the spring of 2021, and in the initial months of 2022. Similarly to what has been observed globally, the number of COVID-19 deaths progressively decreased during the 2022 and the first 4 months of 2023. Still in April 2023 approximately 150-200 COVID-19 deaths per week were registered in Italy.

Table 1 provides our estimates of the excess deaths over the course of the pandemic in Italy. We estimated around 226,000 excess deaths from the onset of the pandemic in Italy in March 2020 to the end of 2022 and no excess deaths between January and April 2023.

Figure 2 gives the excess mortality expressed as the percentage difference compared to the expected number of deaths during the whole of 2022 and up to April 2023 in Italy. During 2022, excess mortality ranged between 4.3% in September to 26.3% in July 2022. In July 2022, part of the excess can be attributed to the extreme temperatures registered in Italy during that month.

Figure 3 shows a comparison between our estimates of excess deaths and the registered COVID-19 deaths
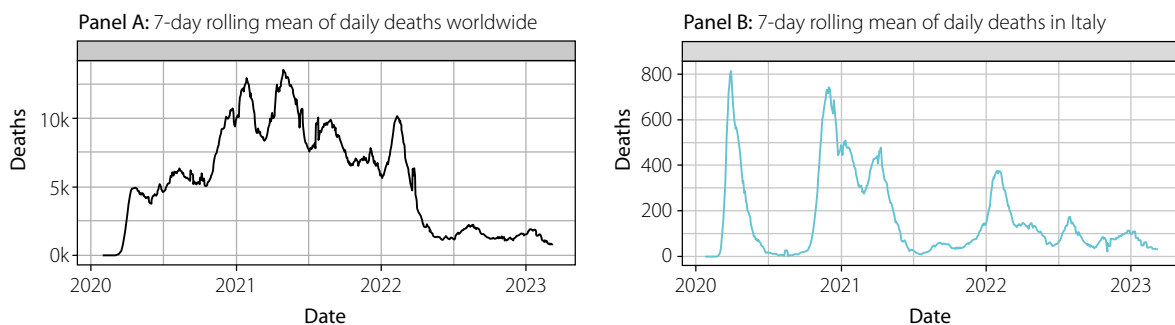
FIGURE 1. Seven-day rolling mean of COVID-19 daily deaths registered globally (Panel A) and in Italy (Panel B) from the beginning of the pandemic up to 9 March 2023

TABLE 1. Observed deaths, expected deaths, and excess deaths from any cause in Italy during the COVID-19 pandemic

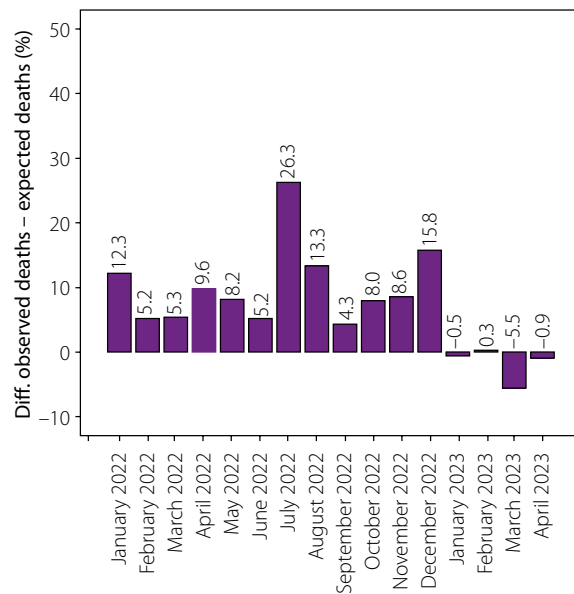| Period	Observed deaths	Expected deaths	Difference	LCL	UCL
2020	628,057	528,716	99,341	97,827	100,854
2021	709,035	648,684	60,351	58,244	6,2457
2022	713,499	647,196	66,303	63,900	6,8705
Jan-Apr 2023	232,475	236,349	−3,874	−4,936	−2,811

LCL – low confidence level, UCL – upper confidence level.

in Italy. Between the beginning of the pandemic and the end of April 2023, Italy recorded 189,796 COVID-19 deaths, whereas our estimate of excess deaths for the same period amount to approximately 226,000 deaths. Excess deaths remarkably exceeded COVID-19 in March-April 2020, November 2020, and in July and December 2022. In contrast, while mortality was lower than expected in January–April 2023, 4878 COVID-19 deaths were registered in that period.

DISCUSSION

The study used the officially registered COVID-19 deaths and excess deaths from all causes to measure the impact of the COVID-19 pandemic in Italy and found a substantial disparity between officially registered COVID-19 deaths and excess total mortality up to April 2023. Excess deaths exceeded COVID-19 deaths by approximately 36,000. Our findings also highlight important differences in the timing and magnitude of the impact of COVID-19 in Italy as compared to that observed globally.

A different impact of the pandemic across countries became evident since the first year of the outbreak. In

FIGURE 2. Percentage difference between observed and expected deaths in Italy from March 2022 to April 2023 by month
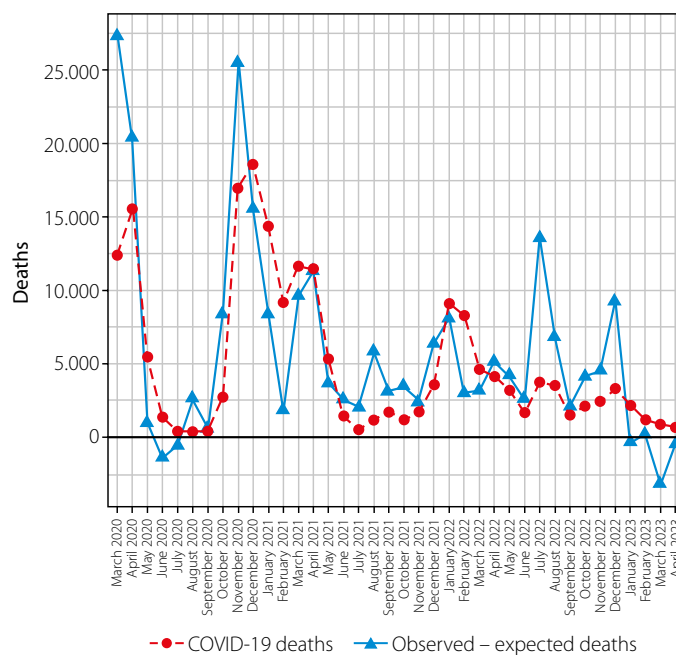
FIGURE 3. Comparison between excess deaths from any cause and COVID-19 deaths monthly registered in Italy from March 2020 to April 2023

2020, there was a reduction in life expectancy in several countries, which exceeded 2 years in men and women in Russia, equalled 2.3 years among men in the United States and 1.6 among women, and was generally higher in East as compared to North and South Europe [8]. In 2021, life expectancy rebounded from the 2020 losses in Belgium, Switzerland, Spain, Italy, France, England and Wales, Sweden, and Slovenia. Conversely, in the US and in several Eastern European countries, such as Bulgaria, the Czech Republic, Estonia, Greece, Croatia, Hungary, Lithuania, Poland, and Slovakia, life expectancy dropped further in 2021 [9].

These disparities probably arose from the complex interplay of various factors, such as the timing and the spread of the different SARS-CoV-2 variants during the pandemic, the age distribution of the population, the level of preparedness of the country, the quality and accessibility of the healthcare system, the level of hospital saturation, the vaccine availability and uptake, and the government responses to contain the spread of infection.

Furthermore, there is an important issue regarding the validity and comparability of official statistics on COVID-19. The ability to identify cases varied across countries as well as the definition of COVID-19 deaths used in official statistics. Moreover, there are concerns about the validity and completeness of reporting. In fact, an important degree of underreporting is expected in many low- and middle-income countries, including China and India. In China around 120,000 COVID deaths were reported since the beginning of the pandemic, but independent estimates ranged between 1 and 1.5 million deaths [10, 11]. However, these estimates are subject to a high degree of uncertainty, depending on the prevalence of infection at different ages, the fatality rate, and mainly the extent to which the elderly have been protected after abandoning the "zero COVID" policy [12].

Similar doubts on the validity of the information on COVID-19 deaths can be raised in India, where official data indicate around 530,000 deaths, but the actual figure could be up to 10 times higher [13, 14].

These considerations highlight the limitations of relying solely on COVID-19 deaths as a measure of the pandemic impact and suggest that total excess deaths provide a better and more accurate measure to quantify the overall health impact. However, it is important to note that while civil registration coverage and completeness approach 100% in the majority of high-income countries, in some low- and middle-income countries, including China and India, civil registration covers only a small share of the population (4% in China and 8% in India) with suboptimal completeness (61.5% in China and 10% in India) [15]. As a result, there remains a substantial degree of uncertainty in estimating excess deaths in these countries.

Regardless of the measure we choose, the significant protection offered by vaccines becomes evident starting from the second half of the 2021 in Italy when most of the population was vaccinated. However, a resurgence in the number of deaths can be observed at the beginning of 2022, attributed to the rapid spread of the Omicron variant in the country [16]. The variant demonstrated higher infectiousness compared to previous variants and partially evaded natural and vaccine-induced immunity [17]. In July 2022, Italy faced an important excess mortality, which was partly attributed to the pandemic and partly a consequence of the heat waves observed in the country [18, 19]. In 2023, although over 5000 COVID-19 deaths were registered between January and April, the number of deaths from any cause was lower than expected. This may be a consequence of a compensatory effect resulting from the depletion ("harvesting effect") of the vulnerable share of the population during the previous pandemic waves.

On a global level, the effects of the vaccines can be only observed during the second half of 2022, probably due to delay in vaccine delivery, shortages, and inefficient vaccine campaigns in certain countries [20].

The underestimation of COVID-19 deaths is not the sole explanation for the discrepancy between total excess mortality and COVID deaths. In fact, important excesses were registered also for specific causes of death, including cardiovascular diseases and diabetes in several countries [21]. This suggest that COVID-19 contributed to worsening the clinical condition of patients affected by those diseases, or that during the acute phase of the pandemic, health care systems were unable to provide adequate care to patients.

The methodology used to estimate excess deaths is the main strength of our study. By calculating the number of lives lost throughout the entire pandemic period, we were able to provide an estimate of the overall impact of the pandemic in Italy. However, this task is not easily achievable for many countries due to the absence of standardized and efficient data collection systems. This introduces a high degree of uncertainty in global estimates.

Finally, the model showed good reliability in a validation study where it was used to estimate the difference between observed and expected deaths in the years preceding the pandemic [22]. Our estimates aligned closely with those form other sources. The WHO estimated a 12% excess mortality in Italy in 2020 and 2021 combined [23], while Our World in Data reported an approximately 15% excess mortality for Italy in 2020, gradually decreasing but remaining above 10% throughout 2021 and 2022 [24]. These differences probably stem from differences in methodology, particularly in the choice of the baseline period considered to estimate expected deaths [25].

CONCLUSIONS

Excess deaths from all causes is a better metric to measure the overall impact of the pandemic as compared to officially registered COVID-19 deaths. The suboptimal coverage and completeness of civil registrations in certain countries make the global estimates provided questionable [26].

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

References

1. Looi MK. Did covid-19 come from a lab leak in China? BMJ 2023; 382: 1556.

2. Adam D. The pandemic's true death toll: millions more than official counts. Nature 2022; 601: 312-315.

3. Alfieri C, Egrot M, Desclaux A, et al. Recognising Italy's mistakes in the public health response to COVID-19. Lancet 2022; 399(10322): 357-358.

4. Alicandro G, Remuzzi G, La Vecchia C. Italy's first wave of the COVID-19 pandemic has ended: no excess mortality in May, 2020. Lancet 2020; 396(10253): e27-e28.

5. Islam N. "Excess deaths" is the best metric for tracking the pandemic. BMJ 2022; 376: o285.

6. Johns Hopkins University Center for Systems Science and Engineering (JHU CCSE). Novel Coronavirus (COVID-19) Cases Data – Humanitarian Data Exchange. 2020. Available from: https://data.humdata.org/dataset/novel-coronavirus-2019-ncov-cases (accessed: 7 July 2023).

7. Istituto Nazionale di Statistica. Decessi e cause di morte: cosa produce l'Istat. 2021. Available from: https://www.istat.it/it/archivio/240401 (accessed: 7 July 2023).

8. 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.

9. Schöley J, Aburto JM, Kashnitsky I, et al. Life expectancy changes since COVID-19. Nat Hum Behav 2022; 6(12): 1649-1659.

10. Dyer O. Covid-19: China stops counting cases as models predict a million or more deaths. BMJ 2023; 380: 2.

11. Ioannidis JPA, Zonta F, Levitt M. What really happened during the massive SARS-CoV-2 omicron wave in China? JAMA Intern Med 2023; 183(7): 633-634.

12. Ioannidis JPA, Zonta F, Levitt M. Estimates of COVID-19 deaths in mainland China after abandoning zero COVID policy. Eur J Clin Invest 2023; 53(4): e13956.

13. Jha P, Deshmukh Y, Tumbe C, et al. COVID mortality in India: National survey data and health facility deaths. Science 2022; 375(6581): 667-671.

14. Banaji M, Gupta A. Estimates of pandemic excess mortality in India based on civil registration data. PLoS Glob Public Health 2022; 2(12): e0000803.

15. Civil registration coverage of cause-of-death (%) 2017; 2017. Available from: http://apps.who.int/gho/data/node.wrapper.imr?x-id=84 (accessed: 7 July 2023).

16. Alicandro G, Remuzzi G, Centanni S, et al. Excess total mortality during the Covid-19 pandemic in Italy: updated estimates indicate persistent excess in recent months. Med Lav 2022; 113(2): e2022021.

17. Willett BJ, Grove J, MacLean OA, et al. SARS-CoV-2 Omicron is an immune escape variant with an altered cell entry pathway. Nat Microbiol 2022; 7(8): 1161-1179.

18. Alicandro G, Gerli AG, Remuzzi G, et al. Updated estimates of excess total mortality in Italy during the circulation of the BA.2 and BA.4-5 Omicron variants: April-July 2022. Med Lav 2022; 113(5): e2022046.

19. Ballester J, Quijal-Zamorano M, Méndez Turrubiates RF, et al. Heat-related mortality in Europe during the summer of 2022. Nat Med 2023; 29(7): 1857-1866.

20. Hopkins J. Understanding vaccination progress by country – Johns Hopkins Coronavirus Resource Center. Underst Vaccin Prog 2022. Available from: https://coronavirus.jhu.edu/vaccines/international (accessed: 7 July 2023).

21. Alicandro G, La Vecchia C, Islam N, Pizzato M. A comprehensive analysis of all-cause and cause-specific excess deaths in 30 countries during 2020. Eur J Epidemiol 2023; 38(11): 1153-1164.

22. Alicandro G, La Vecchia C, Remuzzi G, et al. Excess mortality in Italy in 2020 by sex and age groups accounting for demographic changes and temporal trends in mortality. Panminerva Med 2022; 64(4): 472-478.

23. Msemburi W, Karlinsky A, Knutson V, et al. The WHO estimates of excess mortality associated with the COVID-19 pandemic. Nature 2023; 613(7942): 130-137.

24. Our World in Data. Excess mortality: Deaths from all causes compared to projection based on previous years. Our World Data 2022. Available from: https://ourworldindata.org/excess-mortality-covid (accessed: 15 November 2023).

25. Levitt M, Zonta F, Ioannidis JPA. Excess death estimates from multiverse analysis in 2009-2021. Eur J Epidemiol 2023; 38(11): 1129-1139.

26. 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. Lancet 2022; 399(10334): 1513-1536.