



COVID-19-induced excess mortality in Italy during the Omicron wave.

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ABSTRACT

Background: The existing literature estimates a significantly reduced odds of hospitalisation and death among individuals. However, though less severe than other variants, the Omicron variant may still lead to excess mortality compared to pre-pandemic years.

Methods: A generalized linear mixed model is introduced to model weekly mortality from 2011 to 2019, taking into account seasonal patterns and year-specific trends. Based on the 2019 year-specific conditional best linear unbiased predictions, excess of mortality is estimated.

Results: In Italy, 14 and 11 regions suffered from relevant excess mortality in January and February, respectively. However, the situation is far from being as critical as during previous waves.

Conclusions: We can conclude that no matter which variant (or multiple inter-variant recombination) we are facing, excess mortality will appear in correspondence of any incidence peak.

Introduction

Several studies discussed the milder severity of the Omicron variant of concern (Maslo et al., 2022; Wolter et al., 2022; Abdullah et al., 2022; Divino et al., 2022; Pascarella et al., 2021). The existing literature estimates a significantly reduced odds of hospitalisation and death among individuals. However, though less severe than other variants, the Omicron variant may still lead to excess mortality compared to pre-pandemic years. Excess mortality induced by the pandemic during its first few weeks has been the focus of several researches (Kontopantelis et al., 2021; Modig et al., 2021). The pandemic has had an incredibly high impact on mortality during 2020 and 2021. Here, we estimate Omicron-induced excess mortality at the regional level in Italy by employing a generalised linear mixed model, allowing for seasonal patterns.

Methods

Open-source daily all-cause Italian mortality data from January 2011 to February 2022 are available from the Italian National Institute of Statistics (<https://www.istat.it/it/archivio/240401>). These data were downloaded on April 14th, 2022, and aggregated at the week and region level. The weeks numbered 53, present in leap years, were dropped from the analysis.

The crucial aspect in estimating excess mortality is the definition of a reliable benchmark mortality model, i.e. a model able to perform well in-sample under pre-pandemic conditions. We assume that the weekly mor-

tality $Y_{tj} \sim NB(\lambda_{tj}, \alpha)$ at week $t = 1, \dots, 52$, year $j = 2011, \dots, 2019$ follows a Negative Binomial distribution (similar approaches are discussed in Maruotti et al., 2022; Konstantinou et al., 2022; Blangiardo et al., 2020) with

$$\log(\lambda_{tj}) = (\beta_0 + b_{0j}) + \sum_{i=1}^I \beta_i \sin\left(\frac{2i\pi t}{52}\right) + \sum_{i=1}^I \gamma_i \cos\left(\frac{2i\pi t}{52}\right).$$

Cyclical patterns are captured by the Fourier series, whose number of terms is defined using model selection criteria. To account for year-specific mortality baselines and to partially accommodate autocorrelation of the weekly counts, random effects $b_{0j} \sim N(0, \sigma)$ are introduced. Parameters are estimated by maximum likelihood using adaptive Gaussian quadrature integration for the random effects. In Italy, the Omicron variant was observed since mid December 2021. Accordingly, the weekly predictions of mortality data for January and February 2022 are considered (formally, we consider the first 8 weeks of 2022). The predictive model is trained on data from 2011 to 2019. Excess mortality is obtained by subtracting the expected deaths from the registered all-cause deaths.

Results

Estimated COVID-19-induced excess deaths are reported, along with 95% prediction intervals in Table 1. If zero is included in the intervals, no difference from the expected number of deaths is estimated, i.e. there is no excess mortality. The Omicron effect on deaths is relatively straightforward. Between the end of January and the very first days of

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Table 1

Absolute and percentage estimated excess mortality for weeks 1 to 4 (January 2022) and 5 to 8 (February 2022) in the 20 Italian regions, with prediction intervals in the brackets.

Region	Estimated Excess Mortality Weeks 1-4 2022 (January)	Estimated Excess Mortality Weeks 5-8 2022 (February)	Estimated % Excess Mortality Weeks 1-4 2022 (January)	Estimated % Excess Mortality Weeks 5-8 2022 (February)
Piemonte	378 (185; 557)	17 (-70; 289)	7.8 (4.0; 11.9)	0.3 (-1.4; 5.7)
Valle d'Aosta	1 (-11; 12)	-11 (-22; 0)	0.8 (-9.7; 10.2)	-8.9 (-16.3; 0.0)
Lombardia	1013 (691; 1325)	301 (-17; 604)	11.3 (7.9; 15.2)	3.3 (-0.2; 6.5)
Trentino Alto Adige	4 (-35; 39)	15 (-23; 51)	0.5 (-4.3; 4.9)	1.8 (-2.6; 5.8)
Veneto	662 (449; 722)	146 (-7; 283)	15.7 (10.4; 17.3)	3.3 (-0.2; 6.4)
Friuli Venezia Giulia	156 (102; 200)	57 (9; 102)	12.1 (8.5; 16.0)	4.3 (0.7; 7.6)
Liguria	141 (75; 209)	103 (34; 173)	7.4 (4.0; 11.4)	5.3 (1.7; 8.8)
Emilia Romagna	411 (273; 543)	201 (62; 334)	9.3 (6.3; 12.6)	4.5 (1.4; 7.3)
Toscana	361 (229; 493)	229 (90; 361)	9.4 (6.3; 13.3)	5.9 (2.2; 9.1)
Umbria	45 (5; 86)	37 (-4; 75)	4.9 (0.6; 9.8)	4.1 (-0.4; 7.8)
Marche	140 (69; 206)	54 (-16; 120)	9.3 (4.6; 14.3)	3.5 (-1.0; 7.6)
Lazio	80 (-107; 271)	180 (-2; 359)	1.5 (-2.1; 5.4)	3.5 (-0.0; 6.6)
Abruzzo	16 (-35; 66)	85 (32; 133)	1.2 (-2.7; 5.1)	6.4 (2.3; 9.6)
Molise	-16 (-37; 4)	26 (6; 46)	-4.6 (-11.5; 1.2)	7.6 (1.7; 12.6)
Campania	763 (598; 931)	516 (349; 684)	15.0 (12.4; 19.0)	10.4 (6.8; 13.1)
Puglia	27 (-76; 164)	422 (276; 557)	0.7 (-2.2; 4.7)	12.0 (7.5; 15.0)
Basilicata	60 (31; 88)	-7 (-36; 20)	10.5 (5.5; 16.2)	-1.2 (-5.8; 3.3)
Calabria	177 (107; 244)	133 (63; 202)	9.5 (6.0; 13.6)	7.2 (3.3; 10.5)
Sicilia	819 (651; 971)	468 (302; 625)	16.7 (13.4; 20.5)	9.3 (5.8; 12.3)
Sardegna	229 (165; 293)	260 (194; 324)	15.3 (11.0; 20.5)	16.7 (11.9; 20.8)

February, the death curve peaked, and most regions (14 over 20) suffered from relevant excess mortality, with even 15% more deaths than expected. In February, the situation improved: we estimate excess mortality for 11 regions over 20. The excess mortality in February is limited to Southern and a few Central regions, with an overall much smaller excess mortality than in January, with the exceptions of Abruzzo, Molise and Puglia. Overall, the situation is far from being as critical as during previous waves.

Discussion

Our analysis leads to an obvious question: “is the estimated excess mortality linked to the Omicron variant?”. At first glance, the answer is yes. Integrating our analysis with the officially reported COVID-19 deaths, the answer is still yes, but with some shades. In 2022, the number of official COVID-19 related deaths is higher than the estimated excess mortality. The simplest justification for this result is that some people who died from COVID-19 would have died anyway of other causes (three or more comorbidities are reported for more than 65% of Italian COVID-19-related deaths, according to official reports). Heterogeneity is a fact: estimated excess mortality is clearly region-specific. Indeed, death reporting and the health systems across regions are largely heterogeneous. With the available data, it is impossible to conclude if such differences are due to misreporting the main cause of death. As suggested by a reviewer, such a heterogeneity may also be linked, and partially explained, to the heterogeneous vaccination coverage at the regional level. There is a literature supporting this hypothesis (see e.g.

Zhou et al., 2022; Stoto et al., 2022; Kirpich et al., 2022), but further analyses are required for the Italian case.

A harvesting effect may also explain the differences, and played a role in anticipating the death of more at risk people. That idea should be investigated in detail when deaths-by-cause will be available (see e.g. Grande et al., 2022, for a premiere) together with individual hospital-related information, which may also reveal changes in the mortality rates for non-COVID-19 diseases, not correctly treated during the pandemic as major resources were dedicated to managing them the epidemic. The debate on the presence or not of the harvesting effect during the different COVID-19 waves is still ongoing. Both hypotheses are still on the ground: Rivera et al. (2020), Andrasfay and Goldman (2021) and Canoui-Poitrine et al. (2021) did not find evidence of any harvesting effects in periods following the worst waves of the COVID-19 pandemic; Scortichini et al. (2020) and the Italian National Institute of Statistics (Istat) and Istituto Superiore di Sanità (ISS) (2020b), instead, reported some evidence of harvesting effect in some areas during the multiple waves observed in Italy.

We can conclude that no matter which variant (or multiple inter-variant recombination) we are facing, excess mortality will appear in correspondence of any incidence peak.

Compliance with ethical standards

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Ethical statement This study is compliant with the ethical standards.

Informed consent Considering the design of the study, no informed consent was necessary.

Conflict of interest

We declare that we have no conflict of interest.

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