Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Original Research

Doubled mortality rate during the COVID-19 pandemic in Italy: quantifying what is not captured by surveillance

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ABSTRACT

Objectives: It is important to quantify the true burden of coronavirus disease 2019 (COVID-19) in different countries, to enable informed decisions about imposing and relaxing control measures. COVID-19 surveillance data fails in this respect, as it is influenced by different definitions, control policies and capacities. This article aims to quantify excess mortality and estimate the distribution between COVID-19 and non-COVID-19 causes of death.

Study design: Observational study and mathematical modelling.

Methods: Publicly available data from multiple institutional sources were used and an in-depth analysis was carried out of deaths from all causes between 2015 and 2020 in Italy at the national, regional and local level. Excess mortality over time and space was first explored, followed by an assessment of how this related to COVID-19 surveillance and, ultimately, assuming a fixed male:female ratio, a model was developed and applied to estimate the proportions of COVID-19 and non-COVID-19 excess mortality in 2020.

Results: In Italy, the mortality rate doubled in March and April 2020 compared with data from 2015 to 2019 (+109%, when considering municipalites with >10.000 inhabitants), with excess mortality reaching >600% in large municipalities in northern areas. Notified COVID-19 deaths accounted for only 43.5% (regional range: 43–62%) of excess mortality. It is estimated that more than two-thirds of excess deaths that were not captured by surveillance are non-COVID-19 deaths, which could be a result of the excess burden on the health systems, in addition to reduced demand and supply of other non-COVID healthcare services.

Conclusions: The impact of COVID-19 during the early stages of the pandemic is much larger than official figures have reported. Monitoring excess mortality helps to capture the full effect of the COVID-19 pandemic, which differs between regions in Italy and which might have resulted in significant indirect effects on the well-being of the population. In addition, the COVID-19 pandemic has also resulted in significant indirect effects on the well-being of the population.

Introduction

The rapid spread of coronavirus disease 2019 (COVID-19) has posed a challenge to governments that is unprecedented in the modern era. Given continued uncertainties about infection transmission and effective control measures, it is essential to have timely and accurate data on the burden of disease that the COVID-19 pandemic is generating. These data are needed to inform decisions about imposing and relaxing nonpharmaceutical countermeasures, such as restrictions on movement, and to facilitate learning from experiences of others, both internationally and within countries. It has been previously argued that countries are lacking a robust system of epidemiological intelligence to guide and inform public health action, and that current surveillance systems in most countries, including Italy, merely consist of counting COVID-19 cases and deaths with diverse criteria.[1] How deadly has COVID-19 been with respect to the population (in different areas)? How many people have been infected by the virus and how many

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are dying? The Italian National COVID-19 surveillance system does not enable such questions to be answered. It is known that data of notified COVID-19 deaths underestimate the true burden of COVID-19, as it does not include those who died but did not get tested for coronavirus infection.[2] In addition, the COVID-19 pandemic will have an indirect effect on mortality through different pathways, including health services running at stretched capacity, unmet demand for healthcare services other than COVID-19 and fear in the population to seek medical care. The World Health Organisation (WHO) has provided criteria for coding deaths due to COVID-19, yet there is considerable variation in reported COVID-19 mortality. Consequently, there is growing support for the use of excess all-cause mortality. This has the advantage of avoiding differences in diagnostic recording. It can also be expected to capture the full, both direct and indirect, effect of the COVID-19 pandemic. However, this measure will be most useful if there is also an understanding of how it relates to the narrower definitions of COVID-19 deaths reported in official figures.

It is the responsibility of public health officials to quantify the real direct and indirect impact of the COVID-19 emergency on population health, and to explore its determinants related to the natural history of COVID-19, to its spread at the community level and to its management within and outside health services. In this context, the aim of the current study is to carry out an in-depth analysis of all-cause mortality rates in Italy between 2015 and 2020, at the national, regional and local level, and to compare these to COVID-19 surveillance mortality data. From these data, the current study estimates how much of the excess mortality that was not captured by surveillance is directly and indirectly due to COVID-19, thus deriving meaningful elements to quantify the true burden of the pandemic in Italy.

Methods

Sources of data

Publicly available data were used from multiple institutional sources at the local, regional and national level. The number of deaths from all causes were retrieved from the Italian National Institute of Statistics (Istituto Nazionale di Statistica, ISTAT) for the period from 1st January 2015 to 15th April 2020. Mortality statistics were obtained from the National Resident Population Register (ANPR) and made available by ISTAT.[3] Data for the period from 1st January to 15th April 2020 have been released by ISTAT earlier than usual to support the development of responses to the COVID-19 pandemic.[3] There are 7900 municipalities in Italy, grouped into 170 provinces and 21 regions. Mortality data for the study period were available for 4433 municipalities, which corresponds to 57.2% of the total Italian population. Morality data were retrieved by month, gender and municipality. Population statistics were retrieved from the ISTAT demographic database to compute mortality rates. COVID-19 data were obtained from the national COVID-19 surveillance reporting system, established by the Italian Government on 24th February 2020[4] and managed by the National Institute of Health, and into which regional authorities are required to report daily disaggregated microbiological and epidemiological data. Aggregated COVID-19 surveillance data are published daily on a dedicated publicly available online dashboard.[5] For the current analysis, a COVID-19 death was defined according to the national COVID-19 surveillance reporting system as those occurring in patients testing positive for severe acute respiratory syndrome coronavirus 2(SARS-CoV-2) using reverse transcription polymerase chain reaction (RT-PCR), regardless of the presence of pre-existing diseases that may have contributed to death.[6]

Analysis

The objective was to first quantify excess deaths, then compare them to COVID-19 surveillance data and subsequently estimate the proportion of excess deaths directly or indirectly attributable to COVID-19 in different geographical areas. The baseline is the average number of deaths from all causes in the period 2015–2019 in each of the months of January, February, March and April. When describing data on individual municipalities, those with a population of <10,000 were excluded. The percentage difference in absolute numbers of deaths in 2020 compared with the baseline in each municipality by sex was then calculated, and municipalities were aggregated into provinces and regions.

A model was developed to estimate the excess mortality in 2020 in its different components: first, the increase in all-cause deaths in 2020 was calculated, compared to baseline, by sex in each region that (i) had ISTAT data available for at least 50% of the total population, (ii) had a total population >1 million and (iii) had at least 700 notified COVID-19 deaths between 1st March and 15th April. The increase in absolute numbers of male and female deaths from all causes between baseline and 2020 (Δ_M^{ac} and Δ_F^{ac}) was rescaled for each region, and expressed as per equation (1) (eq. (1)), with $D_{M,F}^{cv}$ representing the number of COVID-19 deaths reported by the national surveillance reporting system, $d_{M,F}^{cv}$ the number of COVID-19-deaths not captured by the national COVID-19 surveillance reporting system and $d_{M,F}^{nocv}$ the number of excess deaths from other causes.

$$\Delta_{M,F}^{ac} = D_{M,F}^{cv} + d_{M,F}^{cv} + d_{M,F}^{nocv}, \tag{1}$$

While there are data for $\Delta_{M,F}^{ac}$ and $D_{M,F}^{cv}$, $d_{M,F}^{cv}$ and $d_{M,F}^{nocv}$ are unknown. The $D_{M,F}^{cv} + d_{M,F}^{cv}$ (total COVID-19 deaths) was set to have a fixed male:female distribution (g^{ratio}) in the range of 58–62%:42–38%. This was calculated by combining the mean male:female COVID-19 death distributions reported from Germany, France, the UK and Spain,[7] with the latest official Italian values reported by the National Institute of Health.[8] d^{nocv} was set to have the same male:female distribution as observed during baseline (defined as $p_{M,F\ baseline}^{ac}$).

From this, eq. (2a) and eq. (2b) were derived and, in turn, $d_{M,F}^{cv}$ was calculated from eq. (1) (eq. (3)).

$$\frac{\Delta_M^{ac} - p_{M\ baseline}^{ac} * d^{nocv}}{\Delta_F^{ac} - p_{F\ baeline}^{ac} * d^{nocv}} = \frac{62}{38} \div \frac{58}{42} = g^{ratio}, \tag{2a}$$

$$d^{nocv} = \frac{\Delta_M^{ac} - g^{ratio} * \Delta_F^{ac}}{p_{M\ baseline}^{ac} - g^{ratio} * p_{F\ baseline}^{ac}} \tag{2b}$$

$$d_{M,F}^{cv} = \Delta_{M,F}^{ac} - D_{M,F}^{cv} - d_{M,F}^{nocv} \tag{3}$$

Using data on the regional male:female distribution of deaths at baseline and in 2020, and assuming a fixed male:female distribution of COVID-19-related deaths (g^{ratio}), the model allows an estimate to be calculated of the proportion of excess mortality attributable to COVID-19 and to non-COVID-19 causes that are associated with the pandemic.

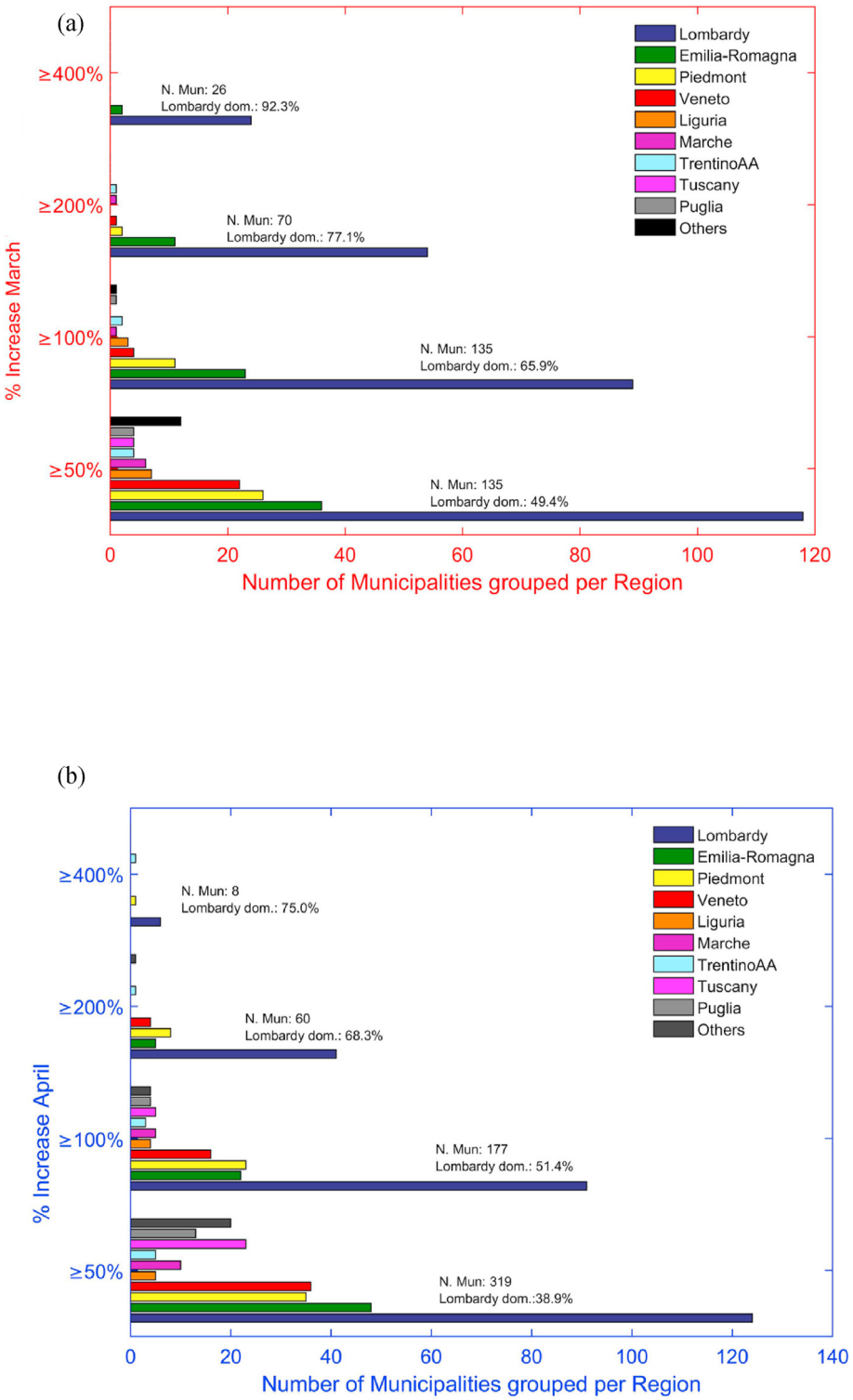

Fig. 1. Italian municipalities (n) percentage increase (≥50%, ≥100%, ≥200%, ≥400%) in all-cause deaths in 2020 compared with 2015–2019 for the periods (a) 1st–31st March, (b) 1st –15th April.

Results

Excess mortality in 2020

Data were analysed on 34.5 million Italian residents in 4433 municipalities. The percentage change in the number of deaths between the 2015–2019 baseline and 2020 was slightly negative in the months of January (−9.6%) and February (−3.1%), but it increased by a massive 61.3% in March and by 51.6% in the first half of April. Between 1st March and 15th April 2020, there were 77,339 deaths compared with the 48,860 expected deaths based on trends from the previous years (a difference of 28,479 deaths). When

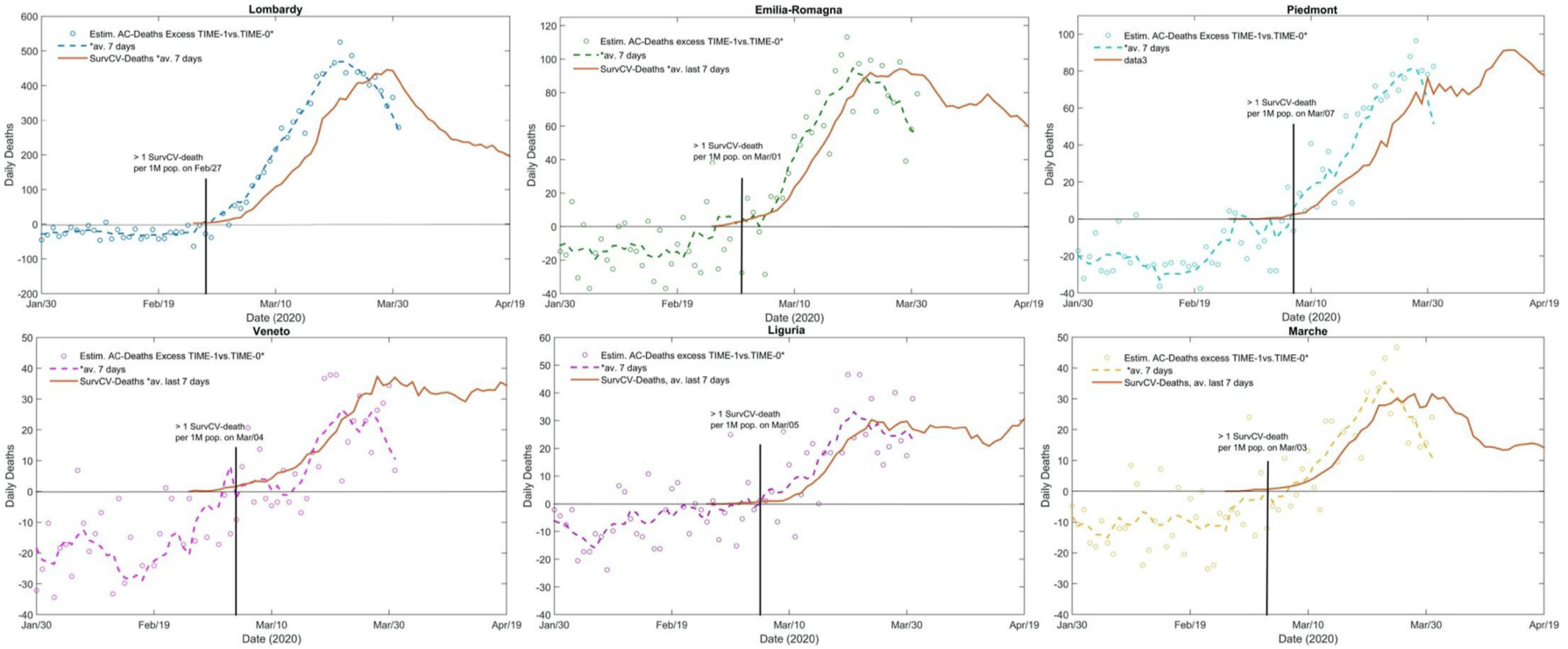

Fig. 2. Daily COVID-19 notified deaths (SurvCV) and all-cause deaths (AC-deaths) TIME-1-TIME-0 difference (n) in the period 31st January–31st March, by region. TIME-1: 2020. TIME-0: Average 2015–2019. The black bar indicates the onset of the COVID-19 epidemic, set at the time when each region SurvCV-deaths surpass the value of 1 death per 1 million population.

Table 1
Comparison of all-cause excess deaths and notified COVID-19 deaths,[a] by region[b] and at the national level, between 1st March and15th April.

Region	Resident population (n)	ISTAT data coverage (%)	Average all-cause deaths 1st March–15th April 2015–2019 (n)	All-cause deaths 1st March–15th April 2020 (n)	Excess deaths in 2020 compared with 2015–2019[c] (n)	Percentage increase in excess deaths in 2020 compared with 2015–2019	Notified COVID-19 deaths[a] (n)	Total excess deaths – COVID-19 deaths difference (n)	% of excess deaths not captured by COVID-19 surveillance
Lombardy	10,060,574	78.4%	10,071.6	27,010	21,616.6	168.2%	11,377	10,239.6	47.4%
Emilia-Romagna	4,459,477	83.8%	5522.8	9291	4495.0	68.2%	2788	1707.0	38.0%
Liguria	1,550,640	76.7%	2165.2	3435	1654.5	58.6%	807	847.5	51.2%
Veneto	4,905,854	72.6%	4701.2	6001	1791.3	27.6%	940	851.3	47.5%
Piedmont	4,356,406	59.8%	4187.8	6954	4629.1	66.1%	2015	2614.1	56.5%
Marche	1,525,271	47.9%	1094.2	1816	1506.7	66.0%	746	760.7	50.5%
Italy	60,359,546	57.2%	48,860.4	77,339	49,754.6	58.3%	21,645	28,109.6	56.5%

COVID-19, coronavirus disease 2019; ISTAT, Italian National Institute of Statistics.
[a] Data from the national COVID-19 surveillance reporting system, ISTAT.
[b] Regions were selected with the following inclusion criteria: (i) total population >1 million; (ii) ISTAT available for at least 50% of total population; (iii) at least 700 COVID-19 notified deaths between 1st March and 15th April.
[c] Rescaled to 100% population coverage.

scaled up to 100% of the Italian population, there was an estimated total of 49,754 excess deaths nationwide. When the analysis is limited to Italian municipalities with a resident population >10,000 (n = 735), the percentage change was, on average, −8.9% for January and +0.5% for February, while it increased by 113.5% in March and by 101.8% in April (108.6% when considering the period: 1st March to 15th April). Data on all municipalities are available upon request. The percentage increase over baseline in the period 1st March to 15th April was ≥400% in 18 municipalities, ≥200% in 63, ≥100% in 144 and ≥50% in 260 municipalities. The Italian municipalities reporting the highest percentage increases in excess deaths are listed in Table S1 in the supplementary material. Four municipalities in the Lombardy Region, part of the province of Bergamo, reported the highest percentage increase in Italy: Nembro (+810%), Alzano Lombardo (+808%), Albino (+685%) and Ponte San Pietro (+590%). When limiting the analysis to the period 1st–31st March (i.e. when the COVID-19 epidemic peaked in Italy), the percentage increase was even greater, at +1117%, +990%, +973% and +723%, respectively, for these four municipalities, decreasing to +104%, +200%, +182% and +313%, respectively, in the first half of April (see Table S1).

In total, 94.4% of the municipalities reporting over 400% increases in excess deaths were in the Lombardy region, and municipalities reporting ≥200% increase were in Lombardy (79.4%), Emilia-Romagna (12.7%), Piedmont (3.2%), Veneto, Marche and Trentino Alto-Adige (1.6% each). The regional distribution of municipalities reporting >50% increases in excess deaths is reported in Fig. 1, separately for the periods 1st–31st March (Fig. 1a) and 1st–15th April (Fig. 1b). This shows that the highest increases (≥400%) were in March and were mainly concentrated in the Lombardy region.

Table S2 in the supplementary material reports data from Italian provinces, showing those where the increase in all-cause excess deaths over the study period was greater than 50%. The highest percentage increases were in the Lombardy provinces of Bergamo (+448%), Cremona (+341%), Lodi (+291%) and Brescia (+255%), followed by Piacenza (+237%) in the Emilia Romagna region. Overall, 8 in 12 provinces in Lombardy, 2 in 9 in Emilia-Romagna, 2 in 8 in Piedmont and 1 in 5 in the Marche region reported at least a doubling of all-cause mortality.

Comparison with official data on COVID-19 deaths

Fig. 2 reports the distribution of officially recorded COVID-19 deaths plotted against the increase in all-cause deaths between 30th January and 31st March 2020 in the six regions with the highest numbers of official COVID-19 deaths in the country. Together, these six regions have accounted for 88% (n = 28,406) of the official COVID-19 deaths in Italy, as of 30th May 2020. Fig. 2 shows that the trends in all-cause excess deaths preceded those for COVID-19, which followed with a slight delay in almost all regions, with the exception of Veneto. In Lombardy, Emilia-Romagna and Piedmont (the regions hardest hit by the COVID-19 outbreak), excess mortality was reported at the beginning of the regional epidemic onset. As can be seen in Fig. 2, excess deaths for all causes preceded COVID-19 deaths occurrence by approximately 1 week, largely surpassing them in absolute numbers. For example, in the Lombardy region, the daily difference between excess deaths for all causes and COVID-19 notified deaths reached 100, while, in contrast, the differences seen in Veneto were on average 10 times smaller.

Table 1 reports excess all-cause deaths for the period 1st March to 15th April by region. These were +168.2% in Lombardy, +68.2% in Emilia Romagna, +66.1% in Piedmont, +66.0% in Marche, +58.6% in Liguria and +27.6% in Veneto. Official COVID-19

Table 2
Estimated proportions of excess mortality attributable to COVID-19[a] and non-COVID-19 causes by region[b] and at the national level.

Region	$p^{ac}_{M,TIME-0}$	$p^{ac}_{M,TIME-1}$	Estimated total COVID-19 deaths $D^{cv} + d^{cv}$ [m:f 62–58%:38–42%]	D^{cv}(*)	d^{nocv} [m:f 62–58%:38–42%]	$\frac{d^{cv}}{D^{cv}+d^{cv}}$ [m:f 62–58%:38–42%]	$\frac{d^{nocv}}{d^{cv}+d^{nocv}}$ [m ÷ f 62–58%:38–42%]
Emilia-Romagna	46.3%	50.7%	3125.0:4192.0	2788	1369.9:303.0	10.8%:33.5%	80.3%:17.7%
Lombardy	46.6%	51.4%	10,903.2:14,713.8	11,377	10,713.4:6902.8	[c]0%:22.7%	[d]100%:67.4%
Liguria	45.2%	47.7%	665.0:872.6	807	989.5:781.9	[c]0%:7.5%	[d]100%:92.3%
Veneto	46.9%	48.1%	662.1:900.3	940	1129.2:891.0	[c]0%	[d] 100%
Piedmont	46.6%	49.5%	2243.6:3028.3	2015	2385.5:1600.8	10.2%:33.5%	91.3%:61.2%
Marche	46.6%	52.6%	1469.8:1986.8	746	36.9:480.1	49.2%:62.5%	4.8%:0%[c]
Italy	47.2%	50.0%	25,683.3:35,163.8	21,645	24,071.3:14,590.8	15.7%:38.4%	85.6%:51.9%

COVID-19; coronavirus 2019; ISTAT, Italian National Institute of Statistics.
$p^{ac}_{M\ baseline}$: % of male deaths in 2015–2019; p^{ac}_{M2020}: % of male deaths in 2020.
Estimated total COVID-19 deaths: notified COVID-19 deaths (D^{cv})* + estimated no. of COVID-19 deaths not captured by surveillance (d^{cv})
$\frac{d^{cv}}{D^{cv}+d^{cv}}$: COVID-19 deaths not captured by surveillance as % of total estimated COVID-19 deaths.
$\frac{d^{nocv}}{d^{cv}+d^{nocv}}$: Non-COVID-19 deaths as % of total excess deaths not captured by surveillance.
m:f: male:female death ratio.
[a] Data from the national COVID-19 surveillance reporting system, ISTAT.
[b] Regions were selected with the following inclusion criteria: (i) total population >1 million; (ii) ISTAT available for at least 50% of total population; (iii) at least 700 COVID-19 notified deaths between 1st March and 15th April.
[c] Value is cut-off to 0% when operation returns negative percentage.
[d] Value is cut-off to 100% when operation returns >100%.

deaths during the same period represent only a fraction of total excess mortality, leaving a large proportion of excess deaths unexplained: from 38% in Emilia Romagna, to around 47% in Lombardy and Veneto, 51% in Marche and Liguria and up to 56.5% in Piedmont (Table 2). In all regions, the proportion of all-cause excess deaths attributed to men at baseline ranged from 46.3% to 46.9%, with the exception of Liguria (45.2%), but increased to 48.1–52.6% in 2020 (+12.9% in Marche, +10.3% in Lombardy, +9.5% in Emilia Romagna, +6.2% in Piedmont, +5.5% in Liguria, +2.6% in the Veneto region and +5.9% in the whole country, Table 2).

Modelling the proportions of excess mortality attributable to COVID-19 and non-COVID-19 causes

Table 2 shows the estimates of the total number of COVID-19 deaths according to the study model, by region (official COVID-19 deaths plus those not captured by surveillance systems), ranging from 10,903 to 14,714 deaths in Lombardy (on the basis of the male:female ratio range assumed by the model), from 3125 to 4192 deaths in Emilia Romagna, from 2244 to 3028 deaths in Piedmont, from 1470 to 1987 deaths in Marche, from 662 to 900 deaths in Veneto and from 665 to 873 deaths in Liguria. Nationally, the estimate is between 25,683 and 35,164 COVID-19 deaths. After subtracting COVID-19 deaths notified through the national COVID-19 surveillance reporting system, we estimate that the percentage of COVID-19 deaths that have not been captured by official figures is highest in Marche (49–62.5% of total estimated COVID-19 deaths), followed by Piedmont and Emilia-Romagna (10–33.5%) and Lombardy, where <23% of the total estimated COVID-19 deaths are missed. In Veneto, the region with the lowest percentage increase in distribution of male deaths between baseline and 2020, the model returned no further COVID-19 deaths, apart from those captured by surveillance. Table 2 also reports the number of estimated non-COVID-19 excess deaths. It is estimated that in all regions, except Marche, non-COVID-19 deaths accounted for the largest proportion of the increase in all-cause excess deaths. However, caution is needed when applying the model to individual regions. When applying the model to the whole country (around 60% ISTAT coverage data), from a total of almost 50,000 all-cause excess deaths (+58%) at the national level, it is estimated that 4000–13,500 deaths are COVID-19 deaths that were not captured by surveillance (15.7–38.4% of total COVID-19 deaths), while approximately 15,000–24,000 deaths are attributable to causes other than COVID-19 (52–86% of total excess deaths that were not captured by surveillance).

Discussion

The death count has doubled in Italy in March and April 2020 compared with the same months in 2015–2019. This is an unprecedented mortality burden increase. In particular, deaths for all causes increased in March 2020 by >600% in more than ten large municipalities in the north of Italy, with a peak increase of >1100%. However, with geographical variability, COVID-19 deaths notified through the Italian national COVID-19 surveillance system accounted for only 40% of the excess mortality. Within excess mortality that was not captured by COVID-19 surveillance, our model quantifies that more than two-thirds of excess deaths might be due to causes other than COVID-19. This study initially looked at excess mortality patterns over time and space, then combined and compared excess mortality data with COVID-19 official statistics, and ultimately modelled the different contribution of COVID-19 morbidity and non-COVID-19 clinical burden. Therefore, the current analysis not only allows quantification of the true population-level health impact of the COVID-19 emergency in Italy, but it also determines meaningful elements to describe and interpret the characteristics of the COVID-19 epidemic at the national and regional level, and enables comparisons with international settings.

The current data do not support the hypothesis previously put forward[9–11] that COVID-19 was present in Italy and causing excess mortality earlier than reported by the national COVID-19 surveillance system, as the number of all-cause deaths in January and February 2020 are in line with what was expected based on trends from previous years. This study reports that the pandemic in Italy has played out in very different ways throughout the country; of note, among large northern Italian regions, Veneto reported the smallest excess death count (27.6% for the period March–April, compared with168% in the Lombardy region). The response to COVID-19 in the Veneto region during the early and most critical phases of the epidemic differed from other regions, including Lombardy, and focused on extensive swab testing, which proved to

be effective in limiting infection transmission, and possibly mortality,[12,13] in addition to providing useful insights on transmission dynamics at the population level.[13] In particular, as reported in *Nature,* the municipality of Vo' in Veneto, where the first Italian COVID-19 death was reported, imposed an early and timely lockdown, with almost 86% of the population tested and a 2.6% population-level prevalence of infection at the start of the municipality lockdown.[13]

In different Italian regions, notified COVID-19 deaths accounted for varying percentages of excess deaths, leaving large proportions of excess mortality unexplained. Although the definition of a COVID-19 death in Italy was established by the national COVID-19 surveillance reporting system[6] and does not vary across regions, it has been previously argued[1] that varying regional control strategies and capacities may have influenced COVID-19 death counts.

While COVID-19 surveillance data across countries are not easily comparable because of different adopted classifications and case/death definitions, it is possible to compare excess mortality data. Although scholars have identified monitoring excess mortality (a consistent measurement of the COVID-19 pandemic scale across time and space)[14,15] as a priority, few comprehensive analyses of excess deaths in 2020 have been published to date.[15–19] With reference to Italy, several recent descriptive studies analysed excess morality in the small city of Nembro (heavily impacted by the COVID-19 outbreak),[20] and in selected major Italian cities,[11,21,22] but with no complete regional-level analysis. Excess mortality data from other countries confirms that, in areas hit by the COVID-19 outbreak, death rates have risen above historical averages.[23] An analysis conducted on US states with data from the Centers for Disease Control and Prevention (CDC)[24] reports excess deaths in the United States between 11th March and 2nd May increased by around six times (24,172 excess deaths in absolute numbers) in New York City, the epicentre of the US COVID-19 outbreak.[25] In Europe, the European Mortality Monitoring Project records excess deaths from 24 countries on a weekly basis, and reported 149,447 excess deaths in European countries between week 10 and 18 of 2020. Another analysis conducted on 14 countries worldwide reported excess deaths to be highest in Spain (17,200 deaths estimate), followed by the UK and Italy.[26–28]

In addition to assessing excess mortality and how it relates with COVID-19 official statistics, the second part of the current analysis estimated how excess deaths that were not captured by surveillance are distributed between additional COVID-19 deaths and deaths due to causes other than COVID-19; the results suggest a large proportion belong to non-COVID-19 related deaths. Although the outputs of the current study's model should be taken with caution, there is a strong rationale, and accumulating data from the literature, suggesting that the COVID-19 pandemic has indirectly increased mortality through different pathways, including decreased demand and supply of other non-COVID healthcare services. As health services were reorganised to manage COVID-19 patients at the hospital and community level (e.g. converting wards into dedicated COVID-19 wards, and postponing elective procedures, hospitalisations and other services), the healthcare needs of patients with chronic conditions may not have been met. In addition, fear of nosocomial SARS-CoV-2 transmission may have stopped individuals seeking care when in need, with reports from several countries showing decreased hospitalisations and emergency admissions.[23,24,29–32] Recent data from a large multicentre Italian study showed hospital admissions for acute myocardial infarction (AMI) decreased by 48.4% compared with 2019, and AMI case fatality increased threefold during the COVID-19 pandemic.[26] In addition, data from another Italian study showed longer times from symptom onset to hospital admission in patients with myocardial infarction during the COVID-19 pandemic compared with previous years.[33] In the UK, attendances at emergency departments dropped by 30% in March 2020 compared with March 2019[27] and, in France, researchers reported a doubled incidence of out-of-hospital cardiac arrests and decreased survival rates.[34] In terms of other chronic diseases, including cancer, preliminary data suggest that the COVID-19 pandemic has resulted in delays in diagnosis, with possible detrimental effects on survival.[35]

Although not conclusive, data from different settings suggest the negative indirect effects associated with the COVID-19 lockdown and healthcare service adjustments are accounting for a substantial proportion of the reported excess mortality. This is among one of the first studies to attempt to quantify the proportions of excess mortality, building the reasoning around the fact that reported COVID-19 deaths for the male:female ratio are different from the non-COVID-19 ratio.[36] If the true COVID-19 death male:female ratio is different to that reported in the official statistics[37] or if other factors have influenced the 2020 male:female mortality ratio, this could bias the current estimates.

The current study has some additional limitations that need to be acknowledged. Data on deaths from the ISTAT do not cover the entire Italian population, thus generalisation of estimates to the whole country introduces some statistical fluctuations, which is further increased by regional heterogenicity in data coverage. However, there is nothing to suggest that trends in deaths are distributed differentially in municipalities that were included in ISTAT statistics compared with those that were not included. To account for incomplete data coverage, the current study reports municipal-level data as a whole and only includes provincial and regional area estimates where data coverage is >50%. In addition, statistical fluctuations were minimised when the model was applied to the Italian national level. Another limitation is that age distribution of the study population was not considered or analysed into different age strata as this would have returned too few data to be imputed in the model; however, age strata was included in the analysis of a recent Italian report.[28]

The current pandemic has caused an unprecedented health burden worldwide; after China, Italy was the first country to be heavily impacted by the COVID-19 outbreak. While it is important to wait several months to get more complete and comprehensive mortality data and to detect any harvesting effect,[28] the current study contributes to the accumulating body of knowledge, unmasking the true negative impact of COVID-19 on population health, and underlining how such impact might be associated with unmet non-COVID-19 medical needs. While raising awareness of the need to build and maintain a robust system of real-time intelligence of the epidemic, including rapid mortality surveillance, the current analysis will help inform the planning, implementation and monitoring of healthcare service delivery as the pandemic progresses, and offers effective guidance to public health action so that nobody, regardless of infection status, is left behind.

Author statements

Ethical approval

Given the study design (observational study) and the sources of data (analysis of publicly available data), no ethical approval was required to conduct the study.

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

Competing interests

The authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2020.11.016.

References

1. Odone A, Delmonte D, Scognamiglio T, Signorelli C. COVID-19 deaths in Lombardy, Italy: data in context. *Lancet Public Health* 2020 Jun;**5**(6):e310. https://doi.org/10.1016/S2468-2667(20)30099-2. Epub 2020 Apr 25. Erratum in: Lancet Public Health. 2020 Jun;5(6):e315. PMID: 32339478; PMCID: PMC7182509.
2. Wise J. Covid-19: death rate in England and Wales reaches record high because of covid-19. *BMJ* 2020;**369**:m1484.
3. Italian National Institute of Statistics. *Decessi e Cause di Morte*. ISTAT; 2020. Available at: https://www.istat.it/it/archivio/240401?fbclid=IwAR2yQEpYziRSvZJx395GPp4nVSHeVzWftn6Id0pVneTn0y2Rwgw57BTYKoc. [Accessed 1 May 2020].
4. Presidency of the Council of Ministers. COVID-19 Italian Integrated surveillance. Available at: http://www.trovanorme.salute.gov.it/norme/dettaglioAtto?id=73469 (accessed 06 May 2020).
5. The Civil Protection Department of the Italian Government. COVID-19 National Surveillance. Available at: http://www.protezionecivile.gov.it/ (accessed 01 May 2020).
6. Onder G, Rezza G, Brusaferro S. Case-fatality rate and characteristics of patients dying in relation to COVID-19 in Italy. *JAMA* 2020 May 12;**323**(18):1775–6. https://doi.org/10.1001/jama.2020.4683.
7. Global Health 5050. COVID-19 sex-disaggregated data tracker. Available at: https://globalhealth5050.org/covid19/ (accessed 10 May 2020).
8. Reuters. Italian scientists investigate possible earlier emergence of coronavirus. Available at: https://www.reuters.com/article/us-health-coronavirus-italy-timing/italian-scientists-investigate-possible-earlier-emergence-of-coronavirus-idUSKBN21D2IG (accessed 26 March 2020).
9. Deslandes A, Berti V, Tandjaoui-Lambotte Y, et al. SARS-COV-2 was already spreading in France in late December 2019. *Int J Antimicrob Agents* 2020:106006.
10. Chinazzi M, Davis JT, Mu K, et al. *Estimating the risk of sustained community transmission of COVID-19 outside Mainland China*. 2020.
11. Michelozzi P, de'Donato F, Scortichini M, et al. Mortality impacts of the coronavirus disease (COVID-19) outbreak by sex and age: rapid mortality surveillance system, Italy, 1 February to 18 April 2020. *Euro Surveill* 2020;**25**(19).
12. Di Bari M, Balzi D, Carreras G, Onder G. Extensive testing may reduce COVID-19 mortality: a lesson from northern Italy. *Front Med* 2020;**7**:402.
13. Lavezzo E, Franchin E, Ciavarella C, et al. Suppression of a SARS-CoV-2 outbreak in the Italian municipality of Vo'. *Nature* 2020;**584**(7821):425–9.
14. Leon DA, Shkolnikov VM, Smeeth L, Magnus P, Pechholdova M, Jarvis CI. *COVID-19: a need for real-time monitoring of weekly excess deaths*. 2020.
15. Vieira A, Peixoto VR, Aguiar P, Abrantes A. Rapid estimation of excess mortality during the COVID-19 pandemic in Portugal -beyond reported deaths. *J Epidemiol Global Health* 2020;**10**(3):209–13.
16. de Lusignan S, Joy M, Oke J, et al. Disparities in the excess risk of mortality in the first wave of COVID-19: cross sectional study of the English sentinel network. *J Infect* 2020:4817.
17. Silva GAE, Jardim BC, Santos C. Excess mortality in Brazil in times of Covid-19. *Ciência Saúde Coletiva* 2020;**25**(9):3345–54.
18. Stang A, Standl F, Kowall B, Brune B, Böttcher J, Brinkmann M, et al. Excess mortality due to COVID-19 in Germany. *J Infect* 2020 Nov;**81**(5):797–801. https://doi.org/10.1016/j.jinf.2020.09.012. Epub 2020 Sep 19. PMID: 32956730; PMCID: PMC7501062.
19. Stokes Andrew C, Lundberg Dielle J, Hempstead Katherine, Elo Irma T, Preston Samuel H. Assessing the impact of the Covid-19 pandemic on US mortality: a county-level analysis. *medRxiv, gennaio* 2020. https://doi.org/10.1101/2020.08.31.20184036. 2020.08.31.20184036.
20. Piccininni M, Rohmann JL, Foresti L, Lurani C, Kurth T. Use of all cause mortality to quantify the consequences of covid-19 in Nembro, Lombardy: descriptive study. *BMJ* 2020;**369**:m1835.
21. Conti S, Ferrara P, Mazzaglia G, et al. Magnitude and time-course of excess mortality during COVID-19 outbreak: population-based empirical evidence from highly impacted provinces in northern Italy. *ERJ Open Res* 2020;**6**(3).
22. Blangiardo M, Cameletti M, Pirani M, Corsetti G, Battaglini M, Baio G. Estimating weekly excess mortality at sub-national level in Italy during the COVID-19 pandemic. *PloS One* 2020;**15**(10). e0240286.
23. De Filippo O, D'Ascenzo F, Angelini F, Bocchino Pier Paolo, Conrotto Federico, Saglietto Andrea, et al. Reduced rate of hospital admissions for ACS during Covid-19 outbreak in Northern Italy. *N Engl J Med* 2020;**383**(1):88–9. https://doi.org/10.1056/NEJMc2009166.
24. Cofano F, Tartara F, Zenga F, Penner F, Lanotte M, Garbossa D. Letter: back pain and accesses to emergency departments during COVID-19 lockdown in Italy. *Neurosurgery* 2020 Aug 1;**87**(2):E211. https://doi.org/10.1093/neuros/nyaa174. PMID: 32355982; PMCID: PMC7197581.
25. Preliminary estimate of excess mortality during the COVID-19 outbreak - New York city, March 11-may 2, 2020. *MMWR Morbidity and mortality weekly report* 2020;**69**(19):603–5.
26. De Rosa S, Spaccarotella C, Basso C, Calabrò MP, Curcio A, Filardi PP, et al. Reduction of hospitalizations for myocardial infarction in Italy in the COVID-19 era. *Eur Heart J* 2020 Jun 7;**41**(22):2083–8. https://doi.org/10.1093/eurheartj/ehaa409. PMID: 32412631; PMCID: PMC7239145.
27. Appleby J. What is happening to non-covid deaths? *BMJ* 2020;**369**. m1607-m.
28. ISTAT. *Impatto dell'Epidemia COVID-19 sulla mortalità totale della popolazione residente primo trimestre 2020*. 2020. Available at: https://www.epicentro.iss.it/coronavirus/pdf/Rapporto_Istat_ISS.pdf. [Accessed 4 May 2020].
29. Parri N, Lenge M, Buonsenso D, Coronavirus Infection in Pediatric Emergency Departments (CONFIDENCE) Research Group. Children with Covid-19 in pediatric emergency departments in Italy. *N Engl J Med* 2020 Jul 9;**383**(2):187–90. https://doi.org/10.1056/NEJMc2007617. Epub 2020 May 1. PMID: 32356945; PMCID: PMC7206930.
30. Tartari F, Guglielmo A, Fuligni F, Pileri A. Changes in emergency service access after spread of COVID-19 across Italy. *J Eur Acad Dermatol Venereol* 2020 Aug;**34**(8):e350–1. https://doi.org/10.1111/jdv.16553. Epub 2020 Jun 4. PMID: 32339340; PMCID: PMC7267617.
31. Lazzerini M, Barbi E, Apicella A, Marchetti F, Cardinale F, Trobia G. Delayed access or provision of care in Italy resulting from fear of COVID-19. *Lancet Child Adolesc Health* 2020 May;**4**(5):e10–1. https://doi.org/10.1016/S2352-4642(20)30108-5. Epub 2020 Apr 9. PMID: 32278365; PMCID: PMC7146704.
32. Kansagra AP, Goyal MS, Hamilton S, Albers GW. Collateral effect of covid-19 on stroke evaluation in the United States. *N Engl J Med* 2020;**383**(4):400–1.
33. Gramegna M, Baldetti L, Beneduce A, et al. ST-Segment-Elevation myocardial infarction during COVID-19 pandemic: insights from a regional public service healthcare hub. *Circ Cardiovasc Interv* 2020;**13**(8). e009413.
34. Marijon E, Karam N, Jost D, Perrot D, Frattini B, Derkenne C, et al. Out-of-hospital cardiac arrest during the COVID-19 pandemic in Paris, France: a population-based, observational study. *Lancet Public Health* 2020 Aug;**5**(8):e437–43. https://doi.org/10.1016/S2468-2667(20)30117-1. Epub 2020 May 27. PMID: 32473113; PMCID: PMC7255168.
35. Ferrara G, De Vincentiis L, Ambrosini-Spaltro A, Barbareschi M, Bertolini V, Contato E, et al. Cancer diagnostic delay in northern and central italy during the 2020 lockdown due to the Coronavirus Disease 2019 pandemic. *Am J Clin Pathol* 2020 Sep 30:aqaa177. https://doi.org/10.1093/ajcp/aqaa177. Epub ahead of print. PMID: 32995855; PMCID: PMC7543252.
36. The L. The gendered dimensions of COVID-19. *Lancet* 2020;**395**(10231):1168.
37. Krieger N, Chen JT, Waterman PD. Excess mortality in men and women in Massachusetts during the COVID-19 pandemic. *Lancet* 2020 Jun 13;**395**(10240):1829. https://doi.org/10.1016/S0140-6736(20)31234-4. Epub 2020 May 27. PMID: 32473099; PMCID: PMC7255340.