

Updated estimates of excess total mortality in Italy during the circulation of the BA.2 and BA.4-5 Omicron variants: April-July 2022

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ABSTRACT

Background: *The impact of new lineages and sub-lineages of Omicron on total and excess mortality is largely unknown. This study aims to provide estimates of excess mortality during the circulation of the Omicron variant in Italy updated to July 2022.* **Methods:** *Over-dispersed Poisson regression models, fitted separately for men and women, on 2011–2019 mortality data were used to estimate the expected number of deaths during the COVID-19 pandemic. The excess deaths were then obtained by the difference between observed and expected deaths and computed at all ages and at working ages (25–64 years).* **Results:** *Between April and June 2022, we estimated 9,631 excess deaths (+6.3%) at all ages (4,400 in April, 3,369 in May, 1,862 in June) and 12,090 in July 2022 (+23.4%). At working ages, the excess was 763 (+4.9%) in April–June 2022 and 679 (+13.0%) in July 2022.*

Conclusions: *Excess total mortality persisted during the circulation of different lineages and sub-lineages of the Omicron variant in Italy. This excess was not limited to the elderly population but involved also working age individuals, though the absolute number of deaths was small. The substantial excess found in July 2022 is, however, largely attributable to high temperatures. At the end of the year, this may translate into 30 to 35,000 excess deaths, i.e. over 5% excess mortality. COVID-19 related deaths reversed the long-term trend toward increasing life expectancy, with the relative implications in social security and retirement schemes.*

1. INTRODUCTION

Italy was among the countries most severely hit by the Coronavirus disease 2019 (COVID-19) pandemic with more than 45,000 excess deaths estimated during the first wave in February–May 2020 [1] and more than 177,000 officially-registered COVID-19 deaths since the beginning of the pandemic to the end of September 2022 [2].

Most deaths occurred in 2020, when vaccines were not available, and in 2021 during the circulation of the Delta variant with suboptimal vaccine coverage. In December 2021, a new variant of SARS-CoV-2, B.1.1.529 (Omicron), started to circulate in the country, and in early January 2022 it became the dominant variant [3]. The circulation of Omicron has been accompanied by a surge in the number of cases (5 million cases registered in January and

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over 17 million to the end of September 2022). This, however, was followed by a smaller increase in hospitalizations and COVID-19 deaths as compared to previous waves [2]. In the following months, different lineages and sub-lineages of Omicron circulated in Italy (from the original lineage BA.1 to the latest ones BA.4-5) [4], whose impact on total mortality remain to be quantified.

In this study, we update previous estimates on excess total mortality in Italy covering the months of April-July 2022, with a focus on mortality at working ages.

2. METHODS

The study is based on national daily mortality data from January 1, 2011 to July 31, 2022 and population data for the calendar years 2011-2022 [5,6].

We estimated the number of excess deaths by the difference between the observed deaths and the number of deaths that would have been expected had the pandemic not occurred. The expected number of deaths were estimated separately for men and women using two over-dispersed Poisson regression models. The models included a linear term for calendar year (to account for temporal trends in mortality), age groups (to capture the demographic changes over the period), a smooth function of week of the year (to capture seasonal variations) as predictors, and the natural logarithm of the population as offset term. A natural spline was used as a smooth function, with number of knots chosen on the basis of the quasi-Akaike Information Criterion (QAIC). Up to 10 equally spaced knots were tested.

Excess deaths were reported at all ages and at working ages (25-64 years) and presented both in absolute terms (i.e. difference between observed and expected deaths) and relative terms (i.e. percent relative differences). To avoid the inclusion of individuals who may still be in education and those who are retired, we defined the working-age population as individuals aged 25-64 years. Excess deaths were provided with 95% Confidence Intervals (CI) obtained through a Monte Carlo simulation. We sampled 10,000 iterations from a multivariate normal distribution for each set of the model's coefficients using the parameter estimates and the variance-covariance matrix. For each iteration, we computed

the difference between the observed and the expected deaths and 95%CI were obtained using normal approximation.

To evaluate the excess mortality due to high temperature in July 2022, we related mean temperatures for the months of July of the period 2015-2022 in six urban areas from northern and central Italy (Turin, Milan, Florence, Bologna, Rome and Naples) to the number of deaths registered in the same areas and in the corresponding periods.

3. RESULTS

Between April and June 2022, 226,232 deaths were registered in Italy; 22,166 (9.8%) of them among individuals of working ages. We estimated an excess mortality over the whole period of 21,721 (+10.6%) deaths at all ages and 1,442 (+7.0%) at working ages (Table 1). Observed deaths were higher than expected in all the four months, although most of the excess was observed in the month of July 2022. Between April and June 2022, we estimated 9,631 excess deaths (+6.3%) at all ages (4,400 in April, 3,369 in May, 1,862 in June) and 12,090 in July 2022 (+23.4%). At working ages, the excess was 763 (+4.9%) in April-June 2022 (123 in April, 338 in May, 302 in June) and 679 (+13.0%) in July 2022.

Figure 1 shows the excess deaths in relative terms, i.e. as percent of the expected number of deaths, estimated at all ages and at working ages. In April, the estimate was lower for individuals of working ages as compared to that obtained for the whole population (+2.3% *vs* +8.4%). In May, the estimates were close to +6.5%, while in June the value was higher at working ages than at all ages (+6% *vs* +3.8%). In July, excess mortality substantially increased, up to +13.0% at working ages and +23.4% at all ages.

Our estimates of total excess deaths were close to the officially-registered COVID-19 deaths in the months of April (4,124 deaths), May (3,190 deaths) and June (1,656 deaths), whereas COVID-19 deaths accounted for only 31% of the total excess we estimated in the month of July 2022 (3,733 COVID-19 deaths *vs* 12,090 excess deaths).

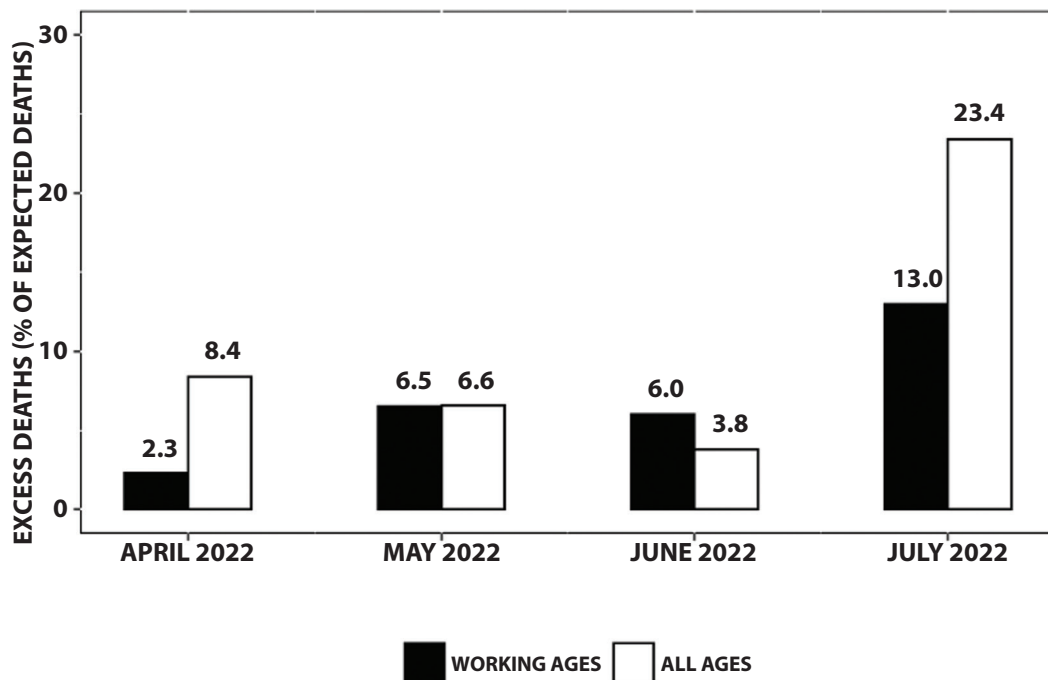
Figure 2 shows the relationship between the average temperatures and the number of deaths registered in the municipalities of Turin, Milan, Bologna,

Table 1. Observed, expected deaths and excess total mortality in Italy between April and July 2022 at working ages (25-64 years) and at all ages by month.

Age group	2022	Observed deaths	Expected deaths ¹	Difference	95%CI
Working ages	April	5,400	5,277	123	99 to 146
	May	5,529	5,191	338	314 to 361
	June	5,332	5,030	302	279 to 324
	July	5,905	5,226	679	655 to 702
	April-July	22,166	20,724	1,442	1,359 to 1,522
All ages	April	56,512	52,112	4,400	4,221 to 4,578
	May	54,520	51,151	3,369	3,191 to 3,546
	June	51,471	49,609	1,862	1,683 to 2,040
	July	63,729	51,639	12,090	11,912 to 12,267
	April-July	226,232	204,511	21,721	21,140 to 22,299

CI: Confidence Interval.

¹Estimated from 2011-2019 mortality and population data, separately by sex, through an over-dispersed Poisson regression model including a linear term for calendar year (to account for the temporal improvement in mortality), age groups as categorical variable (to capture the demographic changes over the period), a smooth function of week of the year with 7 equally spaced knots (to capture seasonal variations), and the natural logarithm of the population as offset term. Values were rounded up to the smallest integer.

**Figure 1.** Excess total mortality in Italy (expressed as percent of the expected deaths) between April and July 2022 at working ages (25-64 years) and at all ages by month.

Florence, Rome and Naples in the months of July for the calendar years 2015-2019. The high temperatures

in July 2022 and 2015 can explain to a 15-20% excess deaths in the six urban areas considered.

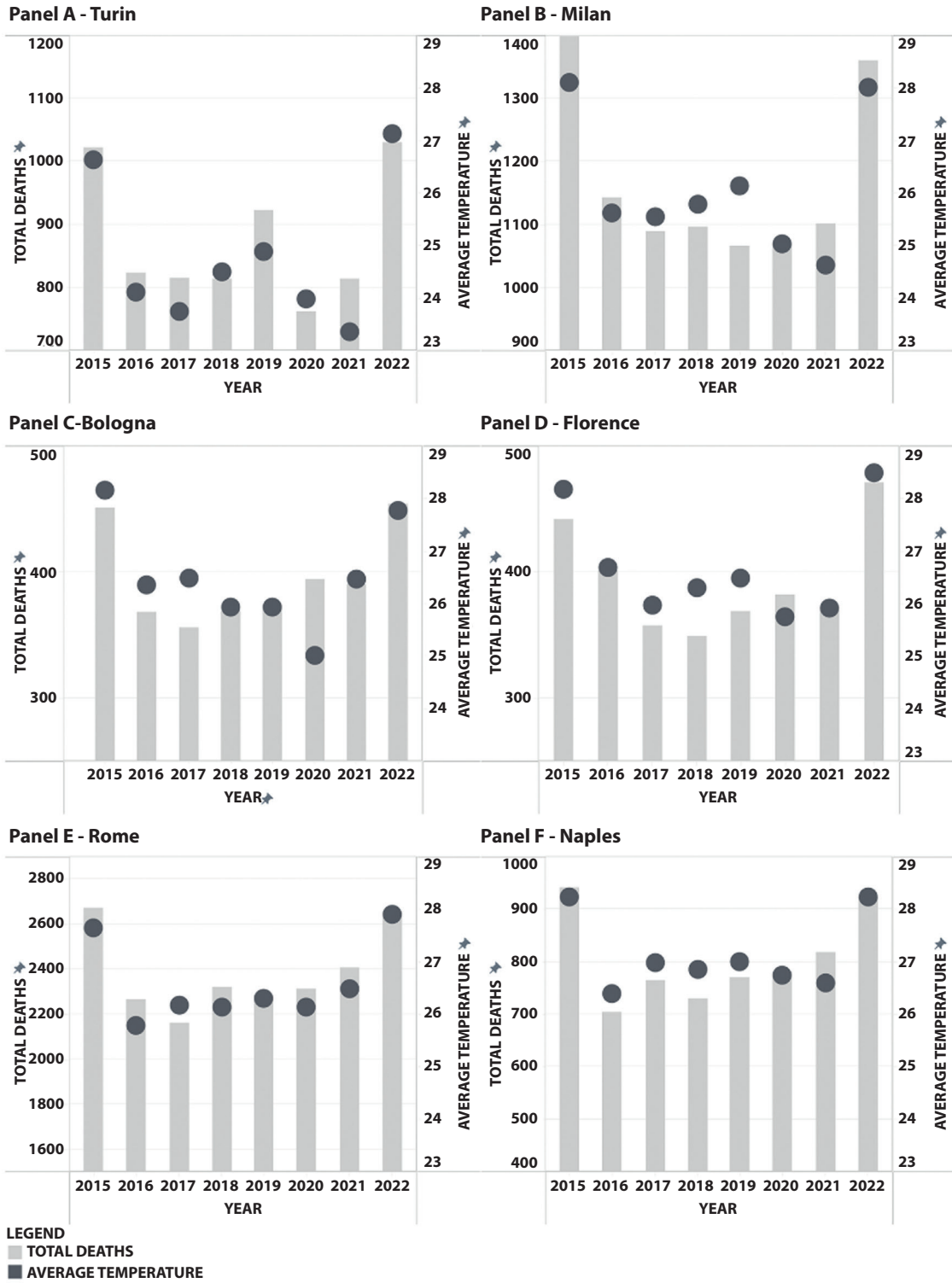


Figure 2. Relationship between average temperatures (°C) and number of deaths registered in the municipalities of Turin, Milan, Bologna, Florence, Rome and Naples in the months of July of the calendar years 2015-2022. Data on average temperatures were downloaded at: <http://www.ilmeteo.it>

4. DISCUSSION

Between April and July 2022, we estimated an average 6% higher total mortality, whereas in July 2022 the excess was +23%. In the working age population, we observed a similar pattern with excesses in the range of 2 to 6% in April-June 2022, which increased to 13% in July 2022.

We reported only a modest excess mortality (+2.5%) at all ages during the initial period of Omicron predominance in Italy (February-March 2022), and no excess at working ages [7]. That finding likely resulted from the combination of a less severe disease induced by Omicron [8,9] and a high level of natural and vaccine-induced protection of the Italian population [10]. However, in spring and summer 2022, when new variants appeared and quickly became predominant, the number of deaths returned higher than expected. This may reflect the waning of vaccine efficacy, since the (booster) vaccination campaign levelled off at the end of the previous winter. However, the reasons behind that remain largely undefined, and in the absence of cause-of-death data in Italy, can be only hypothesized.

The numbers of hospitalization in intensive care units due to COVID-19 did not increase between February and July 2022 [2], indicating that those deaths did not occur in the acute phase of the disease, but may be related to possible sequelae of COVID-19 [11,12]. In fact, a remarkable increased risk of cardiovascular events has been observed among individuals infected by SARS-CoV-2, including young and middle-aged adults [13,14]. Long-term (i.e. over 300 days) cardiac pathology, mainly inflammatory (moderate myocarditis) has been reported in subjects with mild initial COVID-19 illness and no previous cardiac disease. [15]. Moreover, an indirect effect of COVID-19 on other diseases as a consequence of delayed diagnosis and suboptimal care has to be considered [16]. In support of these hypotheses, there are emerging data on increasing mortality from causes other than COVID-19, including heart disease, diabetes and Alzheimer disease/dementia [17,18].

The remarkable excess observed in the month of July 2022 can be largely attributed to the high ambient temperatures registered in that month in Italy. This is evident from the substantial gap between the estimated excess deaths and the deaths attributed to

COVID-19 in July, which was not observed in the previous months. In July 2015, there was a similar increase in ambient temperature in several main Italian cities, and in that year around 12,000 excess deaths were registered compared to the previous year.

Other countries are still observing excess total mortality during the circulation of Omicron. The Office for National Statistics reported no excess in the UK between January and mid-March 2022, but from the second half of March to the end of July 2022, 20,600 (6,000 in July) more deaths than expected were observed, based on the average number of deaths registered in the 5-year before the pandemic (2015-2019) [19]. The number of deaths attributed to COVID-19 in that period was 14,000 (68% of the total excess) and in July 2022 only 3,000 (50% of the total excess).

Between February and June 2022, the average excess mortality was close to 5%. In January and July, the excess was over 10%, but was influenced by the residual of the Delta wave in January and by the high temperatures in July. Assuming a 5% COVID-19-related excess mortality for the remaining months, at the end of the year this may translate into 30 to 35,000 excess deaths.

Our estimates are based on provisional data which may be incomplete for some municipalities due to delay in death registration. This may have underestimated the true excess mortality, especially in the most recent months. Consequently, we need timely mortality data in order to implement an effective monitoring of the pandemic. Considering the high social and economic impact of a premature death at working age, estimates of excess death should be also provided for this population, despite the low risk and the comparatively small total number of deaths.

5. CONCLUSIONS

Our data indicate a persistent excess in total mortality during the circulation of different lineages and sub-lineages of the Omicron variant in Italy. With few exceptions (i.e. the serious flu epidemic in 2015) until 2019 total mortality had been decreasing and hence life expectancy had been increasing in Italy, with implications on social security and retirement schemes, i.e. planned periodic increases of age at retirement. After decades, of increased life expectancy,

the trend has reversed in Italy as in other countries [20], indicating that COVID-19 pandemic continues to have implications on total mortality in high-income countries. The impact was concentrated in the elderly, but an excess mortality is evident at working age too, even if the absolute number of excess deaths is small below age 65.

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