O R I G I N A L   I N V E S T I G A T I O N S / C O M M E N T A R I E S

The spread of COVID-19 in six western metropolitan regions: a false myth on the excess of mortality in Lombardy and the defense of the city of Milan

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Summary. We analyzed the spread of the COVID-19 epidemic in 6 metropolitan regions with similar demographic characteristics, daytime commuting population and business activities: the New York metropolitan area, the Île-de-France region, the Greater London county, Bruxelles-Capital, the Community of Madrid and the Lombardy region. The highest mortality rates 30-days after the onset of the epidemic were recorded in New York (81.2 x 100,000) and Madrid (77.1 x 100,000). Lombardy mortality rate is below average (41.4 per 100,000), and it is the only situation in which the capital of the region (Milan) has not been heavily impacted by the epidemic wave. Our study analyzed the role played by containment measures and the positive contribution offered by the hospital care system. (www.actabiomedica.it)

Key words: COVID-19, Mortality, Metropolitan regions, Hospital care system

Introduction

As history taught us, many airborne transmitted diseases - causing large epidemics - spread along trade routes and had the most dramatic effects in large urban areas in terms of infections, incidence and mortality. As it happened during the Black Death, a centripetal trend is even recurring nowadays (1), with the COVID-19 pandemic that, as of the 14th of April 2020, has surpassed 2 million notified cases (although these data largely underestimate the real situation) and 120,000 confirmed deaths, affecting large metropolitan areas for the most part (2). A precise track of the infection spread, across different geographical areas, is complicated by the globalization that, also, greatly improve the risks posed by trade routes (3), people gathering (4) and work activities (5).

Therefore, it is not by chance that in industrialized countries the diffusion of SARS-CoV-2 had a greater effect in the areas surrounding large urban centers (6): as London, Paris, New York, Madrid, Bruxelles and Milan amongst others. All these cities share similar characteristics and well-established commercial exchanges with China, where the virus dissemination started between the end of 2019 and January 2020.

Preventive actions have changed from the past: in addition to quarantine, health authorities took advantage from limitations of mobility (7), lockdown measures, the establishment of "red zones" (8), contact tracing (6), home fiduciary isolation (9) and the availability of new technologies (10), together with an adequate risk communication (11,12). These measures acquire a crucial importance considering the current lack of treatment and vaccinations.

With respect to the past centuries, the healthcare systems, and in particular hospitals with intensive care capacity, played an important role in saving lives but were also an important mean of infection dissemina-

tion (13), as it happened with the SARS epidemic (14), and at the beginning of the COVID-19 epidemic (15). The infection of patients and healthcare workers in the hospitals of Codogno and Casalpusterlengo – which were the first sites in which cases of local Italian transmission were confirmed (16) – showed how COVID-19 has a high tendency of diffusion in healthcare environments (hospitals) and residential care (nursing homes), that incidentally host individuals that are frail and at high risk (of older age and/or affected by chronic conditions).

This epidemiological study, conducted within the School of Public Health of Vita-Salute San Raffaele University, analyzes six geographical settings that include relevant metropolitan areas, and aims at evaluating the diffusion of COVID-19 and its mortality, to assess the reaction of healthcare systems, and lastly, to estimate the dynamics spread of the epidemic and the efficacy of the healthcare measures implemented.

Methods

For each included metropolitan area, we built a profile which included administrative, demographic and social characteristics (the latter was estimated in terms of daytime commuting population). We retrieved the number of available hospital beds, with a focus on intensive care units, and the measures implemented by health authorities to cope with the epidemic. With respect to COVID-19, we analyzed the number of deaths and draw mortality curves, starting with the day during which the first 3 deaths were declared in each area. Furthermore, we analyzed mortality rate at the level of regional and metropolitan areas, to evaluate centripetal trend of the epidemic. Finally,

we analyzed in details the case of Lombardy and in particular the metropolitan area of Milan due to its peculiar features, and because its mortality rates has been considered to be abnormal (17). Additionally, we examined the containment measures implemented by the healthcare authorities to reduce the inter-human transmission. Moreover, we reported the number of patients admitted, for COVID-19, to two Italian National Institutes for Scientific Research (IRCCS), since the beginning of the epidemic to date. Moreover, we anonymously retrieved their residence.

Results

First, we describe the characteristics of the six metropolitan areas in terms of demographic data, increase in daytime population, and healthcare:

New York – We analyzed the metropolitan area of New York City, with five boroughs (Manhattan, The Bronx, Queens, Brooklyn and Staten Island), a population of 8,388,748 and density of 10,715 people/km² (18). Manhattan is the most densely populated, with 26,821.6 inhabitants/km² (19), and an increase of daytime population of 1,499,757 commuters (20). In New York City there are 23,000 hospital beds (21) (2.74 per 1,000 inhabitants), which increased to 38,400 since to the COVID-19 epidemic (22) (4.57 per 1,000 residents, 67% increase). At the beginning of the epidemic, 2,449 intensive care beds were available in New York City (23), and increased of 62% (total available 3,965) by 10th April 2020 (24). Table 1 shows mortality data starting from the beginning of the epidemic (15th March 2020) (25).

Bruxelles – The Bruxelles-Capital Region has a population of 1,208,542 people and a population den-

Table 1. Cumulative mortality rate (x 100,000) in the six metropolitan areas analyzed

Area	Population x 1,000	Beginning of the epidemic*	Increase of beds in intensive care units	Number of deaths	Cumulative mortality rate°
New York City	8,623	15th March	67.0%	7,429	81.2
Community of Madrid	6,662	06th March	115.6%	5,136	77.1
Bruxelles-Capital	1,209	11st March	40.0%	587	48.6
Lombardy (Milan)	10,088	23rd February	114.0%	4,178	41.4
Ile-de-France (Paris)	12,278	11st March	109.0%	3,040	26.9
Greater London	9,304	7th March	19.8%	2,193	23.0

*Considered as the day during which the first 3 deaths were recorded; °Considered the 30th day since the beginning of the epidemic

sity of 7,489 people/km^2 (26). The central area includes the city of Bruxelles (181,726 inhabitants, and population density of 5,570 people/km^2) (27), and 324,000 people commute there every day, in addition to the city residents and the European Commission visitors (28). Bruxelles-Capital Region has an availability of 6.74 hospital beds per 1,000 population (29). In Belgium, 1,900 intensive care beds increased by 40% during the epidemic (11th March 2020) (30).

Community of Madrid – The Community of Madrid has 6,661,949 inhabitants and a population density of 829.84 people/km^2 (31,32). The metropolitan area of Madrid has 3,266,126 inhabitants and a population density of 5,265 people/km^2, in addition it receives around 345,000 workers daily and 27,000 turists (33). In 2017 the region had 20,458 hospital beds (3.14 per 1,000 people), among public and private structures (34). The 800 intensive care beds of the region increased to 1,725 to treat patients affected by COVID-19 (35). To cope with the high number of patients during the epidemic, the Ifema field hospital has been built, and it can accommodate 5,000 beds in 9 pavilions (35). On the 1st April 2020 the number of hospitalized people in the region of Madrid reached a peak value with 15,227 occupied hospital bed and 1,528 patients in intensive care units (35). On 1st of April 2020, the Ifema hospital hosted 930 patients, 16 of which in intensive care beds. Table 1 shows mortality data starting from the beginning of the epidemic (6th March 2020) (35).

Île-De-France (Paris region) – We analyzed the region of Île-de-France, with 8 Département, a total population of 12,278,210 (18% of metropolitan France population) and a population density of 1,022.25 people/km^2 (36). It includes the city of Paris, divided into 20 arrondissement, with 2,148,271 inhabitants and a population density of 20,382 people/km^2 (37), with a daytime increase in population of 570,000 people commuting from Île -de-France (38). Île-de-France counts 5.94 hospital beds per 1,000 inhabitants (2014 update). In 2018 the region had 1,275 intensive care beds (471 in Paris (39)), that increased by 109% to 1,390 (40) since the beginning of the epidemic. This was achieved by increasing the 3,000 intensive care beds that were already available in the region, which is sustained by private healthcare hospitals by 23.4%

(39). Table 1 shows mortality data starting from the beginning of the epidemic (11th March 2020) (41).

Greater London – The county of Greater London has 8,899,375 and a population density of 5,671/km^2. Inner London forms the central part of Greater London with 12 boroughs and the City of London; it has 3 million residents (42) and a density of population of 9,404/km^2). The daytime population creases by a million of commuters daily (42). In Greater London there are 21,361 NHS hospital beds open overnight, 1,507 of which are reserved for intensive care (43). To cope with the increase in patients due to the epidemic, private hospitals signed an agreement to provide more than 2,000 hospital beds, and 250 between operating rooms and intensive care beds (44). Furthermore, the "NHS Nightingale Hospital London" has been temporarily set up in the ExCeL convention center. It hosts 500 intensive care beds, but it can receive up to 4,000 patients (45). Thanks to this measure, the total number of hospital beds increased by 12.9%, and the number of intensive care beds increased by 49.8%. Table 1 shows mortality data starting from the beginning of the epidemic (7th March 2020) (46).

Lombardy (Milan Region) – The Lombardy Region, with a population of 10,060,574 people and a population density of 422 inhabitants per km^2. The central metropolitan area of Milan, which consists of the city of Milan and other 133 municipalities, with a total of 3,250,315 inhabitants and a population density of 2,063 inhabitants per km^2 (47), in addition to 1,441,409 people that commute every day. The Lombardy Region consists of several highly populated areas in proximity to Milan (Bergamo, Brescia, Monza, etc). The intensive care beds available were 723 at the onset of the epidemic, which increased to a total of 1,547 beds reserved for patients affected by COVID-19 after 30 days. This resulted in an increment of 113.9%, and it includes only 10 of the potential 500 additional beds allocated in the Milano Fiera pavilions. Table 1 shows mortality data (48) starting from the beginning of the epidemic (23rd February) (49).

Figure 1 represents the epidemic progress in the six areas via cumulative daily mortality rate. We decided to put the analytic comparison at day 30 from the beginning of the outbreak (when 3 deaths were reported), due to the different chronological develop-
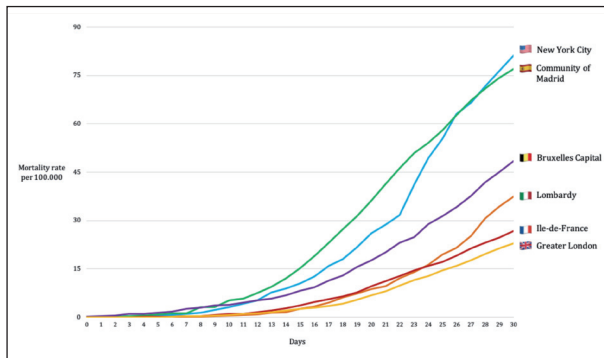
Figure 1. Cumulative daily mortality rate in the six areas

ment in each zone: day 30 is the time at which we calculated the mortality rates for each area (Table 1).

Since China issued the first warnings about the COVID-19 outbreak, European and USA health authorities planned new preventive measures in order to avoid the spread of the virus. These actions (as health check-points in airports, quarantine for people arriving from Hubei region, contact tracing and isolation)

proved to be inefficient in the prevention of a massive implication of the major metropolitan areas of the western world. Italy was the first European country to declare endemic cases, and it was the first country to report outbreaks in Lombardy and Veneto regions (50). Table 2 describes the most relevant actions taken by the Government from February 21st to April 4th 2020. Similar measures were also adopted by the local Governments of the administrative areas analyzed in this report. One of the measures implemented was the increase in the number of hospital beds and intensive care beds, as the normal hospital capacity was not able to host the number of COVID-19 cases requiring hospitalization.

As an example, we reported the cases of the Lombardy region and Greater London areas – as these two entities have similar healthcare systems – in which the public health authorities arranged agreements with private hospitals in order to face the increased demand for healthcare assistance. Figure 2 shows the flatten-

Table 2. Health protection measures against COVID-19 in Lombardy Region, 21 February – 4 April 2020

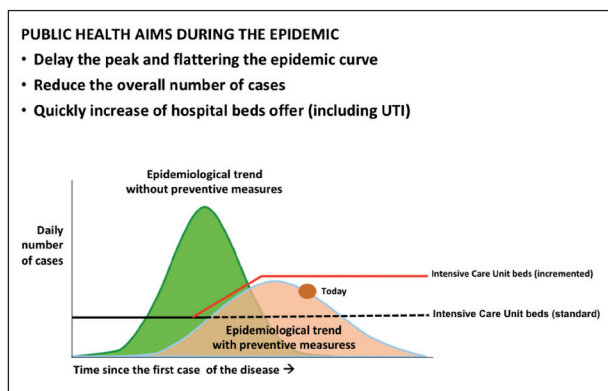| Date	Public Health Measures	Authority
21 February 2020	Mandatory supervised quarantine for 14 days for all individuals who have come into close contact with confirmed cases of disease; Mandatory communication to the Health Department from anyone who has entered Italy from high-risk of COVID-19 areas, followed by quarantine and active surveillance.	Ministry of Health
23 February 2020	Red zones in 11 municipalities in Lombardy Region: adoption of an adequate and proportionate containment and management measures in areas with >1 person positive to COVID-19 with unknown source of transmission.	National Government
23 February 2020	Development of a toll-free number for population	Lombardy Region
08 March 2020	Lock-down: avoid any movement of people except for motivated by proven work needs or situations of necessity (health, food and assistance);	National Government
08 March 2020	• Suspension of deferred and non-urgent hospitalization and outpatient activities. • Reorganization of hospital activities • Establishment of the Unique Post-Hospital Regional Discharge Center aimed at managing the patients' discharge	Lombardy Region
09 March 2020	Public communication campaign on social network #fermiamoloinsieme	Lombardy Region
11 March 2020	Suspension of all commercial activities non-indispensable for production.	National Government
23 March 2020	• Special Care Continuity Units (USCA) aimed at home management of patients with COVID-19 who do not require hospitalization • Identification of accommodation facilities (hotels) for discharged patients with domestic isolation problems • Establishment of a telemedicine service for GPs and their patients	Lombardy Region
30 March 2020	Further identification of day-care structure to isolate asymptomatic or low symptomatic subjects	Lombardy Region
4 April 2020	Use of face mask (or other supply) for the whole population	Lombardy Region

Figure 2. Epidemiological trend and public health measures ("flattening" the curve)

ing of the epidemic curve as a result of public health interventions, with the increase of the hospital capacity, variously needed, in all the different areas analyzed.

We decided to investigate further the Lombardy case, as it was the first to be described in the press and to be of great scientific interest for its alleged excess of deaths (45). The crude fatality rate (number of deaths/number of notified cases) is largely affected by the number of the tests performed and its results are not significant, so we analyzed the mortality rate (Table 1). It showed that, besides the higher number of deaths and the delay of the start of the epidemic in the different areas, the trend documented in the Lombardy region is significantly lower than three areas with the highest mortality (New York, Madrid and Bruxelles). Lombardy region is slightly higher than Paris and London, even though it has a wider surface area.

We believe that such trend recorded in the Lombardy region – despite the earlier start of the epidemic – is due to the fact that the metropolitan area of Milan has never been heavily hit by the epidemic wave, as clearly shown considering mortality rates in the provinces of Lombardy ad surrounding regions (Figure 3) (51). As an example, we took into account the domicile of 1,058 COVID-19 patients admitted to two National Institutes for Scientific Research (IRCCS), situated just outside the areas in which the two outbreaks took place, 50 kilometers outside of Milan (Figure 4). The data shows that most of these patients came from areas located between the cities involved by the first outbreaks and the city of Milan. This suggest that these

two hospitals (as well as the others in the metropolitan area of Milan) have not payed a role as multiplier of SARS-CoV-2 infections as probably happened in smaller-sized hospitals - as for instance hospitals of Lodi and Codogno - in the first phase of the epidemic.

Possible bias

The six areas analyzed have similar economic characteristics, healthcare standards and COVID-19 surveillance data collection procedures, which allowed us to make a reliable comparison of data. The choice of these areas followed administrative borders and the availability of the disaggregated mortality data. If only focusing on the metropolitan area of Milan (3.2
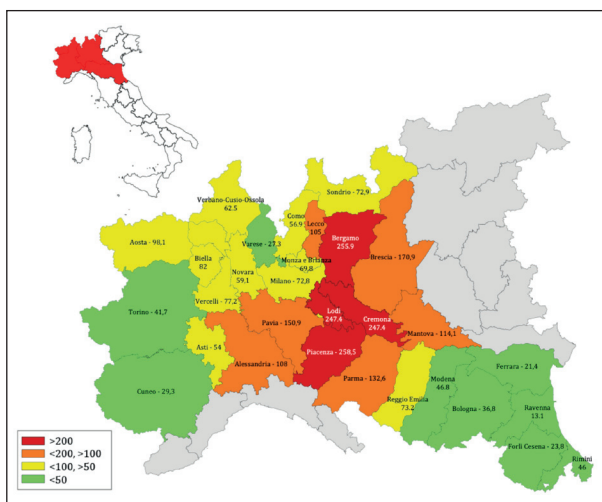

Figure 3. Cumulative mortality rate per 100,000 population in the Provinces of four Regions of Northern Italy, last update 17th April 2020
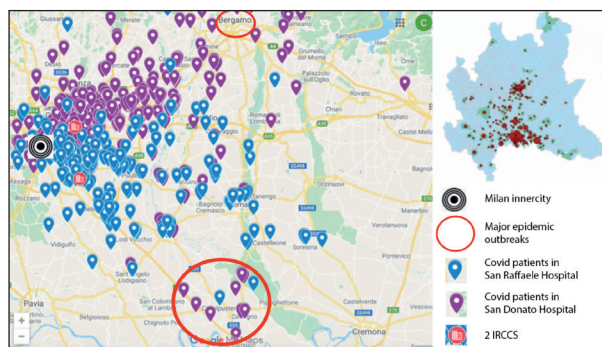

Figure 4. Geographic distribution of COVID cases requiring hospitalization in two major hospitals of Milan (IRCCS)

million inhabitants), mortality rates would have been about 45% lower (data not shown); if a wider area including only the provinces surrounding Milan (Monza, Bergamo and Lodi) had been evaluated (area of 5.5 million inhabitants), the mortality rate would have been comparable to the regional data (data not shown).

Our analysis considered daily COVID-19 mortality rates derived by national surveillance statistics, which are more reliable than infection notifications (confirmed cases). Indeed, notified cases data are largely lower compared to the reality, and highly variable depending on different swab strategies and criteria adopted in different regions (52). Although it cannot be ruled out that a portion of the deaths caused by COVID-19 went undiagnosed, we believe that this possible bias, estimated at 17% (53), is similar in the other five areas (as suggested by international press reports) thereby it doesn't greatly affect the final assertion of our comparative study.

Conclusions

We analyzed the COVID-19 epidemic trend in six areas, comparable from an economic, social and healthcare perspective, using reliable indicators, such as the cause of death. New York City (8.4mln. inh.) and Madrid (6.6mln. inh.) are the two metropolitan areas mostly affected by the epidemic, while the Lombardy region (10mln. inh.) – the first western area affected by the epidemic and, in theory, less prepared – recorded a high number of deaths (over 10,000) but a mortality rate lower than three out of the six regions considered, and a cumulative mortality rate on the 30th day about 50% lower than New York City and the Community of Madrid. One of the reasons contributing to these results, as mentioned earlier, could be that the epidemic has not yet hit the metropolitan area of Milan (3.2mln. inh.), but only smaller cities including Bergamo (1mil. inh.). Two factors could have contributed to the positive "defense" to the metropolitan area with the higher population density and commercial trades: firstly, the efficacy and the promptness (54) of containment and mitigation measures which resulted in increasing physical distancing and then in a reduction people gatherings ; secondly the effectiveness and safety of care pro-

vided by hospitals treating COVID-19 cases (47,48) (considering that hospitals were an important driving force of the transmission of this epidemic worldwide).

An additional refers to the general increase of hospital beds and intensive care beds that was achieved in a short time in all the examined areas, which allowed to face the emergency. In particular, the Lombardy Region (as also done by the Community of Madrid and Ile-de-France) more than doubled the number of beds, both ordinary hospital beds and for intensive care.

Finally, the two countries with a public healthcare system (Italy and UK), which recorded mortality rates below the average, arranged formal agreements with the private healthcare system. This aspect might have given an important contribution to the management of the emergency. Although emergency treatments were provided in all considered areas with the same models (apparently free of charge) in all six areas, the fact that the two countries with a public healthcare system achieved lower mortality rates could be due to the hospital system efficacy combined with the activity of territorial services. In conclusion, we can state that a "Lombardy case" did not occur in terms of a specific mortality excess; moreover, the rapid adaptation of the hospital network has been able to cope with a massive epidemic wave managing, to date, to limit its spread in the area with the highest population density.

A more complete analysis can be carried out for a longer follow up (45 or 60 days since the onset of the epidemic) in which it will be possible to better analyze, for all the six areas considered (and possibly others), the medium-term effect of the containment measures, the actions of primary health care, the ignition of further epidemic outbreaks and the overall management of the epidemic.

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