

Report on the new coronavirus Covid-19 pandemic in Italy

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Research

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Abstract

Background Sars-CoV-2 is a coronavirus associated with human severe acute respiratory disease named Covid-19, first reported in China on December 2019. World Health Organization declared Covid-19 a pandemic on March 20, 2020. This report aims to outline the Italian outbreak characteristics. Italy, as one of first most affected area outside Asian continent, could give experiences to the other countries.

Methods Data on positive cases and Covid-19 patients made available by Italian Health Authorities were reanalyzed and described.

Results Up to April 18, 2020 Italy recorded 175,925 Sars-CoV-2 positive cases (10.68% among health care professionals) and 23,227 Covid-19 deaths. Covid-19 patients median age was 62 years. Male/female ratio was 1.00. Median time between symptoms and diagnosis was 6 days. Between hospitalized patients, the 10% needed intensive care. Median age at death was 80 years, with differences between sexes. Apparent lethality rate was 13.2%. At least one concomitant medical condition was present in 96.4% of patients who died.

Discussion The number of Italian positive cases could be higher and the Italian lethality rate could be lower. The presence of asymptomatic people, known to be a vehicle for Covid-19 also for serious cases, could made slower the decrease of infection and distance the end of the novel coronavirus epidemic.

Background

Sars-CoV-2 is a coronavirus associated with human severe acute respiratory disease named Covid-19, first reported in Wuhan, Hubei province in China on December 12, 2019¹. Up to January 20, 2020, 282 confirmed cases of Covid-19 were reported from four countries including China (278 cases), Thailand (2 cases), Japan (1 case) and the Republic of Korea (1 case)². Up to January 23, 2020, 581 cases were reported in Thailand, Japan, Hong Kong Special Administrative Region, Taipei Municipality, China, Macau Special Administrative Region, United States of America and the Republic of Korea. All these Covid-19 patients had travel history to Wuhan². Up to January 27, 2020 globally 2,798 confirmed cases were reported for novel coronavirus and for the first time Covid-19 cases were reported also in the European region (France first and then in Germany)². On January 31, 2020 when globally 9,826 cases of Covid-19 acute respiratory disease were confirmed, the first two cases were reported in Italy; both had travel history to Wuhan City². The first Italian Covid-19 case due by local transmission, was reported on February 21, 2020, in Codogno, a city belonging to the province of Lodi, at the boundaries between the province of Lodi and the province of Cremona, in the region of Lombardia, in the North of Italy. In no time the number of Covid-19 cases increased considerably and Italy was soon the first most suffering country outside the Asian continent. Covid-19 cases started to be reported also by other countries worldwide. The World Health Organization (WHO) on March 11, 2020 declared Covid-19 a pandemic, pointing to the over 118,000 cases of the coronavirus illness in over 110 countries and territories around the world and the sustained risk of further global spread². As of March 11, South-East Asia, Europe, America, West Pacific, East Mediterranean, and African regions were affected by the spread of Covid-19 epidemic, for a total of 167 countries worldwide². Up to March 17, 2020 more than two million (2,074,529) Sars-CoV-2 cases and 139,378 Covid-19 deaths were globally reported². Worldwide level WHO risk assessment was classified as very high². This report aims to pointed out data and patients characteristics from Italian epidemic. Italy, as one of the first most affected regions could give experiences to other countries.

Methods

Data source. Italian data about Covid-19 were made available by Italian Health Authorities "Protezione Civile" and "Istituto Superiore di Sanità". In detail, "Protezione Civile" daily updated and made available online the number of tests made to evaluate the presence of Sars-CoV-2 infection, the number of Covid-19 positive cases, the numbers of hospitalized, intensive care and homecare Covid-19 patients and the number of Covid-19 deaths by region and overall in Italy³. Daily updated number of positive cases by provinces was made available as well³. "Istituto Superiore di Sanità" weekly updated and published online cases and deaths distribution by age and by sex, disease incubation time and descriptive statistics about patients who died (symptoms, comorbidities, treatment, hospitalization time and complications)⁴. **Data analysis** Cumulative data obtained from previously listed references were reanalyzed and described in this report. Lethality was calculated as the ratio between deaths and positive cases and cumulative incidence as the ratio between positive new cases and Italian inhabitants, according to last census⁵. For the observation time, crude and age standardized incidence rates were calculated as well^{5,6}. STATA 15 (Texas, USA) was used as statistical analysis software.

Results

Italian Covid-19 cases

Overall the number of Italian Sars-CoV-2 positive cases was increasing but the exponential phase, that mark out the first epidemic phase of a virus infection, seemed definitively distance from data. The grow factor, based on number of cases and not on virus reproduction number, was lower than 1 since March 20, 2020. Figure 1 shows the daily increase of new positive Covid-19 cases in Italy. Considering the daily increase, we should consider both the test's execution time and the number of swabs daily made. The number of Sars-CoV-2's RNA evaluation tests changed in time and increased from 2.07/1000 Italian inhabitants on March 15 (18.14% positive) to 8.40/1000 on March 31 (13.70% positive) and it was 18.51/1000 on April 15, 2020 (6.10% positive)^{3,5}. It should be considered that available tests' number was swabs' number. Taking into consideration confirmation's and repeat's tests, it should be reasonable a number of people who were tested that was about the 70% of the swabs' number.

Up to April 18, 2020 according to official data, Italy recorded 175,925 Sars-CoV-2 positive cases, 10.68% among health care professionals^{3,4}. The age and sex distribution of cases is reported in Table 1, incidence is reported as well. Median age was 62 years (0-100 range)⁴ and overall male/female ratio was 1.00. The different behavior in more aged people was probably due to the higher number of women aged more than 90s (male female ratio equal to 0.37, according to last census⁵). Between health care professional Covid-19 patients, median age at diagnosis was 48 years and male/female ratio was 0.47⁴.

From available literature the estimated mean incubation time of Covid-19 was 5.5 days and symptoms occurred by 11.5 days in the 97.5% of infected people⁷. Italy reported a median time between symptoms and diagnosis equal to 3 days for cases recorded on February 20-29 (1,614 cases analyzed), 5 days for cases recorded on March 1-10 (9,732 analyzed), 6 days for cases recorded on March 11-20 (27,679 analyzed) and 7 days for cases recorded between March 21 and April 9 (46,236 analyzed)⁴.

Overall 25.74% of positive cases were hospitalized³. During hospitalization patients were treated by antibiotics (84%), antivirals (56%) and corticosteroids (35%)⁴. The 19.6% of patients was concomitant treated with all of these medications⁴. On April 18, 2020 the 9.85% of all Covid-19 hospitalized patients received intensive care³. Detail on hospitalization status and number of patients who needed intensive care is reported in Figure 2.

Italian Covid-19 deaths

Up to April 18, 2020 according to official data, Italy recorded overall 23,227 Covid-19 deaths³. Considering the daily deaths increase, reported in Figure 2, we should also considered the disease progression time.

The age and sex distribution of patients who died is reported in Table 1⁴, lethality rate is reported as well. On April 18, 2020 Italian lethality rate was equal to 13.2%, 0.4% among health care professionals^{3,4}. Overall lethality increased with age, especially in male patients. Median age at death was 80 years (range 0-100; IQR 73-86), with differences between sexes (83 for women and 79 for men)⁴.

According to data on comorbidities, available for 1,738 patients, at least one concomitant medical condition (mean 3.3, sd 1.9) was present in 96.4% of patients who died⁴. In detail, the 3.6% had no one concomitant pathologies, 14.4% one, 20.7% two and the 61.3% had three or more concomitant pathologies⁴. Most representative comorbidities were hypertension (69.7%), type 2 diabetes (32.0%), ischemic heart disease (27.7%), chronic renal failure (22.0%), atrial fibrillation (21.9%), chronic obstructive pulmonary disease (17.8%), history of cancer in the past 5 years (16.2%) and heart failure (15.5%)⁴.

Between who died, most common symptoms before hospitalization were fever (76.0%), dyspnea (72.0%), cough (38.0%) diarrhea (6.0%) and hemoptysis (1.0%)⁴. The 5.9% of patients did not experienced any symptom at hospital admission⁴. Median time between presence of symptoms and death was 10 days; between hospitalization and death 5 days, and was 4 days longer if patient was moved to intensive care unit⁴.

Most common complications that finally lead to patient's death were acute respiratory distress syndrome (96.7%), acute kidney injury (22.9%), superinfection (12.4%) and acute myocardial injury (9.5%)⁴.

Figure 1. Positive Covid-19 cases, daily increase since February 24, 2020 (up to April 18, 2020)³; as absolute number (N, continuous blue line, in dotted blue line its 6 days moving average) and as percentage (% , brown line). As reported by Italian Authorities in their newsletter, data were daily updated and we should considered a possible delay in data communication by regions due to a such high number of tests performed a day⁴. We should also considered the execution time of test needed to evaluate the presence of virus's RNA.

Age	Male Patients			Female Patients			Cases, M/F	Overall					
	Positive (N)	Death (N)	Lethality (%)	Positive (N)	Death (N)	Lethality (%)		Positive (N)	Cum Inc (%)	Crude Inc Rate	Age Std Inc Rate	Death (N)	Lethality (%)
0-9	596	0	0.00	519	1	0.19	1.15	1,123	0.02	12.03	1.26	1	0.09
10-19	901	0	0.00	897	0	0.00	1.00	1,804	0.03	17.06	1.88	0	0.00
20-29	3,350	5	0.15	4,338	2	0.05	0.77	7,737	0.12	68.05	8.17	7	0.09
30-39	5,344	28	0.52	6,299	12	0.19	0.85	11,686	0.17	90.10	12.16	40	0.34
40-49	9,009	133	1.48	11,452	45	0.39	0.79	20,519	0.22	121.09	16.95	178	0.87
50-59	14,779	606	4.10	15,015	150	1.00	0.98	29,858	0.32	174.14	23.51	756	2.53
60-69	14,963	1,776	11.87	9,024	504	5.59	1.66	24,040	0.33	178.72	20.55	2,284	9.50
70-79	15,577	4,532	29.09	10,097	1,664	16.48	1.54	25,717	0.43	235.26	21.17	6,203	24.12
80-89	12,332	4,992	40.48	14,329	3,071	21.43	0.86	26,706	0.75	409.70	16.39	8,070	30.22
>=90	2,470	970	39.27	7,333	1,483	20.22	0.34	9,813	1.27	691.07	6.91	2,455	25.02
Unk	49	2		54	0			104				2	
Total	79,370	13,044	16.43	79,357	6,932	8.74	1.00	159,107	0.26	143.78	128.96	19,996	12.57

Table 1. Positive cases diagnosed and number of deaths recorded overall, by age and by sex since February 21, 2020 (up to April 16, 2020); information about sex was missing in 380 cases⁴. Number of Italian inhabitants available at last census⁵ was used to calculate cumulative incidence and crude rate. Eurostat 2013 standard population⁶ was used to calculate age standardized rate. Legend: “Unk” is for unknown, “Cum Inc” is for cumulative incidence, “Crude Inc Rate” is for crude incidence rate; “Age Std Inc Rate” is for age standardized incidence rate. Both incidence rates are monthly incidence rate for the observation time period, x100,000); “M” was for male, “F” female.

Figure 2. Distribution of Covid-19 Italian cases by hospitalization status and exitus since February 24, 2020 (up to April 18, 2020)³. Homecare Covid-19 patients, recovered cases or cases still positive that were dismissed from hospital are not included in this graph. As reported by Italian Authorities in their newsletter the number of deaths were deaths occurred in patients who tested positive for Sars-CoV-2's RNA, independently from pre-existing diseases⁴.

Focus on Lombardia, the region where the Italian Covid-19 outbreak began

Italy is organized in 19 regions and 2 autonomous provinces and the most affected Italian area was the region of Lombardia, in the North of Italy. Up to April 18, 2020 Lombardia recorded 65,381 Covid-19 cases (37.2% of all cases), and 12,050 related deaths (51.9% of all deaths)³. In this area the districts of Cremona, Lodi, Bergamo, Brescia and Milano were the most affected cities and according to last official data, their cumulative incidence values were equal to 1.51%, 1.18%, 0.95%, 0.93% and 0.48% respectively^{3,5}.

Codogno and the around area, for a total of 10 municipalities in the province of Lodi, at the boundary of the province of Cremona (Codogno, Castiglione d'Adda, Casalpusterlengo, Fombio, Maleo, Somaglia, Bertonico, Terranova dei Passerini, Castelgerundo and San Fiorano), were quarantined and defined "red zone" since February 23, 2020⁸. Up to March 5, 2020 this area reached 5,830 laboratory-confirmed Sars-CoV-2 cases³. As reported, the quarantine strategy pointed out a valid approach to slowdown the spread of the infection and no positive new cases were recorded on March 10, 2020 in Codogno, where the 99.94% of inhabitants followed the restriction policies⁹.

Due to the increase of cases outside this area, Lombardia and all Italy, was quarantined from March 8, 2020 and a strengthening of restriction policies was made on March 20, 2020⁸. Increase of cases across the most affected cities in Lombardia is reported in Figure 3; Italy compared to Lombardia is reported as well (Figure 4). The effects of restriction policies should be considered also disease incubation time.

Figure 3. Cumulative Sars-CoV-2 cases, by day across the most affected cities in Lombardia since February 24, 2020 (up to April 18, 2020)³. Milano (blue line), Bergamo (green line), Brescia (yellow line), Cremona (red line) and Lodi (purple line). Number of inhabitants (number of municipalities) are reported as well⁵.

Figure 4. Cumulative Sars-CoV-2 cases, by day in Lombardia and overall in Italy since February 24, 2020 (up to April 18, 2020)³. Positive Sars-CoV-2 cases (dark lines) and hospitalized Covid-19 patients (light lines) in Italy (without cases recorded in Lombardia, blue lines) and in Lombardia (red lines) on a semilogarithmic scale. Legend: "Positive cases" includes both hospitalized and homecare Covid-19 patients; "Hospitalized" includes patients admitted to all hospital wards.

Discussion

Sars-CoV-2 is a coronavirus associated with human severe acute respiratory disease named Covid-19, first reported in Wuhan, Hubei province in China on December 12, 2019¹. In Italy the first local Covid-19 case was identified on February 21, 2020 and one month later Italy was the most suffering country outside Asian continent. In the meantime, Covid-19 cases became to be reported also by other countries worldwide and the World Health Organization (WHO) declared Covid-19 a pandemic on March 11, 2020 pointing to the over 118,000 cases of the coronavirus illness in over 110 countries and territories around the world and the sustained risk of further global spread².

Due to symptomatology and prognosis of Covid-19 disease, the first Italian concern was the limited number of intensive care resources: 5,179¹⁰ beds were available on March 1, 2020. The Italian society of Intensive Care (SIAARTI, Società Italiana di Anestesia Analgesia Rianimazione e Terapia Intensiva) published on March 6, 2020 a list of ethical recommendation and guidelines in order to give criteria for access to intensive treatments, to follow if needs exceeded resources¹¹. Italy done more and more effort to ensure the right health care treatments to anyone who needed it. Many public and private fundraisers grown up to help and make faster the setting up of new intensive care unit and camp hospitals by voluntary workers. On March 31, 2020 Italy reached 9,122¹⁰ (+79.2%) intensive care beds, and more new hospitals were built to treat Covid-19 patients, in a fast race against time and virus. Second concern in the fighting with the Italian outbreak was the infection of health care professionals. Medical devices, medical doctors, nurses and healthcare operators, even retired professionals, arrived in Lombardia from other Italian areas, even from abroad arrived to help out with the coronavirus crisis. Italian private societies and Italian University departments worked together to reconvert their equipment to produce personal protective devices and ventilators according to standards for medical use.

From official data³, the apparent Covid-19 lethality rate seemed to be higher than in other most affected countries, as China for example. This was probably due to two main consideration: the high rate of old people in Italy and the Italian recommendations to evaluate a positive case. About first consideration, data could be analyzed using standardized rates, but a longer observation time and shared guidelines among countries should be needed to take advantage from a such type of epidemiological indicator in a scenario of virus infection. About second observation, according to the decree of February 25, 2020 (updated on April 3, 2020¹²) in Italy the presence of viral RNA was evaluated in very suspected Covid-19, symptomatic ILI (Influenza-Like Illness) and SARI (Severe Acute Respiratory Infections) cases¹³, not considering the asymptomatic cases. This observation was important for the estimation of the number of Sars-CoV-2 positive subjects and so for the lethality attributed to Covid-19 in Italy. The epidemiological study, unique in Italy, set up in Vo' Euganeo, the city that recorded the first Covid-19 case in Veneto (the most affected Italian region, after Lombardia and Emilia Romagna); showed the presence of asymptomatic people. All inhabitants of Vo' Euganeo at the beginning of Covid-19 epidemic, between February 29 and March 5,

2020, were test for the presence of Sars-CoV-2's RNA. Seventy/2,778 subjects were positive, 14/70 subjects were hospitalized and 1/14 died¹⁴. We would have seen for Vo' Euganeo, as positive people 14 symptomatic cases and considering the one death that occurred in Vo' Euganeo, the first Covid-19 death that occurred in Italy; as lethality rate 1/14 (7.1%) rather than the rate 1/70 (1.4%). It could be reasonable that the number of Italian positive cases could be higher and the Italian lethality rate could be lower. On the other hand, some deaths could been not considered, especially among old people who died at home or at elderly residences without the awareness of their Sars-CoV-2 status, as locally reported. Overall Italy counts 3,420 elderly residences (19.8% in Lombardia)¹⁵. On April 14, 1,082/3,420 elderly residences answered the survey conducted by Italian health authority "Istituto Superiore di Sanità"¹⁵. According to the survey's report, between February 1 and April 14, 6,773 deaths occurred (49.7% between March 16 and March 31, 45.0% in Lombardia): 364/6,773 were officially positive Covid-19 deaths and 2,360/6,773 were people who died because of flu like symptoms¹⁵. In the month of March (March 1-28, 2020) in Lombardia, Italian Health Authorities recorded 5,944 Covid-19 deaths³ (underestimation was possible considering a plausible delay in deaths recording) and Italian Institute of Statistics (ISTAT), recorded for the same region (Lombardia) and period (March 1-28, 2020) 16,250 (all causes) deaths against a mean of past March (2015-2019) equal to 5,698.2 (sd 195.3) that is for Cremona +372.5% compared to (all causes) deaths recorded on March in past years (2015-2019 mean), Lodi +371.7%, Bergamo +576.4%, Brescia +268.4% and Milano +88.3%¹⁶. Considering previous months since January 1, 2020 and according to ISTAT mortality data (all causes deaths) released on April 17, in Lombardia the weekly deaths increase was over than 20% same week in previous years (mean 2015-2019) since the 3rd week of February only in the province of Lodi (+23.0%)¹⁶. In the last week of February (all causes) deaths increase was higher than 20% in Lodi again (+117.1%), Bergamo (+30.6%) and Cremona (+22.1%)¹⁶. In last week of February there was an increase of (all causes) deaths also for other two provinces in Lombardia, Pavia (+38.8%), and Como (+38.1%)¹⁶. Overestimating deaths (hypothesis of deaths increase entirely due to Covid-19), and considering 2.3% as a more plausible value of lethality¹; in Lombardia the number of positive people could be higher than official data, reaching in the most affected cities a cumulative incidence value about 20%, even greater for a lesser lethality rate. We should however considered that available data are temporary data and available knowledge on Covid-19 is temporary knowledge. Globally, on April 18, 2020 Sars-CoV-2 is a relatively new coronavirus and Covid-19 is a relatively new disease. Data should be reanalyzed when new knowledge will be available, before delineate a strong hypothesis about more reasonable number of positives Sars-CoV-2 cases and Covid-19 deaths and evaluate differences between countries.

Conclusion

Since the Covid-19 outbreak began, Italy made many efforts: quarantine and national restrictive policies, new healthcare professionals hiring and fast building of new camp hospitals and intensive care units; in a fast race against time and virus. Even if slower, the increase of Covid-19 did not stop and restriction policies, that prevented both much further deaths and the spread of infection in Central and South Italy; could be not sufficient. Asymptomatic subjects, people without information about their positive status and without symptoms, could be themselves unaware vehicles for Covid-19, also for serious cases¹⁷. They could made slower the decrease of infection and distance the end of the novel coronavirus epidemic. Italy really never stopped and two months later the detection of the first local Covid-19 case, the Italian government was planning the economic recovery. Many new kits to make faster the evaluation of the presence of virus's RNA in the blood, or make possible the evaluation of immunoglobulins against Sars-CoV-2 or digital tools for contact tracing were or are under validation; and the efficiently organization of district medicine to plan a "Phase 2 of epidemic" that will have to be safe and clever to restart the economy without restart the epidemic. In the meantime new hopes arose from experimental trials with past and new drugs¹⁸, in a worldwide war against a such challenging submicroscopic nonliving molecule named Sars-CoV-2.

Abbreviations

Covid-19	CoronaVirus Disease 19
ILI	Influenza-Like Illness
IQR	InterQuartile Range
ISTAT	"Istituto Nazionale di Statistica"
N	Number
RNA	RiboNucleic Acid
SIAARTI	"Società Italiana di Anestesia Analgesia Rianimazione e Terapia Intensiva"
SARI	Severe Acute Respiratory Infections
Sars-CoV-2	Severe acute respiratory syndrome CoronaVirus 2
sd	Standard Deviation
WHO	World Health Organization

Declarations

Ethics approval and consent to participate

Not applicable

Availability of data and material

Data described in this report were published by Italian Health Authorities and they are full available following the references.

Competing interests

The author declare that she has no competing interests.

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Authors' contributions

BMD is the only author.

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Not applicable

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Figures

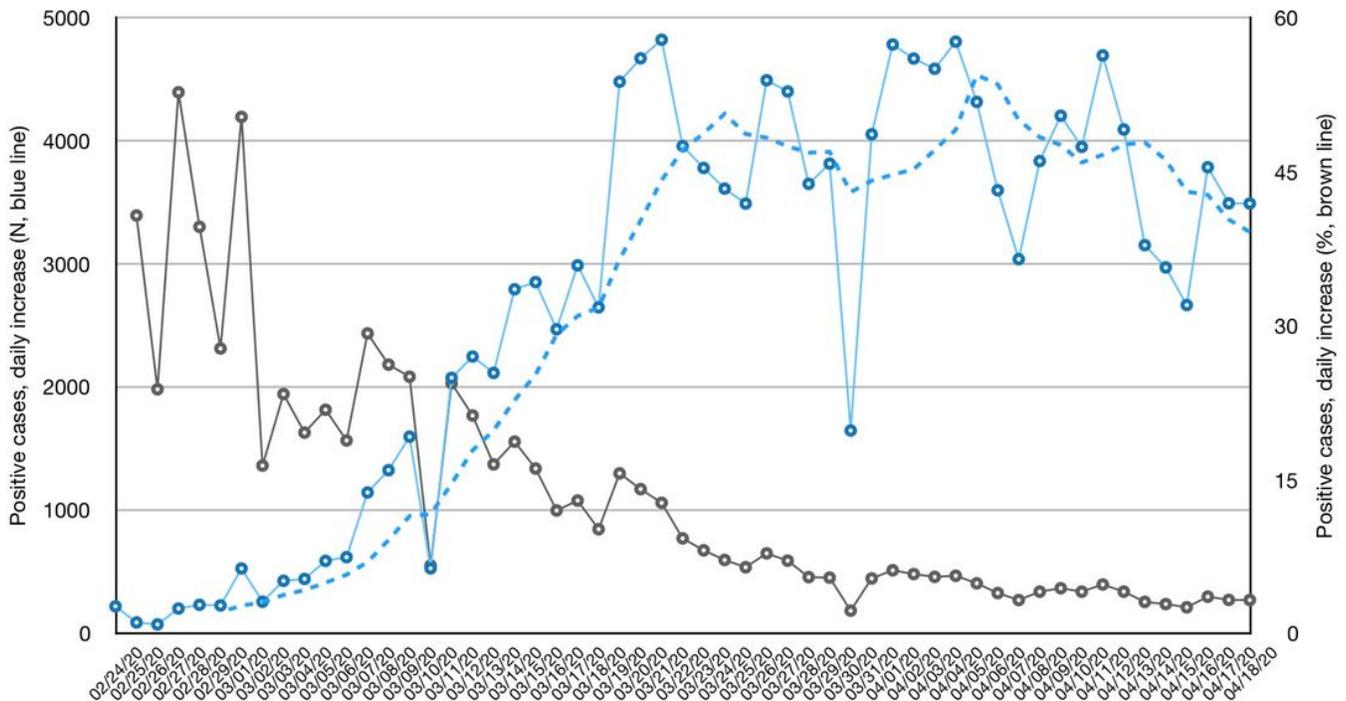


Figure 1
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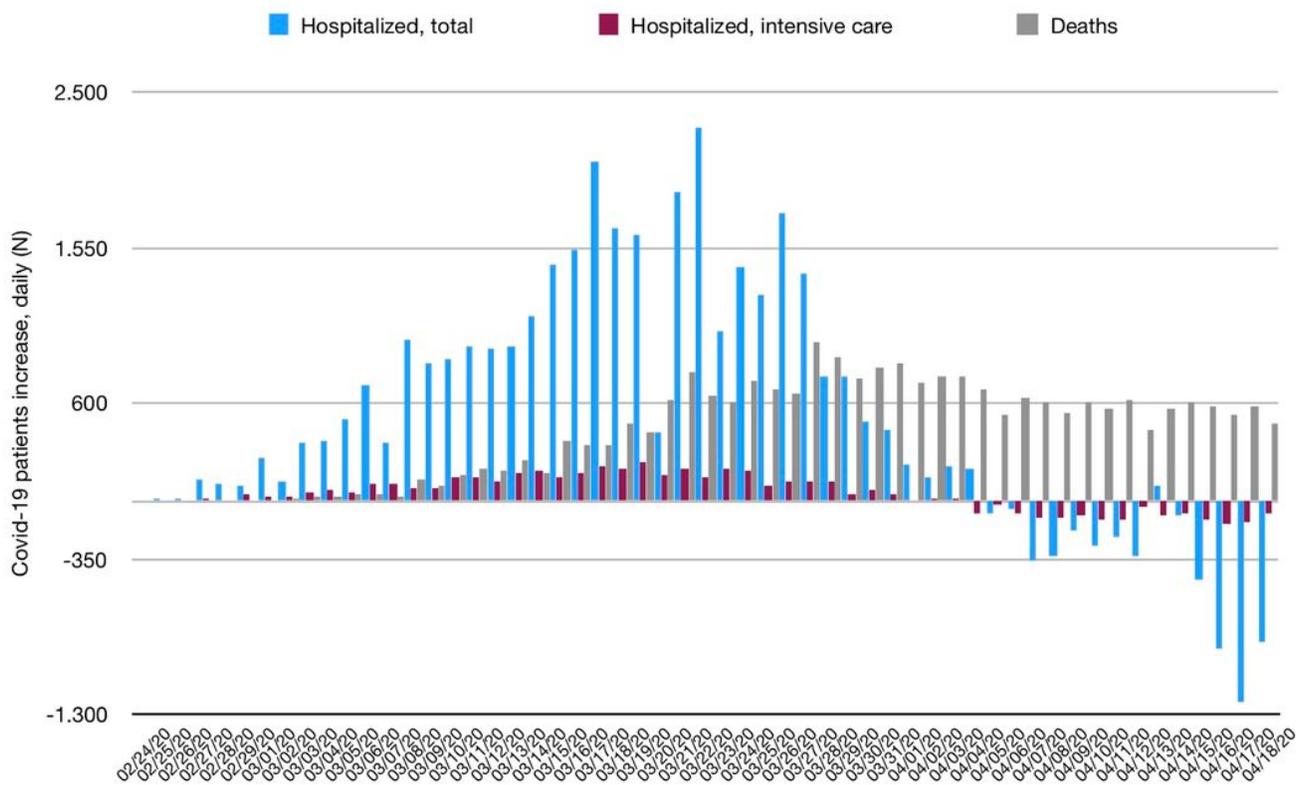


Figure 2

Distribution of Covid-19 Italian cases by hospitalization status and exitus since February 24, 2020 (up to April 18, 2020)³. Homecare Covid-19 patients, recovered cases or cases still positive that were dismissed from hospital are not included in this graph. As reported by Italian Authorities in their newsletter the number of deaths were deaths occurred in patients who tested positive for Sars-CoV-2's RNA, independently from pre-existing diseases⁴.

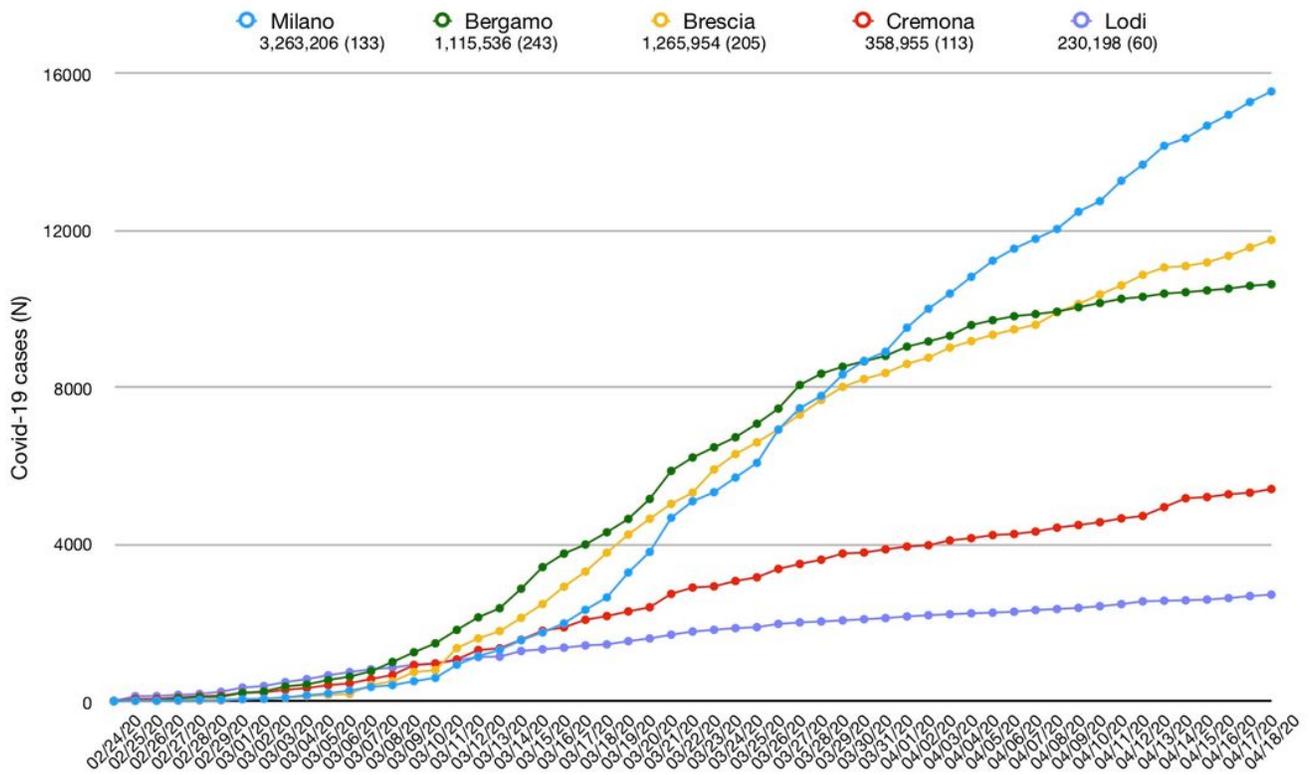


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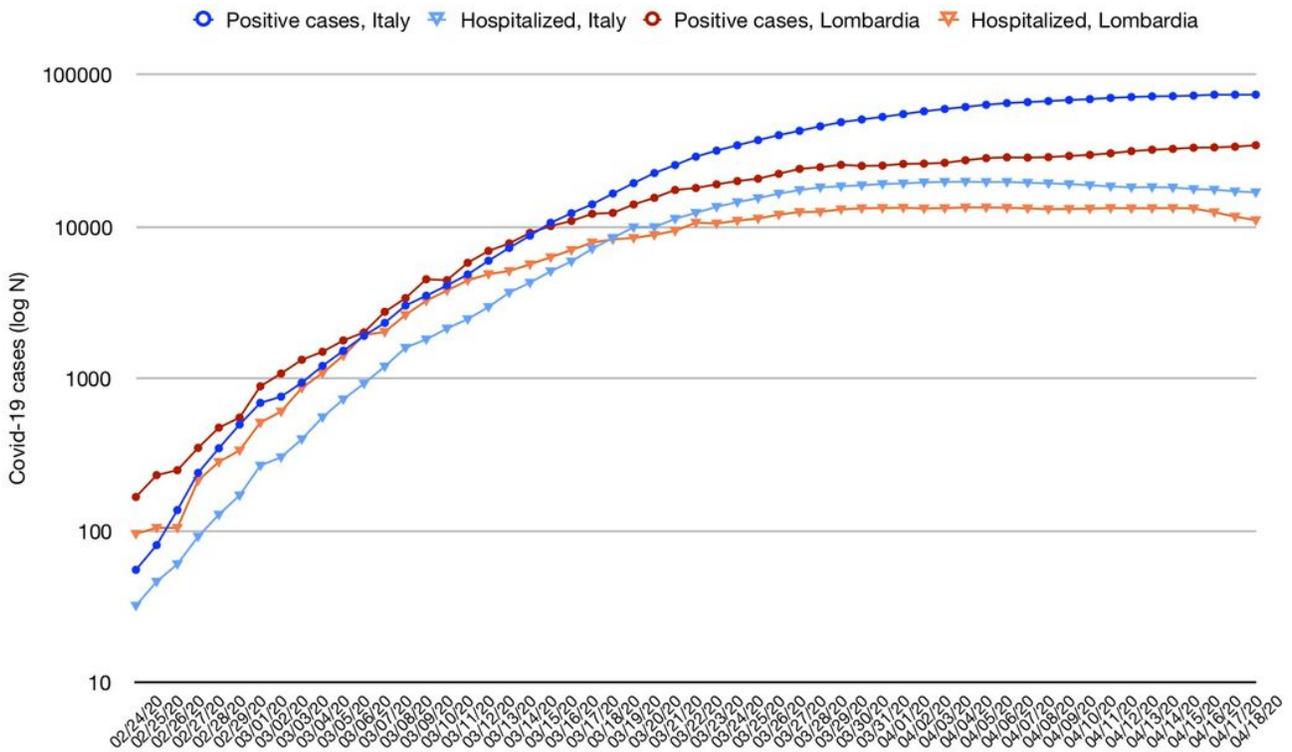


Figure 4

Cumulative Sars-CoV-2 cases, by day in Lombardia and overall in Italy since February 24, 2020 (up to April 18, 2020)³. Positive Sars-CoV-2 cases (dark lines) and hospitalized Covid-19 patients (light lines) in Italy (without cases recorded in Lombardia, blue lines) and in Lombardia (red lines) on a semilogarithmic scale. Legend: "Positive cases" includes both hospitalized and homecare Covid-19 patients; "Hospitalized" includes patients admitted to all hospital wards.