Assessment of the Overall Mortality during the COVID-19 Outbreak in the Provinces of Milan and Lodi (Lombardy Region, Northern Italy)

Valutazione della mortalità generale nelle province di Milano e Lodi durante l'epidemia di COVID-19

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ABSTRACT

OBJECTIVES: to describe the overall mortality increase in the provinces of Milan and Lodi – area covered by the Agency for Health Protection of Milan – during the COVID-19 epidemic in the first four months of 2020, compare it with the same time period in the years 2016-2019, and evaluate to what extent the mortality can be directly attributed to the outbreak.
DESIGN: cohort study.
SETTING AND PARTICIPANTS: using a new information system developed during the pandemic, we gathered data on the number of daily deaths in the population residing in the provinces of Milan and Lodi by Local Health Unit (ASST) and age groups. To describe the case fatality of COVID-19, we performed a record linkage with a database specially constructed during the epidemic to identify deaths that occurred in confirmed cases.
MAIN OUTCOME MEASURES: mortality and excess mortality were analysed by comparing the number of observed deaths in the first 4 months of 2020 with the average deaths of the years 2016-2019 in the same calendar period and with expected deaths, estimated using a Poisson model. Furthermore, a measure of relative risk was calculated as observed/expected ratio with a 95% confidence interval.
RESULTS: the increase in mortality for all causes occurring in the study population in the first 4 months of 2020 was 48.8%, 30.8% for ages between 60 and 69, 43.9% for ages between 70 and 79, and 56.7% for subjects above 80 years of age. Focusing on the epidemic period, from 1 March to 30 April, the excess is quantifiable as more than 2-fold and mainly concerns the population over 60 years of age. The excess mortality was observed in all local health units (ASSTs). The highest increments were in the province of Lodi and the North-East of Milan (ASST Nord). In the ASSTs of Lodi and Melegnano-Martesana the mortality excess was detectable from March 15th, while for the other ASSTs the increase began in the first week of April.
CONCLUSIONS: evaluation of overall mortality in the provinces of Milan and Lodi during the first wave of the Covid-19 epidemic showed a significant excess compared to the first 4 months of the years 2016-2019, mainly in the population over 60 years of age. However, this excess cannot be completely attributed directly to COVID-19 itself. This phenomenon was more intense in the Lodi ASST, with daily deaths up to 5 times higher than expected.

Keywords: COVID-19, mortality, excess mortality

WHAT IS ALREADY KNOWN

- **The province of Lodi was the first to experience the outbreak of COVID-19 in Europe.**
- **Lombardy was particularly hard hit by the COVID-19 epidemic, and case fatality in Lombardy was one of the highest in the world.**
- **COVID-19 mortality is higher in frail elderly people.**

WHAT THIS PAPER ADDS

- **A 48.8% excess of overall mortality was observed in the provinces of Milan and Lodi. A 122% excess was observed when considering the period from 1 March to 30 April.**
- **Mortality in subjects over 80 years of age showed a 56.7% excess, which could not be completely explained by COVID-19-specific mortality.**
- **In subjects under 70 years of age, mortality due to COVID-19 almost completely explained the excess mortality observed during the epidemic outbreak.**
- **Excess mortality was recorded in most of the towns in the two provinces examined, but occurred earlier and was higher in the province of Lodi.**

RIASSUNTO

OBIETTIVI: descrivere l'incremento della mortalità generale nelle province di Milano e Lodi – territorio afferente all'Agenzia di tutela della salute di Milano – nel periodo dell'epidemia di COVID-19 dei primi quattro mesi del 2020 rispetto allo stesso periodo di calendario degli anni dal 2016 al 2019 e valutare quale parte della mortalità può essere direttamente attribuita all'epidemia.
DISEGNO: studio di coorte.
SETTING E PARTECIPANTI: mediante un sistema informativo sviluppato ad hoc durante la pandemia, sono stati raccolti i dati sul numero di decessi giornalieri della popolazione residente nelle province di Milano e Lodi, divisi per Azienda sociosanitaria territoriale (ASST) e macroclassi d'età. Al fine di descrivere la mortalità specifica nei casi COVID, è stato effettuato un *record linkage* con un *database* per identificare i decessi occorsi nei casi accertati.
PRINCIPALI MISURE DI OUTCOME: è stata analizzata la mortalità con i relativi eccessi, confrontando i decessi osservati con i decessi medi calcolati nel primo quadrimestre degli anni dal 2016 al 2019 e con quelli attesi stimati mediante un modello di Poisson. Inoltre, è stata calcolata una misura di rischio relativo (rapporto osservati/attesi) con intervallo di confidenza al 95%.
RISULTATI: l'incremento della mortalità per tutte le cause registrato nella popolazione in studio, nei primi 4 mesi del

2020, è del 48,8%, del 30,8% per età comprese tra i 60 e i 69 anni, del 43,9% tra i 70 e gli 79 anni, e del 56,7% per età superiori. Focalizzandosi sul periodo epidemico, dall'1 marzo al 30 aprile, l'eccesso è quantificabile in più di 2 volte e riguarda principalmente la popolazione con più di 60 anni. L'eccesso di mortalità è stato osservato in tutte le ASST. Gli incrementi maggiori si sono avuti nella provincia di Lodi e nei comuni a Nord-Est di Milano (ASST Nord). Nelle ASST di Lodi e Melegnano Martesana l'eccesso di mortalità è stato osservato a partire dal 15 marzo, mentre per le altre ASST l'incremento è iniziato nella prima settimana di aprile.

CONCLUSIONI: la valutazione della mortalità generale nelle province di Milano e Lodi durante la fase epidemica di COVID-19 ha mostrato un importante eccesso rispetto al primo quadrimestre degli anni 2016-2019, principalmente a carico della popolazione con più di 60 anni e non completamente attribuibile all'azione diretta del virus. Questo fenomeno ha avuto intensità maggiore nell'ASST di Lodi, con decessi giornalieri fino a 5 volte superiori all'atteso.

Parole chiave: COVID-19, mortalità, eccessi di mortalità

INTRODUCTION

Mortality represents the most relevant indicator in public health to assess the health status of a population and measure the impact of extreme events, such as heat waves, environmental pollution, and epidemics. The COVID epidemic caused an increase in overall mortality that was measured at national level by the daily mortality surveillance systems. These systems were activated by the Ministry of Health to monitor and prevent the effects of seasonal emergencies (SISMG) in Italian metropolitan areas.[1] SISMG is based on the data of 34 sample municipalities, regional capitals, and cities with a population exceeding 250,000 inhabitants.

The rapid mortality assessment system,[1] which is currently the only existing reference for Italy, showed a 90% excess compared to the expected value for the city of Milan as of 12 May 2020, with 53%, 76%, and 119% excess mortality for age groups 65-74, 75-84, and 85 and older, with a mortality rate which returned to its expected values in the last week of May.

In light of the epidemic spread in the population, the initial onset in the province of Lodi, the subsequent spread to the province of Milan, and the fact that the national surveillance systems only include the city of Milan (which represents one third of the population of the area), the Agency for Health Protection of Milan (ATS) planned a mortality update system that made rapid assessment of overall mortality in the entire population. The routinely used overall mortality detection system has a latency of about 6 months, and it would not have allowed for the necessary almost real-time evaluations of the increase in deaths, not only in confirmed COVID-19 patients, but even in the general population. The goal of this study was to quantify and describe, with respect to age and area of residence, mortality and its excess for all causes and in COVID-19 positive patients, as recorded in the first four months of 2020, compared to the same period in the years 2016-2019, in the population of the provinces of Milan and Lodi.

MATERIALS AND METHODS

POPULATION AND CONTEXT

Lombardy's Regional Law no. 23/2015[2] established Milan's ATS in 2016, merging the Local Health Units (ASL) of the city of Milan with ASLs Milano 1, Milano 2 (which covered the Province of Milan as a whole), and Lodi, which includes the province of the same name, thus serving an area comprising 193 municipalities and a population of 3.5 million people.[3] In addition to the ATS, which is mainly responsible for health service planning, the same law established local healthcare units (Aziende Socio Sanitarie Territoriali - ASST) which are sub-areas including one or more hospitals (see table S1, on-line supplementary materials) and are entrusted with providing healthcare services, a task formerly carried out by ASLs. Each of the 193 towns of the ATS was assigned to a specific ASST. In this study, the municipality of Milan was considered as a single ASST, aggregating the 3 ASSTs that cover it (Niguarda, Fatebenefratelli Sacco, and SS. Paolo e Carlo).

The mean annual deaths in the entire area of Milan's ATS are about 33,000.

OFFICIAL REGISTRIES

Milan's ATS has access to the database of the office of vital statistics of the residents in the city of Milan, activated in 2002, which is largely used to monitor acute events in the population, such as the effects of the 2003 heat wave; the office of vital statistics was later also extended to include the municipality of Sesto San Giovanni.

The New Regional Register (*Nuova Anagrafe Regionale*, NAR)[4] registers all residents and healthcare users of the 193 towns of the ATS; it receives data from 170 municipal registers and is periodically updated through the system of the national registry of resident population (*Anagrafe Nazionale della Popolazione Residente*, ANPR),[5] established by the Ministry of the Interior according to article 62 of Legislative Decree 82/2005 (eGovernment Code).[6] This system is not currently active for 23 municipalities of the ATS, which cover a population of about 200,000 people. During the epidemic, therefore, a specific flow of notifications was set up from the municipal registers to the ATS. Updates from this new notification system were entered in the NAR database by ATS workers usually employed in assisting healthcare users in the task of choosing or changing their General Practitioner (GP).

This system was also updated using the notifications of deaths in the cohort of cases, provided by mayors and GPs

(subsequently verified on the appropriate vital statistics registers) who were asked to participate actively, each according to their own responsibilities/competences, in a multi-source information system developed by the Epidemiology Unit of Milan's ATS from the earliest stages of the epidemic. This system, based on a web portal with differentiated access, made it possible to trace cases and monitor compliance with the provisions of the Decrees of the President of the Council of Ministers (DPCM).[7] GPs participate in this information system by monitoring the health status of COVID-19 cases among their patients, and notifying new symptomatic cases, while prefectures and mayors have real-time access to the minimum amount of information on cases and contacts needed for the tasks of, respectively, monitoring that the DPCM measures are followed, and providing social aid.
At the end of the lockdown phase, the mortality information of the two monitoring systems was consolidated in a unique database containing the deaths up to 30 April, in order to allow an assessment of the daily mortality observed in the first four months of 2020 compared to previous years.

METHODS OF ANALYSIS

First of all, the 2020 daily mortality was compared with the average of daily deaths which occurred in the first four months of the years 2016-2019. In particular, absolute and relative measures of difference were calculated (% variation). Deaths in the first four months of 2020 and in the period of reference 2016-2019 were computed and displayed for the whole population, and stratified it into five age groups: <50 years, 50-59 years, 60-69 years, 70-79 years, and ≥80 years.[8] In order to describe COVID-19 case fatality, we performed record linkage with the specific database to identify deaths that occurred in confirmed cases; observations were censored on 30 April.
Excess daily mortality was then estimated as the difference between the deaths observed between 1 January and 30 April 2020 and expected deaths, which were obtained using a Poisson model on the mortality of the same period in the years from 2016 to 2019:[9] the linear predictor had a cyclical component corresponding to weekly variation (i.e., cosinor model) expressed by two covariates ($\sin(2\times\pi\times(t-1)/120)$ and $\cos(2\times\pi\times(t-1)/120)$, where t represented the time in weeks, from 1 to 18, and 120 the days of the period considered.[9,10]
The addition of a linear trend component (i.e., stationary cosinor model[10]) was also evaluated through a model selection based on the likelihood-ratio test and the AIC (Akaike Information Criterion: the lower the value, the better the model); predictions were then obtained from the model, and considered as expected values for the calculation of excess mortality. The 95% prediction intervals for excess deaths were obtained by bootstrapping (using 10,000 replications) the predictions of the Poisson model.[9,11] Finally, in addition to the total estimate of excess mortality, a relative risk (RR) measure (observed / expected ratio) was also provided, with a 95% confidence interval.
Furthermore, for each ASST, we graphically analysed the smoothed time trends of the deaths, obtained by interpolation with spline functions,[10,12] representing both the daily mortality of the first four months of 2020 and mortality excess as defined above. Finally, a descriptive geographical analysis of the relative percentage difference between the deaths observed in 2020 and the means of the preceding four-year period in the 193 municipalities of the study area was carried out. In this case, the relative percentage difference was subdivided into classes defined by the quintiles, and therefore equally numerous. Analyses were performed using R 3.6.3,[13] SAS 9.4,[14] and ARCGIS PRO.[15]

RESULTS

MORTALITY TIME TREND ANALYSIS

With respect to the daily overall mortality trend (figure 1), a decrease in deaths can be observed in the month of January 2020, compared to the average in the four preceding years. This was followed by a progressive increase, which endured until for several days, between mid-March and mid-April, up to over 250 daily deaths occurred (with a more than 2.5-fold increase compared to the average daily mean).
Analysis stratified by age (figure S1, see on-line supplementary materials) clearly shows that the surplus in mortality was mainly in the population over 60, but that excess mortality was present already in the 50-59 age class, although with lower numbers.

EXCESS ESTIMATES

Descriptive evaluation of the time trends showed that a decrease in observed deaths was recorded in January 2020, followed by a gradual increase in mortality, with a substantial excess from mid-March to mid-April. After that, a reduction can be observed up until 30 April, when the mean mortality level of the preceding years was reached.
Evaluating the entire period, it was possible to quantify the excess in a 48.8% increase in the mortality observed in the first four months of 2020, as reported in table 1.
The variation amounted to 30.8% for ages between 60 and 69, 43.9% for ages between 70 and 79, and 56.7% for over 80 years of age.
Limiting the analysis to the time window from 1 March to 30 April, the excess amounted to 122.4% globally, 85.2% in the population between the ages of 60 and 69, 114.0% in people aged 70 to 79, and 139.2% for those over 80 years of age.
Expected values calculated using the Poisson model provided values similar to those calculated as daily mean of deaths in the first four months of the four preceding years. The procedures for the model selection for the calculation of mortality excess are presented in table S2. Overall, the esti-

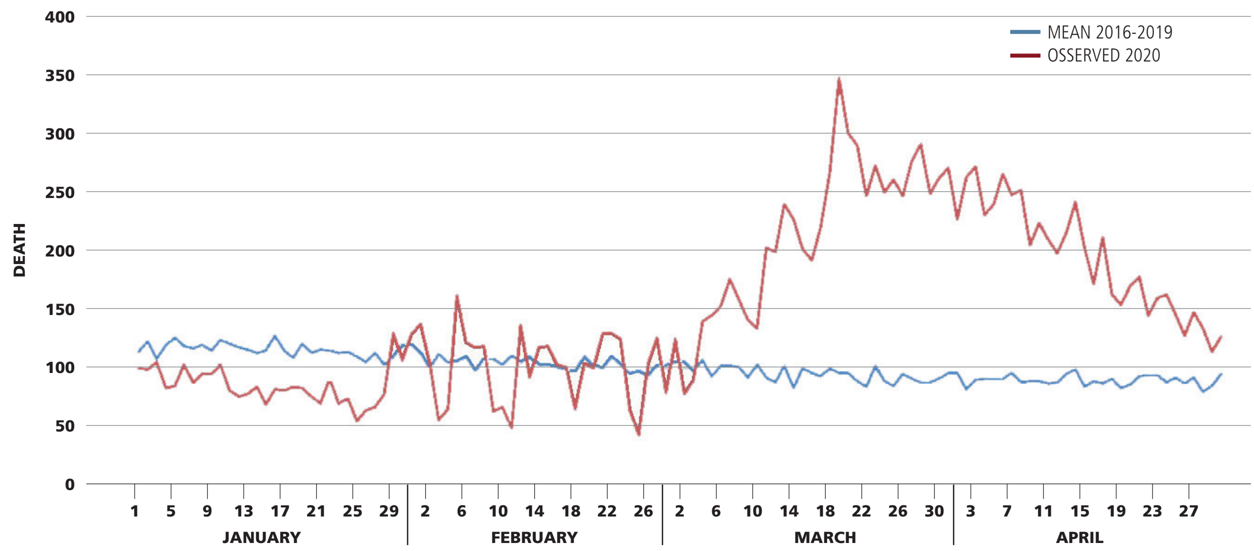

Figure 1. Comparison of daily death trends from 1 January to 30 April, 2020 vs average of 2016-2019.
Figura 1. Confronto dell'andamento dei decessi giornalieri dal 1 gennaio al 30 aprile, 2020 vs media 2016-2019.

ATS	TOTAL	<50 YEARS	50-59 YEARS	60-69 YEARS	70-79 YEARS	≥80 YEARS
1 JANUARY - 30 APRIL						
Deaths 2020	17,959	298	620	1,362	3,581	12,098
Mean 2016-2019	12,068	312.5	505.5	1,041	2,488.5	7,720.5
Difference	5,891	-14.5	114.5	321	1,092.5	4,377.5
Δ%	48.82	-4.60	22.65	30.84	43.90	56.70
Expected*	12,068.0	312.5	505.5	1,041.0	2,488.5	7,720.5
Excess** (95%CI)	5,891.0 (5,673-6,107)	-14.5 (-49-20)	114.5 (69-158)	321.0 (258-385)	1,092.5 (992-1,191)	4,377.5 (4,207-4,550)
RR (95%CI)	1.49 (1.34-1.64)	0.95 (0.85-1.07)	1.23 (1.09-1.38)	1.31 (1.18-1.44)	1.44 (1.29-1.61)	1.57 (1.41-1.74)
1 MARCH - 30 APRIL						
Deaths 2020	12,470	169	400	927	2,546	8,428
Mean 2016-2019	5,606.5	150.25	242.75	500.5	1,189.5	3,523.5
Difference	6,863.5	18.75	157.25	426.5	1,356.5	4,904.5
Δ%	122.42	12.47	64.78	85.21	114.04	139.19
Expected*	5,606.5	150.25	242.75	505.5	1,189.5	3,523.5
Excess** (95%CI)	6,863.5 (6,717-7,008)	18.75 (-5-43)	157.25 (126-188)	426.5 (382-469)	1,356.5 (1,289-1,423)	4,904.5 (4,787-5,019)
RR (95%CI)	2.22 (2.06-2.40)	1.13 (0.96-1.30)	1.65 (1.44-1.88)	1.85 (1.70-2.02)	2.14 (1.94-2.35)	2.39 (2.21-2.58)

ATS: Health Protection Agency / *Agenzia di tutela della salute*; **Δ%:** percentage variation / *variazione percentuale*; **RR:** relative risk / *rischio relativo*;
95%CI: 95% confidence interval / *intervallo di confidenza al 95%*
*predicted by the Poisson model / *previsti dal modello di Poisson*; ** observed-expected / *osservati-attesi*

Table 1. Distribution of deaths (2020 vs 2016-2019).
Tabella 1. Distribuzione dei decessi (2020 vs 2016-2019).

mate of the number of excess deaths derived from the model amounted to 5,891 deaths (5,673-6,107), with a percentage variation of +48.8% and a 1.49 RR (1.34-1.64).
The estimate of excess deaths for people between 60 and 69 years of age was 321 deaths (258-385), with a 1.31 RR (1.18-1.44); for ages 70-79 it was 1,093 (992-1,191), with a 1.44 RR (1.29-1.61); for ages over 80 it was 4,378 (4,207-4,550) with a 1.57 RR (1.41-1.74). Figures 2 and S2 show the daily excess trends. It must be pointed out that the reduction in mortality in the month of January was ascribable particularly to the older age classes.
The analysis was also replicated by ASST. Tables 2 and 3 show the descriptive analyses of observed and mean deaths (2016-2019), and excess estimates (observed-expected). Figures S3 and S4 show the smoothed daily trends of deaths and excess deaths. The charts show a dip in the month of January, due to the lower mortality in 2020.

Apart from this common feature, it is interesting to notice how the Lodi and Melegnano Martesana ASSTs present an anticipation in deaths compared to the other ASSTs, and compared to the ATS as a whole, showing how mortality peaked there around 15 March, while the peak for the other ASSTs was in the first week of April. A similar image emerges from the excess trends, allowing to quantify the number of extra deaths, which on some days was of over 30 cases in the Lodi ASST.

ESTIMATING EXCESS DEATHS THAT CAN BE ATTRIBUTED TO THE EPIDEMIC

After this preliminary analysis, the main question was whether the observed excess mortality was partly or entirely due to the COVID epidemic. Analysing the daily mortality among positive cases and summing the latter to the mean daily mortality (2016-2019), it was possible to graphically evaluate the overall daily mortality in the first four months of 2020 (figure 3).

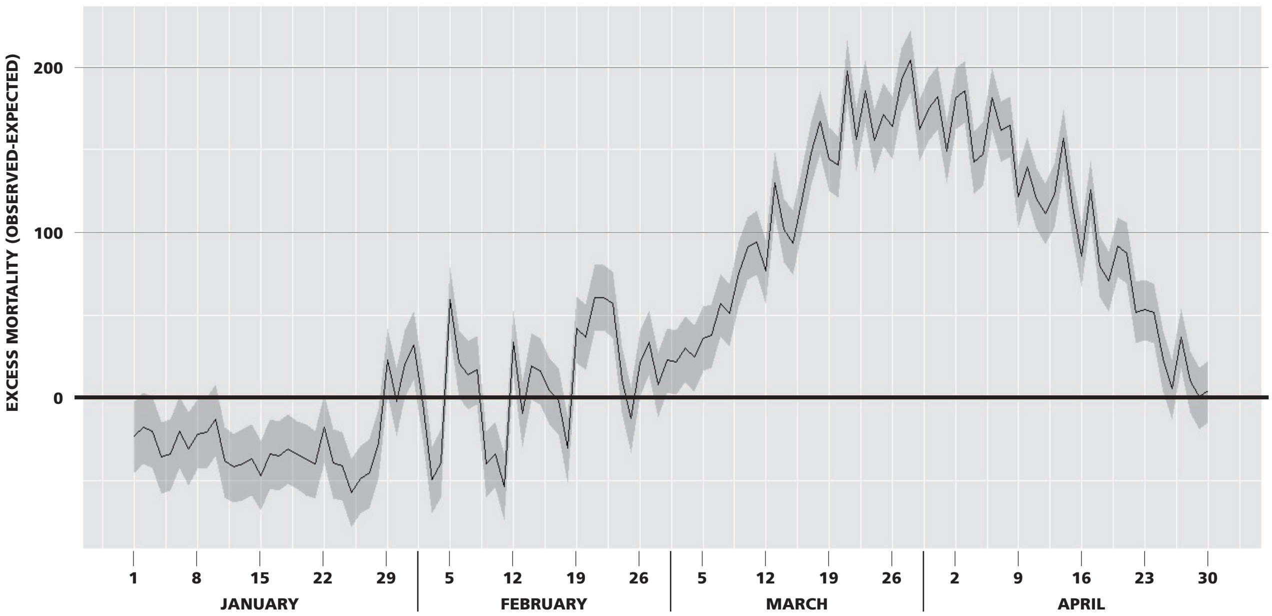

Figure 2. Time series of excess mortality (observed-expected).
Figura 2. Serie storica degli eccessi di mortalità (osservati-attesi).

ASST	DEATHS 2020	MEAN 2016-2019	DIFFERENCE	Δ%
Lodi	1,754	871	883	101
Melegnano	3,061	1,901	1,160	61
Nord Milano	1,450	924	526	57
Ovest Milanese	2,163	1,622	541	33
Rhodense	2,181	1,556	625	40
Milano	7,350	5,195	2,155	41

ASST: Local Healthcare Unit / *Azienda sociosanitaria territoriale*; **Δ%**: percentage variation / *variazione percentuale*

Table 2. Distribution of deaths, by ASST (2020 vs. 2016-2019). Period: 1 January-30 April.
Tabella 2. Distribuzione dei decessi, per ASST (2020 vs 2016-2019). Periodo: 1 gennaio-30 aprile.

ASST	OBSERVED	EXPECTED*	EXCESS** (95%CI)	RR (95%CI)
Lodi	1,754	871	883 (826-941)	2.02 (1.72-2.35)
Melegnano	3,061	1,901	1,160 (1,074-1,246)	1.61 (1.45-1.78)
Nord Milano	1,450	924	526 (466-584)	1.57 (1.42-1.72)
Ovest Milanese	2,163	1,622	541 (462-623)	1.33 (1.22-1.46)
Rhodense	2,181	1,556	625 (549-703)	1.40 (1.27-1.54)
Milano	7,350	5,195	2,155 (2,011-2,297)	1.41 (1.24-1.61)
ATS Milano	17,959	12,069	5,891 (5,673-6,105)	1.49 (1.34-1.64)

ATS: Health Protection Agency / *agenzia di tutela della salute*; **ASST:** Local Healthcare Unit / *Azienda sociosanitaria territoriale*; **RR:** relative risk / *rischio relativo*; **95%CI:** 95% confidence interval / *intervallo di confidenza al 95%*
* predicted by the Poisson model / *previsti dal modello di Poisson* ** observed-expected / *osservati-attesi*

Table 3. Distribution of mortality excess, by ASST. Period: 1 January-30 April 2020.
Tabella 3. Distribuzione degli eccessi di mortalità, per ASST. Periodo 1 gennaio-30 aprile 2020.

Analysing mortality from 22 February to 30 April in the general population and in COVID positive cases, an overall difference of 3,598 deaths is observed, of which 2,770 in subjects 80 years or older and 444 deaths in subjects between 70 and 79 years of age: we can therefore suppose that in these two age groups there may exist a fraction of deaths with no lab-confirmed COVID diagnosis. Furthermore, for age classes under 70 years of age, the difference is 384, suggesting that most of the excess in this age class can be explained by events linked to the epidemic (figure S5).

GEOGRAPHICAL ANALYSIS OF THE MORTALITY

Assessment of excess mortality was also carried out using descriptive geographical representations, showing the extent of observed excess for each of the 193 municipalities that make up the ATS, in terms of percentage differences, both in the general population and by age class. Figures 4 and S6 show the maps for the entire period analysed, from 1 January to 30 April. As can be observed, many municipalities show very high values, especially in the provinces of Lodi and among the towns in the North East of the

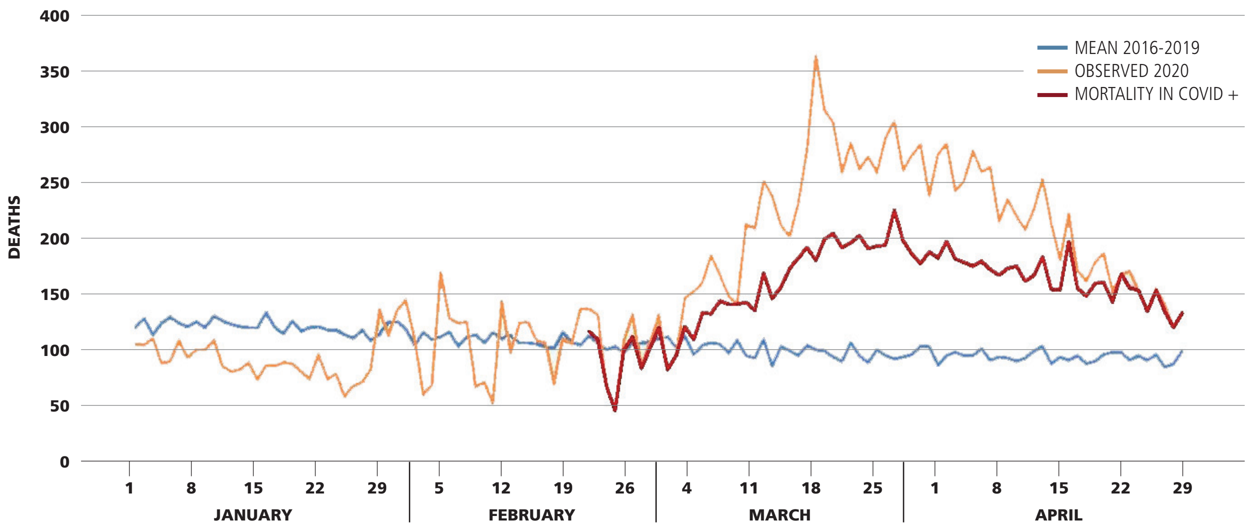

Figure 3. Comparisons of daily death trends from 1 January to 30 April for the general population: observed 2020 vs expected 2016-2019 vs COVID-19.
Figura 3. Confronti dei decessi giornalieri nel periodo dal 1 gennaio al 30 aprile nella popolazione generale: osservati 2020 vs attesi 2016-2019 vs COVID-19

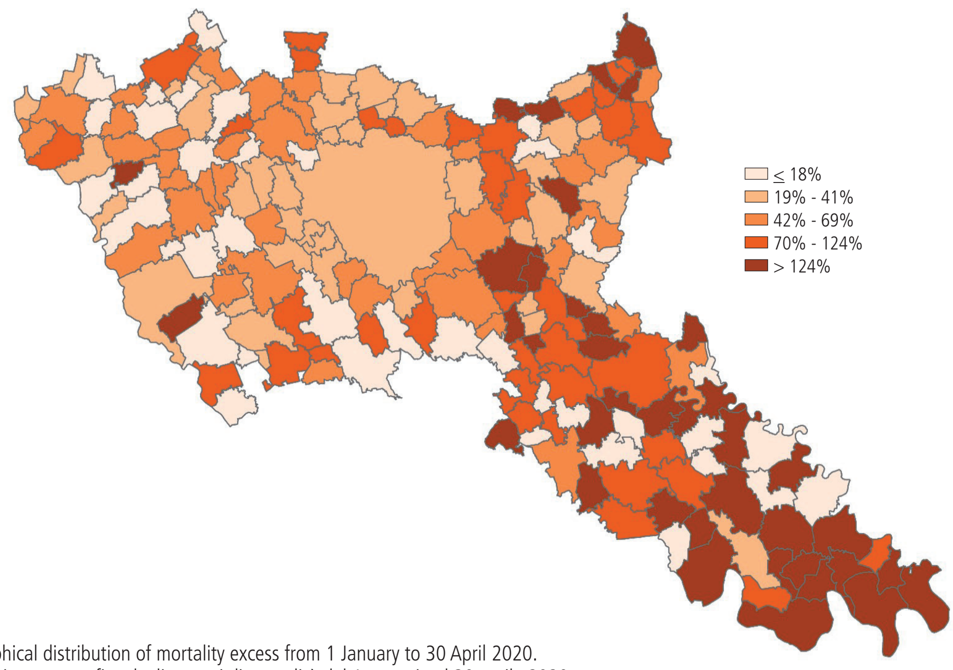

Figure 4. Geographical distribution of mortality excess from 1 January to 30 April 2020.
Figura 4. Distribuzione geografica degli eccessi di mortalità dal 1 gennaio al 30 aprile 2020.

province of Milan. Geographical analysis stratified by age (figure S6) shows how the highest excess mortality can be attributed to the higher age classes.

DISCUSSION

This work, based on the development of rapid systems for the study of overall mortality in a population of 3.5 million people, showed an increase in mortality of 48.8% for the period from 1 January to 30 April and of over 120% from 1 March to 30 April.

The data made available during the epidemic showed COVID case fatality ratios varying significantly across European states. The European Centre for Disease Prevention and Control (ECDC),[16] in a report published on 12 June 2020, listed Belgium as having the highest case fatality ratio, with 84.5 deaths per 100,000 people, followed by the United Kingdom with 62 per 100,000 people. In third and fourth place were Spain and Italy with 58.0 and 56.5 per 100,000, respectively. The differences recorded between countries are mainly due to the fact that no uniform rules concerning the diagnosis of Covid-19 and the attribution of the cause of death during the "first wave" of the pandemic were adopted internationally, nor even between Italian regions.[17-19] As to the way swab testing was performed, the guidelines of the Italian Ministry of Health changed during the epidemic.[17] Furthermore, the gradual increase in testing capacity brought the Italian mean of daily tests performed per 1,000 people (7-day moving average) from 0.04 on 2 March to 1 on 12 May.[120]

As for international comparisons, we have to be aware that a number of countries report the number of people tested, while others, including Italy, report the number of tests, which also includes for each subject tests carried out after the first diagnostic test. These considerations influence the denominator of the COVID-19 fatality ratio. As to the numerator, it is influenced by the definition of death from COVID-19. In agreement with the WHO definition, for surveillance purposes[21] a number of countries also included deaths in subjects with symptoms compatible with COVID-19 with no microbiological confirmation. Many countries, including Italy, report all deaths in subjects who tested positive as COVID-19 deaths, while others have more restrictive definitions and do not consider cases of patients already in medically compromised conditions.

More detailed analyses of the deaths, which should be reported along with any pre-existing medical conditions, would allow for more in-depth evaluation of the causal link between SARS-COV-2 infection and death, and would make cross-country comparisons more meaningful.[22] For instance, The ISTAT/ISS report on the impact of the COVID-19 epidemic,[8] which analysed about 5,000 death certificates of microbiologically positive subjects, concluded that COVID-19 infection was directly responsible for death in about 89% of cases – with as high as 10% differences in the various age classes – and that 72% of deaths had at least one concurrent cause. A further consideration to take into account is that in regions suffering greater health stress it is plausible to expect that part of the deaths are not classified as pertaining to SARS-COV-2 positive subjects due to the scarce resources available to carry out post-mortem testing, especially at the beginning of the epidemic, when diagnostic capacity was limited. The above considerations on the difficulties in calculating and comparing case fatality ratios are the reason for the choice made in this work of measuring the overall mortality data and their trends during the epidemic phase and compare them with the overall mortality of previous years, for the same calendar period. This approach has the advantage of making evaluations carried out for different areas and at different epidemic stages comparable. The assessed variations provide a reliable indicator of the direct and indirect effects of the pandemic in the population, even in the presence of severe healthcare system stress. Our analysis shows that deaths that are not associated with a confirmed COVID-19 infection are concentrated in the over 70 (and particularly over 80) population, while excess deaths in subjects under 70 years of age were substantially due to the epidemic, i.e., infected subjects who underwent testing. In this respect, however, it should be pointed out that a fraction of COVID -19 mortality in the younger age classes could have replaced mortality due to other causes, such as deaths from trauma or workplace accidents, which likely decreased as a consequence of the lockdown. In any case, further evaluations will be needed with regards to the unexplained deaths. For the time being, we can only suppose that part of the unexplained deaths may be attributed to infected subjects who were not tested due to the rapidly lethal course of the disease, including deaths in nursing homes in the early stages of the epidemic. However, a second group of these deaths is likely tied to the failed capacity of the healthcare system to deal with non-COVID health emergencies during the epidemic and lockdown. The general population paid a very high price and mortality that can be attributed to swab-confirmed COVID cases does not completely explain the observed excess mortality.

A further reflection needs to be made on the seasonal distribution of the death risk trend, in particular in elderly frail subjects, who have a greater risk in the presence of stress, be it extreme weather or a pandemic. The study showed that in the month of January 2020, fewer deaths than expected were recorded, especially in the population over 70 years of age. The causes are yet to be determined, but the mild temperatures and the lower pathogenicity of the seasonal flu epidemic might justify part of the observed reduction. This would explain the significant and rapid excess in mortality recorded in the over 70 population in the months of March and April, relative to a reservoir of deaths that had not occurred up to that moment, but which in the presence of very strong external pressure were concentrated in a few weeks. It is possible, moreover, to suppose that the elderly population who survived the first wave of the epidemic has better resistance, which will cause a decrease in their risk of death after the epidemic, in a harvesting effect.[22]

Despite the solid information sources and methods used, it is possible there are still potential unreported deaths, considering the complexity of the information system, as well as deaths in ATS residents that occurred outside the region. This possibility cannot be ruled out, in consideration of the migrations which preceded the lockdown, but its scope should be limited by the fact that half of COVID deaths in Italy were recorded in Lombardy.

Nevertheless, the study made it possible to highlight a significant excess mortality during the March-April Covid-19 epidemic in Lombardy and to carry out a series of quantitative assessments. It also uncovered the need to explore the causes of death in subjects without a COVID-19 diagnosis, and identify mortality predictors in the population under 70, in order to reduce the impact of future epidemic waves.

CONCLUSIONS

Evaluation of overall mortality in the provinces of Milan and Lodi – the area covered by the Milan ATS – during the epidemic phase of COVID-19, showed a 48.8% excess compared to the first four months of the years 2016-2019 and more than 120% compared to the months of March and April, mainly involving the over 60 population. Excess deaths which occurred in the under 70 population would seem to be attributable to the COVID-19 epidemic. This phenomenon was clearly visible in all ATS areas, and in particular in the Lodi ASST, where on some days over 5 times more deaths than expected were recorded.

Finally, the current level of analysis could be raised by developing and using:

1. models that make it possible to define the characteristics of the population that died both in the case set and in deaths that were not tested for COVID;

2. cause-specific mortality, which ATS Milano is implementing by going all out to code the over 18,000 recorded deaths, a task which will be completed in October.

Availability of mortality by cause will make more in-depth comparisons of cause-specific excess mortality possible, which, since to date deaths from trauma and workplace accidents – for which a significant decrease is expected due to the national lockdown – are not even considered, will allow us to pinpoint the causes most affected by the excess mortality. As always, mortality evaluation will enable the development of public health policies to be applied in extreme events such as pandemics.

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