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Phase 2 COVID-19

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Foreword

The identity of public health in COVID-19 times

The COVID-19 has hit the world with devastating clinical, economic and social burden. If any constructive element arises from this tragedy, it is a greater awareness of the key role of public health, which will also be instrumental in the way out of the crisis. Defined in broader terms as the science of protecting the safety and improving the health of communities through education, policy making and research for disease prevention, public health action has guided COVID-19 surveillance and monitoring (1,2), the adoption of containment and mitigation measures (3), has informed the management and organization of healthcare delivery in emergency and has fuelled health communication and education to the general population.

The collective dimension of health and wellbeing is the ultimate aim in the fight against COVID-19. The public health community feels strong the responsibility of contributing towards this aim at the policy, research and practice levels. At the research level the Covid-19 pandemic has led to an unprecedented focus of the world's scientific community on one topic (4). At *Acta Biomedica* we have encouraged and supported the production and dissemination of public health research outputs since the very beginning of the COVID-19 outbreak (5,6). With this supplement on COVID-19 we renew our efforts towards evidence gathering, well aware of the role of public health evidence in informing the planning, implementation and evaluation of COVID-19 response (7). We are glad to present the current supplement that brings together important updates: researchers from Vita-Salute San Raffaele University assess age-standardized COVID-19 mortality rates in selected metropolitan regions around the world putting Lombardy region COVID-19 burden data into context (8). Colleagues from the University of Parma – at national reference laboratory for COVID-19 as well for influenza surveillance (9) - report key findings from four-month long virological surveillance of COVID-19 reflecting on the clinical and public health meaning of decreasing viral loads (10). Aspects related to health services delivery and management during the COVID-19 outbreak are explored by Castaldi et al. (11) and Rovere Querini el at. (12), the latter presenting one of the first cases of COVID-19 hospital follow-up clinics. Infection control in healthcare settings and its determinants are explored by Pasquarella et al (Parma) (13) reporting preliminary interesting data on surfaces contamination, by Squeri et al (Messina) (14)reporting on healthcare workers surveillance and contact tracing in Southern Italy, and by Auxilia et al (Milan) (15) reporting on hospital acquired infections trends during the COVID-19 emergency. Guidelines and safety protocols to be adopted for balneotherapy are outlined by Clementi et al (16). Academic Architects, experts in Public Health, from Politecnico di Milano, in co-operation with colleagues from Sapienza University of Rome (17) provides meaningful insight on design aspects related to quality of care and safety in healthcare facilities, but also related to quality housing and its impact on health and wellbeing during COVID-19 lockdown and beyond (18,19). As some stimulating reflections focus on how to prepare to manage the long-term impact of the COVID-19 public health emergency in Italy both within (20) and outside (21) the healthcare sector, we are confident solid ongoing research projects (22) will soon provide further outputs to keep advancing public health knowledge and inform its action towards population health and wellbeing.

Carlo Signorelli
Anna Odone
Marco Vitale

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Original article

COVID-19 mortality rate in nine high-income metropolitan regions

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Abstract. We analyzed the spread of the COVID-19 epidemic in 9 metropolitan regions of the world with similar socio-demographic characteristics, daytime commuting population and business activities: the New York State, Bruxelles-Capital, the Community of Madrid, Catalonia, the Île-de-France Region, the Greater London county, Stockholms län, Hovedstaden (Copenhagen) and the Lombardy Region. The Lombardy region reported the highest COVID-19 crude mortality rate (141.0 x 100,000) 70-days after the onset of the epidemic, followed by the Community of Madrid (132.8 x 100,000) New York State (120.7 x 100,000). The large variation in COVID-19 mortality and case-fatality rates for COVID-19 in different age strata suggested a more accurate analysis and interpretation of the epidemic dynamics after standardization of the rates by age. The share of elder populations (>70 years) over total population varies widely in the considered study settings, ranging from 6.9% in Catalonia to 17.0% in Lombardy. When taking age distribution into consideration the highest standardized mortality rate was observed in the State of New York (257.9 x 100,000); with figures in most of the European regions concentrated between 123.3 x 100,000 in Greater London and 177.7 x 100,000 in Bruxelles-Capital, lower in French and Danish regions. We also report and critical appraise, when available, COVID-19 mortality figures in capital cities, nursing homes, as well as excess mortality at country level. Our data raise awareness on the need for a more in-depth epidemiological analysis of the current COVID-19 public health emergency that further explores COVID-19 mortality determinants associated with health services delivery, community-level healthcare, testing approaches and characteristics of surveillance systems, including classification of COVID-19 deaths. (www.actabiomedica.it)

Key words: COVID-19, Mortality, Metropolitan regions, Elderly population

Introduction

The COVID-19 pandemic had major impacts in urban settings, (1), including in London, Paris, New York, Madrid, Bruxelles and Milan, among others. All these metropolitan areas share similar characteristics and well-established commercial exchanges with China, where SARS-CoV-2 transmission started between the end of year 2019 and the beginning of 2020.

Containment measures have evolved over time: in addition to quarantine, health authorities have undertaken limitations of mobility (2), lockdown measures (3), have established "red zones" (4), contact tracing (1), home fiduciary isolation (5), supported by advances in technology (6), and better risk communication (7-9). These non-pharmacological preventive measures have played a crucial role, also considering the current lack of effective drugs and vaccines for COVID-19 (10, 11).

In a previous preliminary analysis (4) we compared crude COVID-19 mortality rates 30 days after the onset of the epidemic, exploring different epidemic dynamics, health systems' response and healthcare delivery management in different settings. The current study, developed around the same theoretical framework(12), builds on previous findings and analyzes nine metropolitan areas, with the aim of further assessing the spread of COVID-19 and its mortality, taking into consideration several characteristics, including age distribution. We also explore and expand on the impact of implemented containment measures and healthcare systems response (12). Specifically, we take into consideration COVID-19 mortality rates (crude and age-standardized) up to 70 days (10 weeks) after the onset of the epidemic period during which the COVID-19 epidemic curve slowed down in all considered settings.

Methods

We considered COVID-19 mortality instead of notification rates, acknowledging the highest reliability of such indicator. Study settings have been chosen considering geographical, societal, and economic characteristics, and considering the availability and comparability of official COVID-19 mortality data.

For each of the nine regions, we built a profile which included administrative, demographic, and social characteristics (the latter was estimated in terms of population age distribution and number of nursing homes). With respect to COVID-19, we analyzed the number of deaths and draw mortality curves, starting on the day during which the first 3 deaths were reported by surveillance systems in each area. Furthermore, we analyzed mortality rate at the regional and metropolitan level to evaluate centripetal trend of the epidemic. Finally, we analyzed in detail the case of Lombardy and with its the metropolitan area of Milan, the European region hit first and whose mortality rates has been considered to be abnormal (13).

Due to the wide differences in age distribution across study settings (proportion of people older than 70 years ranging from 6.9% Catalonia to 17.0% Lombardy), in addition to crude mortality rates, we calculated mortality rates standardized by age using the indirect method and the age-specific mortality rates of Lombardy Region as reference population.

Results

First, we describe the characteristics of the nine metropolitan areas in terms of demographic data, population age distribution, and nursing homes:

NEW YORK STATE – New York State has a population of 19,378,102 inhabitants and a population density of 159 inhabitants/km^2 (14). The capital region is New York City with a population of 8,388,748 inhabitants and a population density of 10,715 inhabitants/km^2 (14). Considering the population age distribution of the region (Table 1), only 7.7% of the whole population is older than 70 years (Figure 1). In the region there are 450 nursing homes, where 3,405 confirmed death and 2,522 probable death for COVID-19 occurred until the 30th of May 2020 (representing the 20% of the total COVID-19 death recorded in the area) (15). For the period 1st February- 30th May 2020, the excess mortality rate not attributed to COVID-19 is 21.5% (8,077/36,644) higher compared to the same period of 2019 (16, 17). Crude and age-standardized cumulative mortality rate of the Region are shown in Figure 2. Crude cumulative mortality rate of the capital is shown in Table 2, data starting from the beginning of the epidemic (15th March 2020) (18). Crude and age-standardized weekly mortality rate are shown in Figure 3.

BRUXELLES-CAPITAL – The Bruxelles-Capital Region has a population of 1,208,542 inhabitants and a population density of 7,489 inhabitants/km^2 (19). The central area includes the city of Bruxelles (181,726 inhabitants, and population density of 5,570 inhabitants/km^2) (20). Considering the population age distribution of the region (Table 1), only 9.4% of the whole population is older than 70 years (Figure 1). In the region there are 146 nursing homes, where 643 confirmed death for COVID-19 occurred until the 7th of June 2020 (representing the 49.2% of the total COVID-19 death recorded in the region)

Table 1. Population age distribution stratified in four age groups, in the nine Regions

Age (in years)	New York State	Bruxelles	Com. Madrid	Catalonia	Ile de France	Greater London	Stockholms län	Hovedtsnden	Lombardy
0-59	82.8%	82.3%	76.7%	87.7%	79.5%	84.7%	79.0%	77.8%	71.3%
60-69	8.7%	8.2%	10.3%	5.4%	9.6%	7.3%	9.3%	9.7%	11.8%
70-79	5.0%	5.4%	7.5%	3.9%	6.5%	4.8%	7.8%	8.4%	9.9%
80+	3.5%	4.1%	5.5%	3.0%	4.4%	3.1%	4.0%	4.0%	7.1%

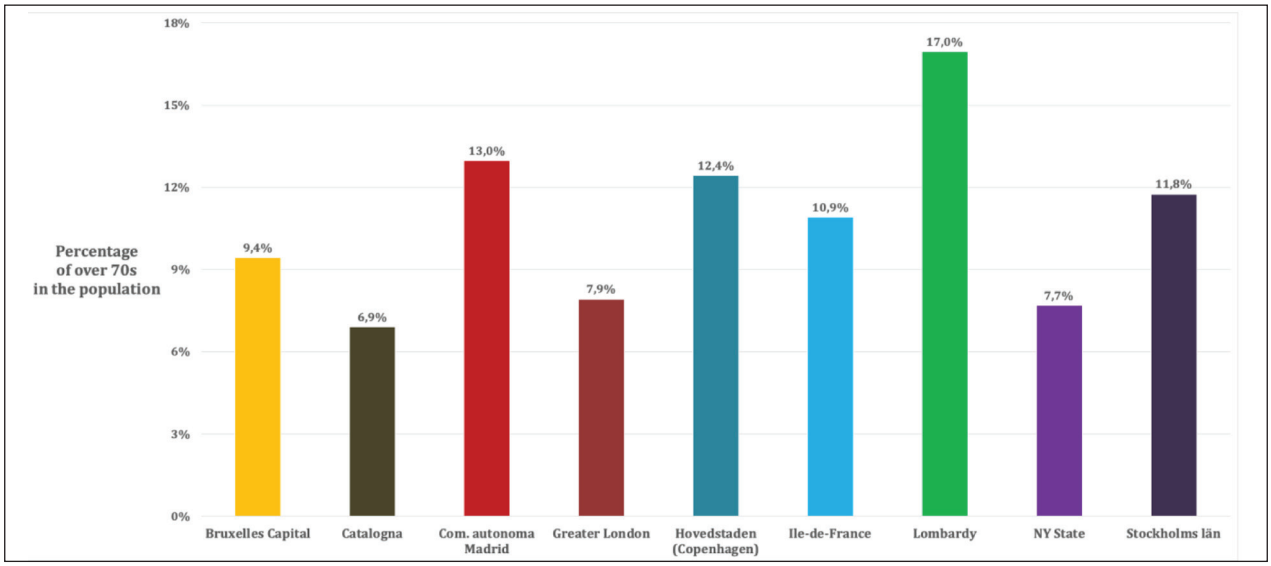

Figure 1. Population age distribution older than 70 years, in the nine Regions

(21). For the period 24th February- 24th May 2020, the excess mortality rate not attributed to COVID-19 is 9.2% (134/1,455) higher compared to the same period of 2019 (22). Crude and age-standardized cumulative mortality rate of the Region are shown in Figure 2. Crude cumulative mortality rate of the capital region is shown in Table 2, data starting from the beginning of the epidemic (11th March 2020) (23). Crude and age-ad weekly mortality rate are shown in Figure 3.

COMMUNITY OF MADRID – The Community of Madrid has 6,661,949 inhabitants and a population density of 829.84 inhabitants/km^2 (24, 25). The capital region is Madrid with 3,266,126 inhabitants and a population density of 5,265 inhabitants/km^2(25). Considering the population age distribution of the region (Table 1), only 13.0% of the whole population is older than 70 years (Figure 1). In the region there are 700 nursing homes, where 1,251 confirmed death and 4,728 probably death for COVID-19 occurred (representing the 68.8% of the total COVID-19 death recorded in the region) (26). For the period 1st January-24th May 2020, the excess mortality rate not attributed to COVID-19 is 42.1% (6,325/15,011) higher com-

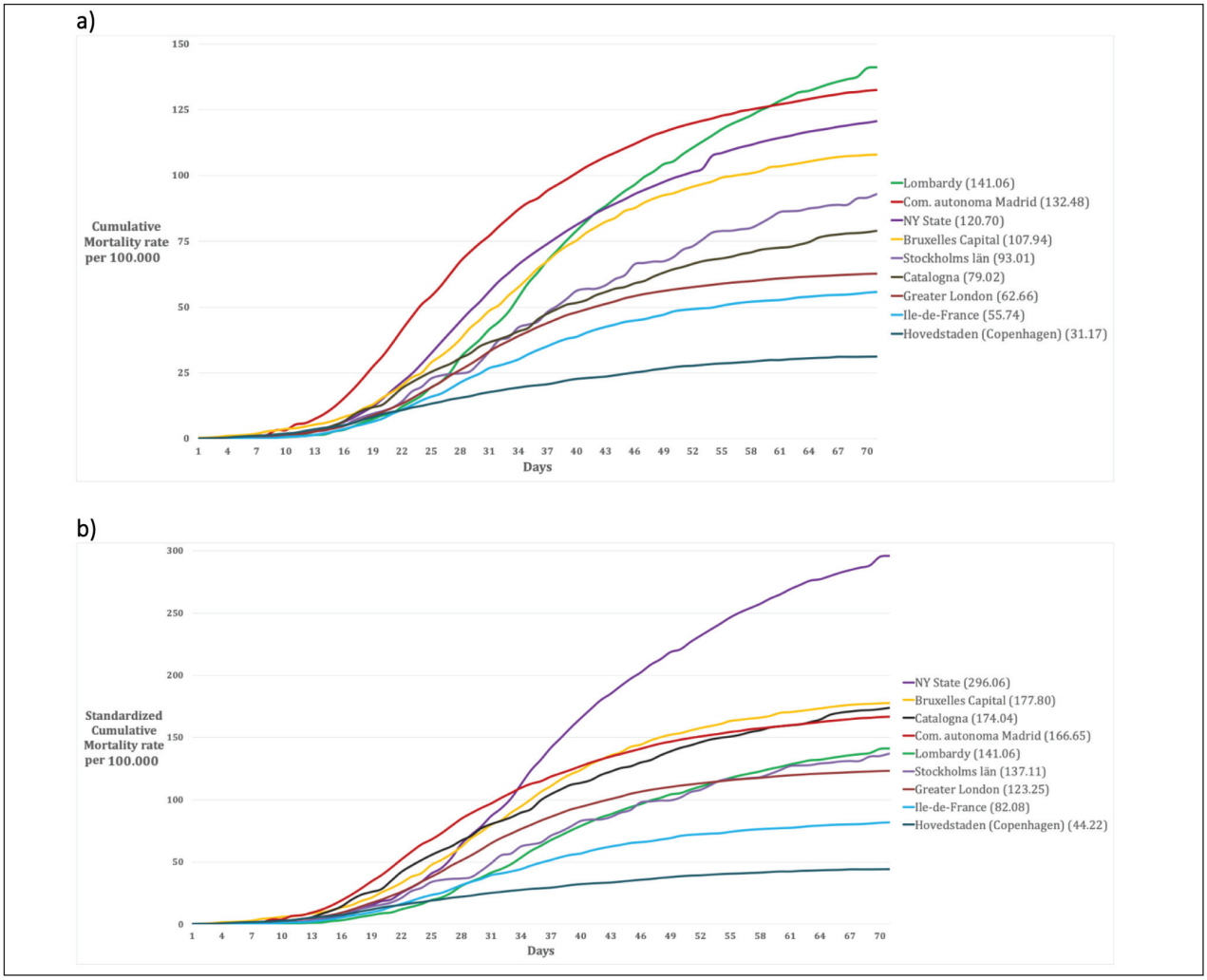

Figure 2. 70 days-Cumulative mortality rate in the nine Regions (a) crude, and (b) age-standardized

pared to the same period of 2019 (27, 28). Crude and age-standardized cumulative mortality rate of the Region are shown in Figure 2. Crude cumulative mortality rate of the capital region is shown in Table 2, data starting from the beginning of the epidemic (6th March 2020) (29). Crude and age-standardized weekly mortality rate are shown in Figure 3.

CATALONIA – Catalonia has 7,619,494 inhabitants and a population density of 235.63 inhabitants/km^2 (25). The capital region is Barcelona with 1,636,762 inhabitants and a population density of 15,992.21 inhabitants/km^2 (25). Considering the population age distribution of the region (Table 1), only 6.9% of the whole population is older than 70 years (Figure 1). In the region there are 1,073 nursing homes, where 4,084 confirmed death for COVID-19 occurred (representing the 73.1% of the total COVID-19 death recorded in the region) (26). For the period 1st January- 24th May 2020, the excess mortality rate not attributed to COVID-19 is 51.5% (5,919/11,494) higher compared to the same period of 2019(27, 28). Crude and age-standardized cumulative mortality rate of the Region are shown in Figure 2. Crude cumulative mortality rate of the capital region is shown in Table 2, data starting from the beginning of the epidemic (10th March 2020) (29). Crude and age-standardized weekly mortality rate are shown in Figure 3.

Table 2. Summary of demographic characteristics of the nine considered areas; proportion of deaths in nursing homes and other epidemiological characteristics

Area	Population x 100,000	Population density inh./km²	Beginning of the epidemic *, week of the peak	Deaths in nursing homes (%)§	Crude cumulative mortality rate°	Definition of COVID-19 death
New York State	8,623	159	15th March; 4th week	20	120.7	People who tested positive and who did not have a positive COVID-19 laboratory test, but their death certificate lists as the cause of death "COVID-19" or an equivalent (18)
New York city	8,388	10,715			191.3	
Bruxelles- Capital	1,209	7,489	11th March; 5th week	49.2	107.9	Both confirmed and probable deaths (64)
Bruxelles	181	5,570			n.a.	
Community of Madrid	6,662	829	6th March; 4th week	68.8	132.8	Before April, the 17th only people who tested positive in hospital. After, independent of the place of death.
Madrid	3,266	5,265			n.a.	
Catalonia	7,619	235	10th March; 4th week	73.0	79.0	Before April, the 17th only people confirmed and probable cases. After, same as the rest of Spain.
Barcellona	1,636	15,999			n.a.	
Ile-de-France	12,278	1,022	11th March; 4th week	50.0	55.7	Only hospitalized patients who test positive for SARS-CoV-2 (excluding death occurred in community or in nursing homes) (65)
Paris	2,148	20,382			76.39	
Greater London	9,304	5,671	8th March; 5th week	14.0	62.7	Only hospitalized patients who test positive for SARS-CoV-2 (included post-mortem test)(66)
Inner London	3,000	9,404			56.6	
Stockholms län	2,119	325	6th March; 5th week	32.0	93.0	Patients who test positive for SARS-CoV-2, independently of the cause of death (67)
Stockholms	960	5,129			96.9^	
Hovedstaden	1,846	718	16th March; 4th week	n.a.	31.2	Patients who test positive for SARS-CoV-2, independently of the cause of death (68)
Hillerød	33	155			n.a.	
Lombardy	10,088	422	23rd February; 5th week	50.0	141.0	Patients who test positive for SARS-CoV-2, independently of the cause of death (69)
Milan	3,250	2,603			72.8+	

*Considered as the day during which the first 3 deaths were recorded; °Considered the 30th day since the beginning of the epidemic; § based on total COVID-19 deaths; ^ until 15th June 2020; + until 17th April; n.a. not available

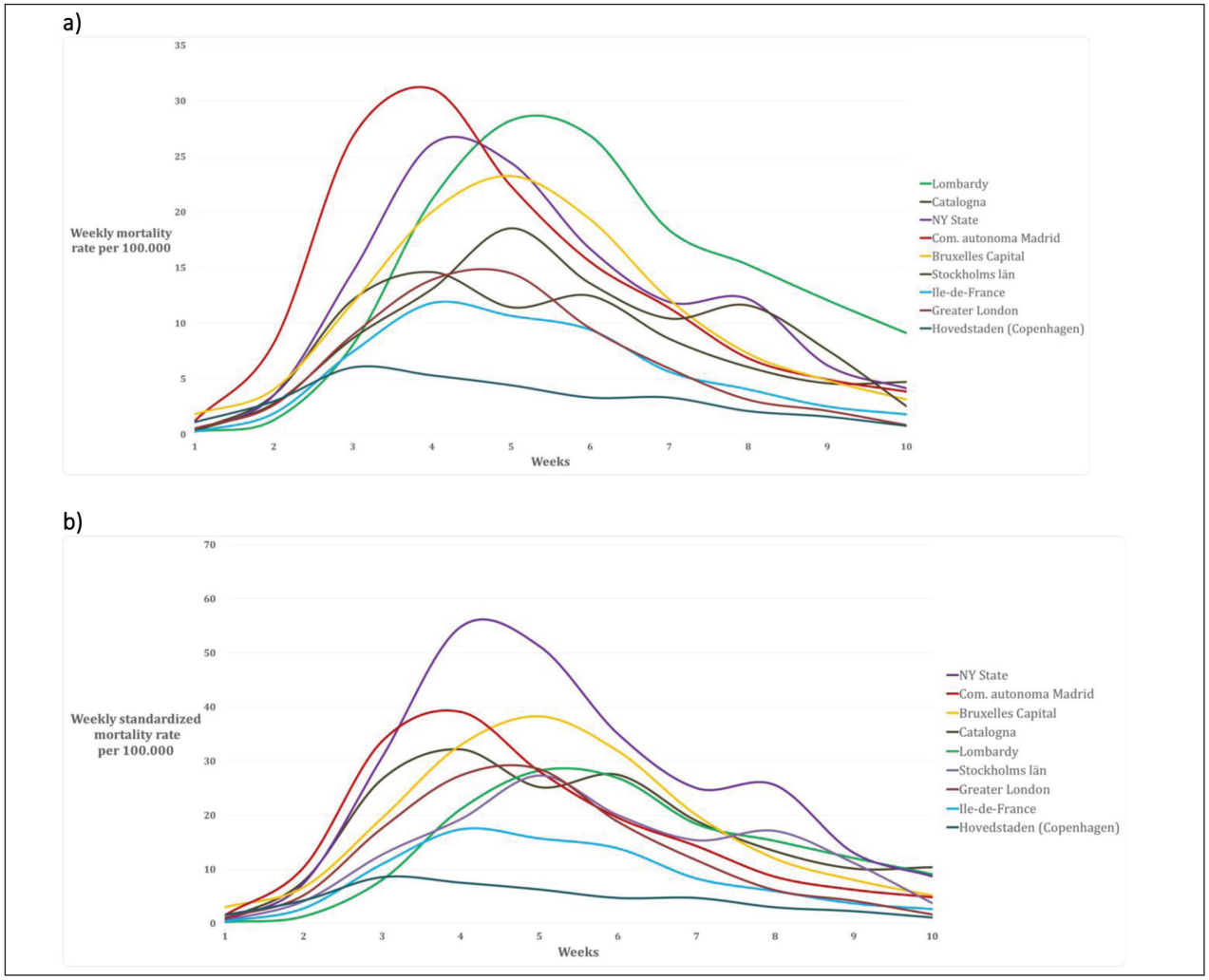

Figure 3. Cumulative weekly mortality rate in the nine Regions (a) crude, and (b) age-standardized

ÎLE-DE-FRANCE (Paris region) – We analyzed the region of **Î**le-de-France, with 8 Département, a total population of 12,278,210 inhabitants (18% of metropolitan France population) and a population density of 1,022.25 inhabitants /km^2 (30). The capital region is Paris, divided into 20 arrondissement, with 2,148,271 inhabitants and a population density of 20,382 inhabitants /km^2 (31).

Considering the population age distribution of the region (Table 1), only 10.9% of the whole population is older than 70 years (Figure 1). In the region there are 760 nursing homes (32), where 5,621 confirmed death for COVID-19 occurred until 28th May 2020 (representing approximately the 50% of the total COVID-19 death recorded in the country) (33). For the period 11th March- 20th May 2020, the excess mortality rate not attributed to COVID-19 is 37.5% (4,102 /10,952) higher compared to the same period of 2019 (34). Crude and age-standardized cumulative mortality rate of the Region are shown in Figure 2. Crude cumulative mortality rate of the capital region is shown in Table 2, data starting from the beginning of the epidemic 11th March 2020) (35). Crude and age-standardized weekly mortality rate are shown in Figure 3.

GREATER LONDON – The county of Greater London has 8,899,375 inhabitants and a popula-

tion density of 5,671 inhabitants /km^2. Inner London forms the central part of Greater London with 12 boroughs and the City of London; it has 3 million inhabitants (36) and a density of population of 9,404 inhabitants/km^2). Considering the population age distribution of the region (Table 1), only 7.9% of the whole population is older than 70 years (Figure 1). In the region there are 426 nursing homes (37), where 803 confirmed death for COVID-19 occurred in the period 10th April – 16th May 2020 (representing the 14% of the total COVID-19 death recorded in the region) (38). For the period 9th March- 16th May 2020, the excess mortality rate not attributed to COVID-19 is 51,5% (5,919/11,494) higher compared to the mean value of the previous five years (39). Crude and age-standardized cumulative mortality rate of the Region are shown in Figure 2. Crude cumulative mortality rate of the capital region is shown in Table 2, data starting from the beginning of the epidemic (8th March 2020) (40). Crude and age-standardized weekly mortality rate are shown in Figure 3.

STOCKHOLMS LÄN – Stockholms län has 2.1 million inhabitants and a density of 325.17 inhabitants/km^2. The capital region is Stockholm city with 960 thousand inhabitants and a population density of 5,129.47 inhabitants /km^2) (41). Considering the population age distribution of the region (Table 1), only 11.8% of the whole population is older than 70 years (Figure 1). In the region there are 400 nursing homes (42), where 630 confirmed death for COVID-19 occurred in the period 10th April – 16th May 2020 (representing the 32% of the total COVID-19 death recorded in the region) (42). For the period 9th March- 16th May 2020, the excess mortality rate not attributed to COVID-19 is 13.1% (298/2,275) higher compared to the same period of 2019 (43). Crude and age-standardized cumulative mortality rate of the Region are shown in Figure 2. Crude cumulative mortality rate of the capital region is shown in Table 2, data starting from the beginning of the epidemic (6th March 2020). Crude and age-standardized weekly mortality rate are shown in Figure 3.

HOVEDTSNDEN (Copenhagen region) – Hovedtsnden has 1,846,023 inhabitants and a population density of 718.57 inhabitants /km^2. The capital region is Hillerød with 33,088 inhabitants and a population density of 155.34 inhabitants /km^2) (44). Considering the population age distribution of the region (Table 1), only 12.4% of the whole population is older than 70 years (Figure 1). In the region there are 229 nursing homes (45), data on confirmed deaths occurred in nursing home is not available. For the period 15th March- 26th May 2020, the excess mortality rate not attributed to COVID-19 is -1.9% (-206/10,741) higher compared to the same period of 2019 (43). Crude and age-standardized cumulative mortality rate of the Region are shown in Figure 2. Crude cumulative mortality rate of the capital region is shown in Table 2, data starting from the beginning of the epidemic (16th March 2020). Crude and age-standardized weekly mortality rate are shown in Figure 3.

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 capital region is the 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/km^2 (46). Considering the population age distribution of the region (Table 1), 17% of the whole population is older than 70 years (Figure 1). In the region there are 717 nursing homes (47), where approximately 50% of the total COVID-19 death recorded in the region has been occurred (data not published). For the period 23rd February- 2nd May 2020, the excess mortality rate not attributed to COVID-19 is 66.5% (27,334/41,083) higher compared to the same period of 2019 (48). Crude and age-standardized cumulative mortality rate of the Region are shown in Figure 2. Crude cumulative mortality rate of the capital region is shown in Table 2, data starting from the beginning of the epidemic (23rd February 2020) (49). Crude and age-standardized weekly mortality rate are shown in Figure 3.

Figure 2 and 3 represent the epidemic spread in the nine metropolitan regions with the cumulative daily mortality rate, the standardized mortality rate, the crude weekly mortality rate and the weekly age-standardized mortality rate. We decided to conclude

the analytic comparison after 10 weeks (day 70) from the onset of the outbreak (Table 2).

Since the first reports of the COVID-19 pandemic, in China (50), data showed a higher hospitalization rate among elderly (older than 65 years) (51), and a sever clinical manifestation among patients with comorbidities (52). According to TESSy data, deaths are approximately 40% among people aged 65-79 years, and approximately 50% among people older than 80 years (52). As emerges from this data, COVID-19 serious clinical cases impacted the most on elder populations.

Figure 1 shows how Lombardy is the region with the highest proportion of elder populations, with a proportion of over 70-year-olds 70% higher when compared with the other Regions studied (17% vs. 10%). Considering this important difference in population distribution, the age-standardized mortality rates were calculated. Although Lombardy was the first European region to be affected by the epidemic (53), the cumulative age-standardized mortality rates of Lombardy are in the average and lower than the community of Madrid, Catalonia, Brussels-Capital, and New York State. For the latter, the estimated cumulative age-standardized mortality is approximately double compared to Lombardy (Figure 2 b).

Considering that high-risk subjects are frequently guests of nursing homes, and also accounting for the numerous outbreaks reported in these settings across European countries (42), we report on COVID-19 burden in our study settings. The proportion of COVID-19 deaths recorded in the nursing homes is, according to available data, between 14% and 73% of total COVID-19 deaths, in almost all the regions analyzed, but in the two Spanish regions the proportion exceeded 60% (54). However, it is necessary to take into account that different diagnostic test strategies, as well as different definitions of COVID-19 deaths, have been adopted in the various countries, potentially reducing the identification of cases. Moreover, especially at the beginning of the epidemic, there was a global shortage of reagents – useful for carrying out the molecular test – as well as health personnel (both in laboratory and for clinical assistance) (55). These factors must be taken into account in the interpretation of the total and not attributed to COVID-19 excesses mortality rates, which however are almost homogeneous in the 9 Regions except one (New York).

Although the Lombardy case was the first to be described by the media, it is of great scientific interest as well (56), since even the alleged excess of deaths compared to the other regions (57), this is not confirmed by our results. Given that the crude mortality rate (number of deaths for COVID-19 / reference population per unit of time) is largely affected by the age distribution of the population; and considering that COVID-19 has a greater disease burden among the elderly, it is appropriate to estimate age-standardized mortality. The standardized age mortality rate allows to increase the level of comparability and expresses the mortality rate that the population would have if the age distribution would be the same as the reference population (standard).

Possible bias

The nine areas analyzed have similar economic characteristics, healthcare standards and COVID-19 surveillance data collection procedures, which allowed us to make a reliable data comparison. The choice of these areas followed administrative borders and the availability of the disaggregated mortality data.

Our analysis considered daily COVID-19 mortality rates derived by national surveillance statistics, which are more reliable than infection notifications (laboratory confirmed cases). Indeed, notified cases data are largely lower as compared to true disease and infection burden, and highly variable depending on different testing strategies and criteria adopted in different regions (58, 59), although it cannot be ruled out that a portion of the deaths caused by COVID-19 went undiagnosed. In Table 2 we reported the definition of COVID-19 death adopted in each considered region. It should be noted that in surveillance systems in Ile de France and Greater London region only deaths occurred in hospital settings have been included. This could explain, at least partially, the lower value of the recorded mortality rate in these regions. However, we believe that this possible bias does not affect much our comparative estimates. Actually, mortality is more reliable than other types of data. Finally,

we explored excess mortality rates, because this measure allows to also estimate the indirect impact of the COVID-19 epidemic. Excess mortality also takes into account deaths potentially occurring due to lack of access to treatment, due to indirect effect of lockdown measures, of other non-COVID patients.

Conclusions

We analyzed the COVID-19 epidemic trend in nine regions and areas comparable from an economic, social, and healthcare perspective, using reliable indicators, such as the cause of death. In all considered areas the epidemic curve began to decrease around the 4th and 5th week, slowing down at 10 weeks since epidemic onset, with a mortality peak during the 4th week in all study settings but in Lombardy, Stockholms län and Bruxelles-Capital during the 5th week. However, in all cases the curves showed the classic model of logistic growth (60). This postponement of the peak of deaths could be attributed to the different type of adopted response approach. For instance, in Lombardy COVID-19 clinical management was more hospital-based, and then had a mixed approach (hospital and home) (61). This may have influenced the total number of confirmed deaths, as all hospitalized patients were tested for COVID-19. Of note that this region is the one with the highest number of elder populations. The age distribution in the 9 regions shows significant differences and, in this context, it appears particularly important, being the mortality rate for COVID-19 highly variable at different ages (about 100 times higher in the ≥80 group compared to the group <60 years). This aspect deserves further investigation to assess whether age itself is a risk factor, independently from the presence of comorbidities, as suggested in some studies (62). Having said that, it seems more logical to consider age-standardized mortality, because it reduces differences among regions, with the only exception of New York State (excess mortality), Hovedstaden (Copenhagen) and, in part, of Il-de-France (apparently lower mortality). The latter could find explanation, at least partially, in the different testing strategies of testing and definitions adopted by surveillance systems, including definition of COVID-19 death. However, these aspects cannot completely explain all the differences, also taking into consideration different epidemic dynamics and clinical evolution.

Lombardy remained the only region in which the capital-region (Milan) was not significantly affected by the epidemic wave, the city having mortality rates lower than the rest of the region. We have already expanded on potential explanation of this phenomenon (4). However, it should be noted that COVID-19 mortality rate in Lombardy, which was one of the lowest at 30 days since outbreak onset, grew more than in other regions starting form 5th week onwards, with a slower drop compared to other areas. A similar trend was recorded in Stockholms län. New York (both the entire State and the metropolitan area) largely exceed all the other considered regions in terms of COVID-19 mortality. This area is characterized by a younger population, a greater metropolitan population density, presence of many neighborhoods with foreign populations, a medium-low economic level, and a private health system. These elements might have played a role in excess mortality from COVID-19.

However, these data deserve further investigation, considering the different management approaches of phase 1 of the epidemic (mainly hospital with containment measures) compared to phase 2 (when efficient action at the community level is highly required and when nursing homes outbreaks could have played a significant role, particularly among the elderly and fragile patients).

In conclusion, it can be said that the impact of the COVID-19 epidemic has been significant in terms of mortality in at least 7 of the 9 metropolitan areas considered. Furthermore, COVID-19 mortality trends were relatively homogeneous even slightly shifted in time (onset of the epidemics). In addition, the Lombardy region reported the highest crude COVID-19 mortality (especially in the second phase of the epidemic) although then similar to the other European regions after standardization by age, having Lombardy elder populations with consequently high prevalence of chronic conditions. Future research on overall mortality over a longer period of time will allow to better assess the overall impact of the COVID-19 epidemic on population health. At the same time, the harvesting effect that anticipated death in patients with chronic

diseases, the possible excess of non-COVID-19 mortality during the epidemic peak due to non-use of health services, and the reasons behind lower reported mortality in some geographical areas need to be further investigated. Having reliable data to inform and support future outbreak response strategies will not only help reducing mortality but will also support public health action at the population level (63).

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Original article

Virological surveillance of SARS-CoV-2 in an Italian northern area: comparison of Real Time RT PCR cycle threshold (Ct) values in three epidemic periods

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Abstract. Aim of the study was to investigate the differences in Ct values in nasopharingeal swabs collected in three SARS-CoV-2 epidemic periods: first one from February 23 to March 25 (14 days from lockdown started on March 11); the second one from March 26 to May 18 (14 days from the end of strict lockdown on May 4) and the third one from May 19 until June 15. Viral RNA was detected in nasopharyngeal swabs obtained both from inpatients and outpatients. COVID-19 infection was confirmed according to the Ct values for N1 and N2 genes ascertained by Real-Time RT-PCR assay as described by the CDC. We calculated the prevalence of nasopharyngeal swabs tested positive for SARS-CoV-2, the mean and median of the Cts and the percentage of samples equal or below the Ct value of 25 in the 3 periods considered. The average value of Ct increased, going from 24.80 in the first epidemic period to 26.64 in the second period to 28.50 in the third period ($p < 0.001$). The percentage of samples with Ct lower than or equal to 25 also decreased sharply from 54.7% to 20.0%. These findings need to be integrated with epidemiological and clinical data. (www.actabiomedica.it)

Key words: SARS-CoV-2, nasopharyngeal swab, Real-Time RT PCR, cycle threshold, surveillance

Introduction

The SARS-CoV-2 epidemic has affected the Italian territory since February 2020 with the first 2 cases notified on January 30 in two subjects coming from China and with the first autochthonous official case notified on February 18 in Lombardy region in the Northern of Italy. Since then, after peaking in the third week of March, it has resulted in a total of 239,709 infections and 33,542 deaths as of June 23, 2020 (1).

Emilia-Romagna was one of the most affected regions with a cumulative incidence of 638.5 cases per 100,000 inhabitants and 4255 deaths; in particular, in the province of Parma, 3631 cases were notified from 23 February to 23 June 2020 (2).

At the beginning of the epidemic, there were 2 laboratories accredited at the WHO national center of the Istituto Superiore di Sanità (ISS) for the surveillance of respiratory virosis in Emilia-Romagna, identified on the basis of the experience acquired in the field of epidemic and pandemic flu viruses (3,4). With the progress of the epidemic event, other laboratories were gradually authorized by regional Health Authority reaching the current number of 11 which serves a population of 3,500,000 inhabitants.

The gold standard for laboratory diagnosis of COVID-19 infection is reverse transcription (RT) real-time PCR test: since the sequence of SARS-CoV-2 was shared, several molecular diagnostic tests through specific primers and probes were designed for the rapid detection by Real-time RT-PCR (6,7). In real time PCR the cycle threshold (Ct) values are inversely related to viral RNA copy numbers (8). ECDC underlines that SARS-CoV-2 detection for diagnosis of patients with COVID-19-like symptoms is essential for patient care, triage and isolation in healthcare facilities. SARS-CoV-2 detection can also be used for screening close contacts for asymptomatic infection and disease as part of contact tracing or outbreak investigations. Testing is also used to screen for infection in crucial target groups like healthcare and social workers as part of local surveillance programmes (8).

The aim of the study was to investigate the differences in Ct values in nasopharingeal swabs (NS) collected in three SARS-CoV-2 epidemic periods.

Methods

We retrospectively divided the surveillance's period into three phases: the first one from February 23 to March 25 (14 days from lockdown started on March 11); the second one from March 26 to May 18 (14 days from the end of strictly lockdown on May 4) and the third one from May 19 until June 15. Viral RNA was detected in NS obtained both from inpatients and outpatients. COVID-19 infection was confirmed according to the Ct values for N1 and N2 genes ascertained by RT-PCR assay as described by CDC (10). We calculated the prevalence of NS test positive for SARS-CoV-2, the mean and median of the Cts and the percentage of samples equal or below the Ct value of 25 in the 3 periods considered. We applicated Chi-square test to assess any differences in distribution by period and the two side Analysis of Variance test to assess differences in mean Ct values. All test were considered statistically significant at $p<0.05$. Analysis were performed by SPSS 26.0 (IBM, Chicago, ILL).

Results

From 23 February 2020 to 15 June 2020, 31,030 swabs were analysed, of which 3557 (11.5%) tested positive for SARS-CoV-2, with a different and statistically significant distribution in the three periods considered (Table 1).

During the phase characterized by the epidemic peak, 44.3% of the samples tested positive, this per-

Table 1. Negative and positive samples and Ct values in the three periods considered

Study Period	Overall	Negative samples		Positive samples (*)		Ct values (°)					Ct below or equal to 25 (%) (§)
	No.	No.	%	No.	%	Mean	St.dev	Median	Lowest	Highest	
23 February - 25 March (+ 14 days after lockdown)	4173	2326	*55.7%*	1847	*44.3%*	24.80	4.77	25.00	10.00	35.00	54.7%
26 March - 18 May (+ 14 days after phase 2 begin)	14,149	12,850	*90.8%*	1299	*9.2%*	26.64	4.85	28.00	10.00	35.00	36.7%
19 May - 15 June (phase 2)	12,708	12,297	*96.8%*	411	*3.2%*	28.50	4.40	30.00	10.00	35.00	20.0%
Overall	31,030	27,473	*88.5%*	3557	*11.5%*	25.89	4.92	27.00	10.00	35.00	44.2%

(*) Chi Square test: $p<0.001$; (°) Analysis of Variance: $p<0.001$; (§) Chi Square test: $p<0.001$

centage dropped to 9.2% in the second period considered and then decreased further in the third period coinciding with phase 2 of the epidemic event (3.2%).

In the three identified periods, the average value of Ct increased, going from 24.80 in the first epidemic period to 26.64 in the second period to 28.50 in the third period (p <0.001). The percentage of samples with Ct lower than or equal to 25 also decreased sharply from 54.7% to 20.0%.

Discussion

Our study is a description of the Ct values trend in relation to different period of epidemic, showing a statistically significant increase in CTs, which indicates a reduction of RNA viral copies. However, in the first phase of the epidemic, the samples came largely from hospitalized patients with medium-severe clinical symptoms, while in the third part most of the samples came from non-hospitalized subjects involved in local screening activities. Many samples, especially in the second period under study, were so-called "healing samples", that is, performed in subjects declared clinically healed and then performed at least 14 days after the onset of symptoms. Beyond the clinical significance, it is difficult to establish the real epidemiological significance of such low viral loads, considering the different framework of population tested. These hypotheses need to be verified with specific studies aimed at integrating epidemiological and clinical date.

Acknowledgment

We sincerely thanks all Colleagues and Volunteers that supported our Laboratory during the epidemic period.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Original article

Post-COVID-19 follow-up clinic: depicting chronicity of a new disease

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Abstract. *Background and aim of the work:* The coronavirus disease-19 (COVID-19) outbreak is posing considerable challenges to healthcare systems and societies worldwide. While the knowledge on the acute phase of the disease has rapidly expanded, little is known on the consequences of COVID-19 following clinical remission. We set up a multidisciplinary COVID-19 follow-up outpatient clinic to identify and address the clinical needs of COVID-19 survivors. Here we describe the features of our follow-up programme. *Methods:* The multidisciplinary assessment comprises a complete physical examination, respiratory evaluation (peripheral oxygen saturation, respiratory rate, dyspnoea assessment, lung ultrasound and pulmonary function), cardiovascular assessment (electrocardiography, echocardiography), nutritional assessment (anthropometrics, mini Nutritional Assessment screening tool), neurological examination including cognitive tests, and mental health assessment. All data are prospectively collected, and blood is sampled for biobanking. *Results:* Since 7 April to 5 June, 2020, 453 out of the 1388 COVID-19 survivors managed at our University Hospital have been evaluated at the Outpatient COVID-19 Follow-up Clinic. The characteristics of the follow-up cohort are similar to those of the whole cohort of COVID-19 in terms of demographics, comorbidities, and COVID-19 severity upon ED presentation, indicating that the follow-up cohort is representative of the whole cohort. *Conclusions:* Continuous patient monitoring might give an answer to the numerous unsolved questions about what comes next in this pandemic and beyond. This will help physicians and researchers establish strategies to face future pandemics and develop preventative and therapeutic strategies for similar hyperinflammatory conditions. (www.actabiomedica.it)

Key words: COVID-19, follow up, outpatient

Introduction

Coronavirus disease-2019 (COVID-19) is a novel disease caused by the Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2). Since its first description in December 2019, COVID-19 soon progressed into a major public health concern, prompting the scientific society to join forces to respond consciously to this common challenge (1). Rapidly accumulating clinical experience on COVID-19 paved the way for an extensive and prompt characterization of the acute phase of the disease. However, we lag behind in the knowledge of COVID-19 evolution in survivors.

Available data on long-term sequelae of previous coronavirus diseases are scarce, and their reproducibility in SARS-CoV-2-infected patients is questionable (2,3). Besides pulmonary function, COVID-19 may

affect renal (4), cardiovascular (5), and neuropsychiatric (6) health, as well as nutritional status (7). The extent to which these alterations may persist remains obscure.

With the aim of identifying and addressing the clinical needs of COVID-19 survivors, we implemented a multidisciplinary COVID-19 follow-up outpatient clinic at our hospital. Patient data and blood samples are collected prospectively in an attempt to combine patient care and answer crucial questions about the pathophysiology of COVID-19 and the consequences of the disease.

Our multidisciplinary model

This follow-up programme is part of the COVID-BioB study, a large observational investigation performed at San Raffaele University Hospital, a tertiary health-care hospital in Milan, Italy. The study protocol was approved by the Hospital Ethics Committee (protocol no. 34/int/2020) and registered on ClinicalTrials.gov (NCT04318366). All patients enrolled in the follow-up programme provided a signed informed consent prior to any study procedures.

All hospitalized patients are offered to participate in the follow-up programme. For patients managed at home after discharge from the Emergency Department (ED), telephonic consultation by a trained physician discriminates patients for whom the follow-up visit is recommended. Outpatient visits are scheduled at 4 weeks, 3 months and 6 months after hospital discharge.

The Outpatient COVID-19 Follow-up Clinic's team comprises internists, neurologists, psychiatrists, cardiologists, nutritionists and nephrologists. Data about the initial presentation of COVID-19 and the disease course are retrospectively scrutinized from medical records in the presence of the patient and integrated with detailed medical history. Complete physical examination and vital sign assessment including measurement of peripheral oxygen saturation with a pulse oximeter are performed on all patients. Respiratory rate is measured by counting respiratory chest movements of over a period of 60 seconds. The modified Medical Research Council (mMRC) scale for dyspnoea is used to quantify residual shortness of breath. The respiratory assessment is complemented by lung ultrasound. Cardiovascular assessment includes electrocardiography and echocardiography. Patients are asked to self-rate their health status on a visuo-analogue scale (VAS)(8). The nutritional assessment includes measurement of height and body weight, as well as of waist circumference as an estimate of adiposity (9). The Mini Nutritional Assessment (MNA) screening tool is used to evaluate nutritional status, with an MNA value ≤7 defining malnutrition and a score between 8 and 11 identifying patients at risk of malnutrition(10). Complete neurological examination is performed to exclude neurological *sequelae*. Cognitive function is inspected through the Montreal Cognitive Assessment (MoCA) score(11), where a score <24 in the absence of known history of neurocognitive disease identifies cognitive impairment. Mental health counselling is an integral component of the follow-up evaluation. Quality of life assessment through the World Health Organization Quality of Life (WHO-QOL) –BREF questionnaire(1) and screening of insomnia, anxiety, and post-traumatic stress disorder (PTSD) through validated indicators (12-14) are performed in all patients.

Demographic, anthropometric, clinical and instrumental data are prospectively collected. Blood samples are centrifuged to separate plasma, serum, peripheral blood white cells, and supernatant, which are then aliquoted and frozen for subsequent use. Samples and data are available to the entire research community, upon reasonable request.

Our patients

Since the beginning of the Outpatient COVID-19 Follow-up Clinic on 7 April 2020, as of 5 June 2020 453 patients have been evaluated.

Patients admitted to our University Hospital as of 5 June were 1167, of whom 860 (73.8%) hospitalized. Of these, as of the same date, 187 (21.7%) had died, 628 (73%) had been discharged, and 45 (5.3%) were still hospitalised.

Of the 453 patients evaluated at the Outpatient Clinic, 363 (57.8% of the hospitalised cohort) had

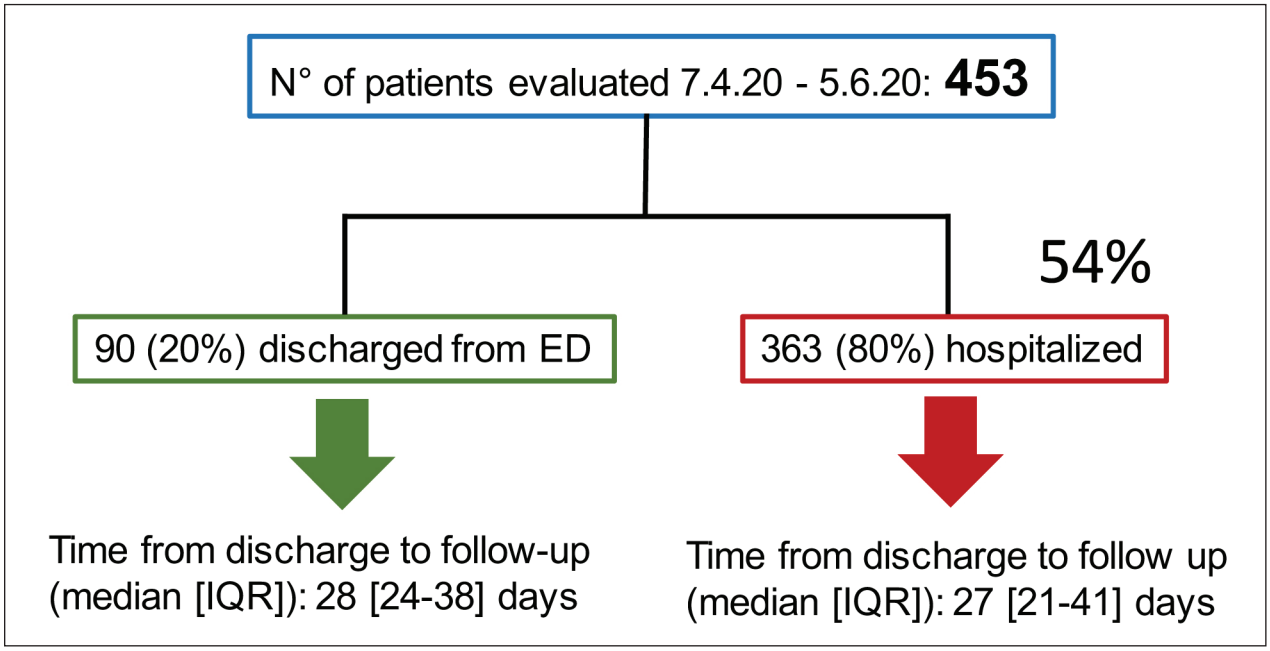

Figure 1. Study flow chart

been hospitalised and 90 discharged home from the ED (Figure 1). Reasons for patients' failure to follow-up included: *i)* missed phone calls (40%), *ii)* refusal to follow-up due to subjective recovery or work commitments (20%), *iii)* long distance of the hospital from home (15%), *iv)* stay in rehabilitation institutes (15%), and *v)* impossibility to physically reach the hospital due to transportation difficulties (10%).

Patients evaluated at the follow-up visit so far are representative of the whole cohort of COVID-19 survivors seen at our University Hospital, having comparable features in terms of demographics, comorbidities, and COVID-19 severity at ED presentation (Figures 2 and 3). Most patients were males in both groups of patients. Median (interquartile range, IQR) age in the entire COVID-19 population and in the follow-up cohort was 59 (49-70) and 59 (49-68) years, respectively ($p>0.05$).

The ratio of arterial oxygen partial pressure (PaO_2) in mmHg to fractional inspired oxygen (FiO_2) expressed as a fraction (PaO_2/FiO_2), serum levels of C-reactive protein (CRP) and lactate dehydrogenase (LDH), and absolute lymphocyte count at ED presentation served as markers of disease severity. Median (IQR) PaO_2/FiO_2 was 304.8 (251.4-349) in the COVID-19 cohort and 309.5 (261.9-348.7) in the follow-up group ($p>0.05$). Median (IQR) absolute lymphocyte count was 1 (0.8-1.4) $x10^9$/L in both patient groups. Median serum levels of CRP and LDH in the entire COVID-19 population were 55.5 (19.1-109.2) mg/L and 325 (254-429) U/L, respectively. On the other hand, the follow-up cohort had median (IQR) levels of CRP and LDH of 54.6 (19-104.8) mg/L and 321 (256-415.2) U/L, respectively. No significant difference in serum CRP and LDH levels at ED presentation was found between the two patient cohorts ($p>0.05$) (Figure 4).

Questions that this project will allow us to answer

Awareness of what to expect from the second phase of this pandemic is crucial to minimise long-term morbidity and mortality associated with COVID-19. Following survivors over time might reveal unexpected COVID-19 *sequelae* and help guarantee prompt and informed medical care. Residual lung damage may be present after the resolution of the

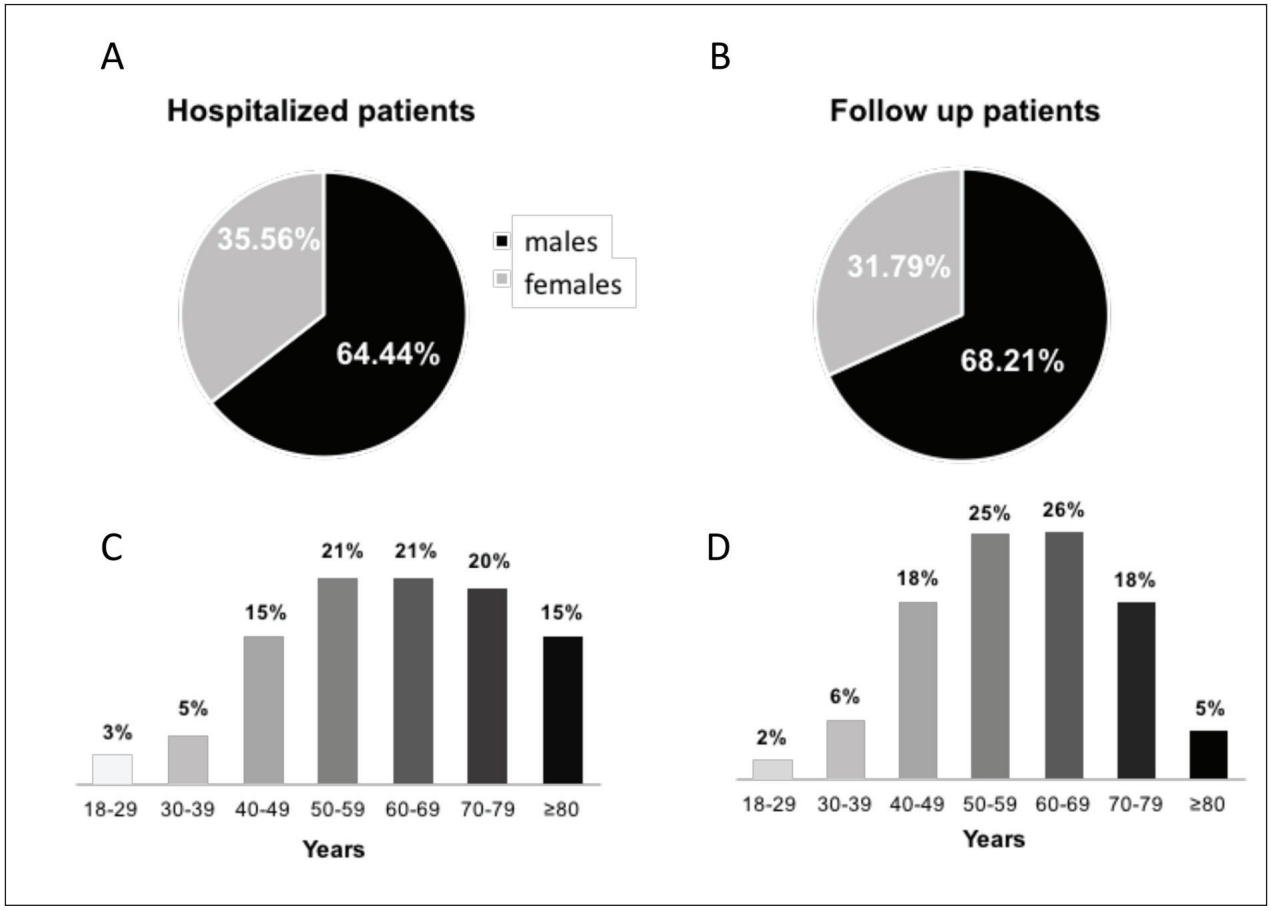

Figure 2. Comparison of demographics between hospitalized and follow-up COVID19 patients

acute phase of the disease (15). Indeed, fibrosis may supersede tissue inflammation independently of viral eradication (16). Besides clinical parameters and reported shortness of breath, PFT and lung ultrasound may provide an objective insight into pulmonary function and disclose persistent subclinical lung alterations. Chronic cardiovascular damage in COVID-19 has been hypothesised (17) . In this sense, periodic electrocardiographic and echocardiographic evaluations by an expert cardiologist may be needed to monitor both electric and mechanic heart function over time. Nutritional status is also a matter of concern in COVID-19 patients, systemic inflammation-related hypercatabolism representing a potential mechanism (18) . Patients surviving to acute respiratory distress syndrome tend to lose lean body mass during acute illness in favour of fat mass, which may be detrimental for functional recovery (19). In patients with a less severe pulmonary involvement, gastrointestinal symptoms (20). and smell and taste disturbances (21) associated with SARS-CoV-2 infection may play a role. Nutritional counselling is therefore crucial to COVID-19 patients. Cognitive function following COVID-19 should also be assessed, due to the potential impact of both direct viral pathogenicity and immune-mediated mechanisms on the development of cognitive *sequelae (22)*. Psychological health might be undoubtedly endangered by COVID-19. Fear of disease complications and restriction of human contact may generate anxiety, and in some cases post-

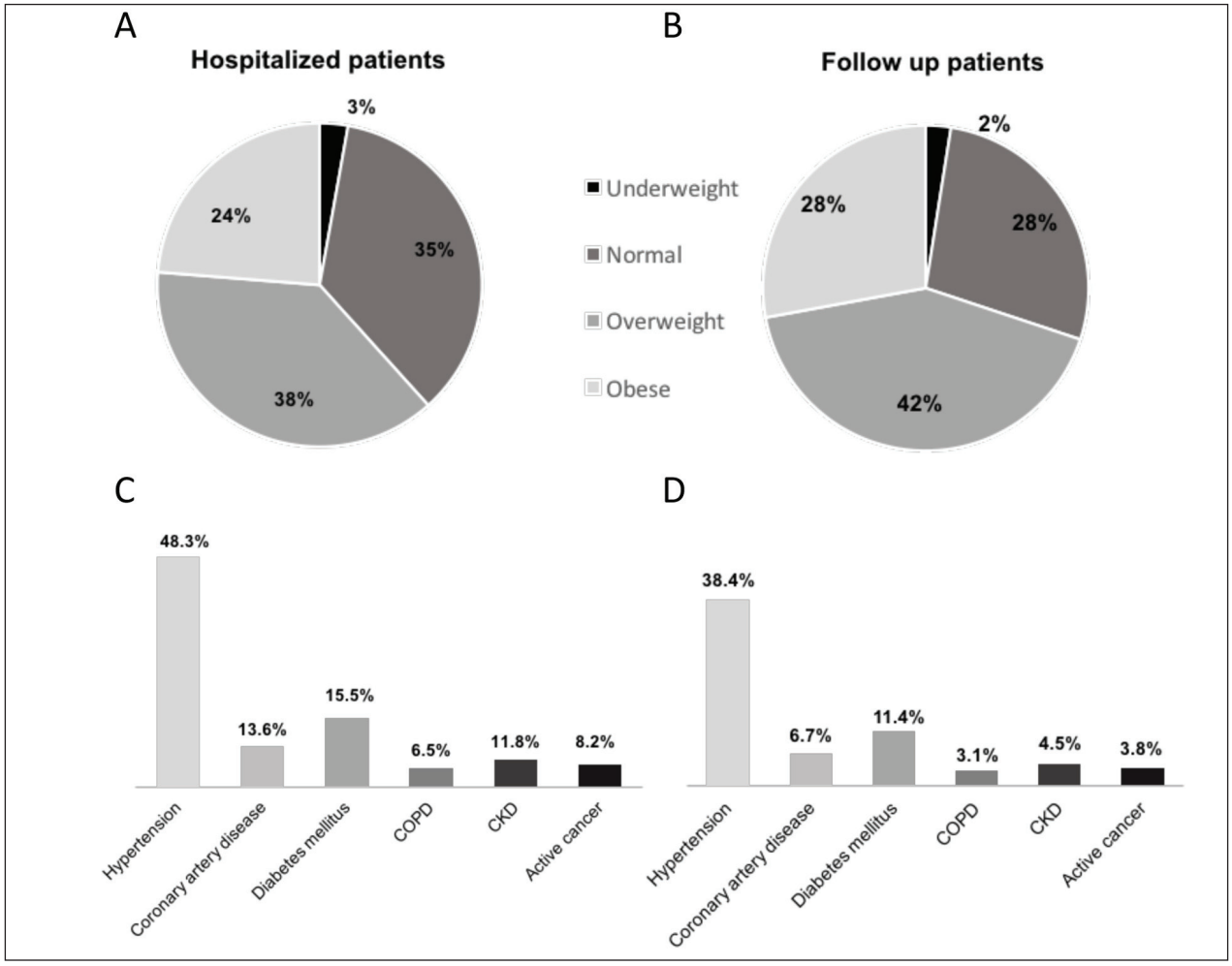

Figure 3. Comparison of comorbidities between hospitalized and follow-up COVID19 patients. COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease

traumatic stress disorder may develop (23). Adequate mental counselling is therefore critical to investigate neuropsychological *sequelae* of COVID-19 and to preserve mental well-being.

Besides the clear contribution to the advancement in the knowledge of COVID-19 *sequelae*, the prospective collection of blood samples implemented at our Outpatient COVID-19 Follow-up Clinic represents an invaluable source of biologic material to be used for research in COVID-19. Patients will be subsequently evaluated (internal medicine, neurological and psychiatric assessment) and biospecimens retrieved at 3 and 6 months post-discharge, which guarantees an attentive care-delivery system which may have important implications for both patient care and research. Patients who suffered from severe COVID-19 (those admitted to the Intensive Care Unit or requiring high-flow oxygen therapy or non-invasive ventilation) will undergo a specific pulmonary follow-up through pulmonary function tests (PFT), impulse oscillometry and lung CT scan.

In conclusion, continuous patient monitoring might give an answer to the numerous unsolved questions about what comes next in this pandemic and beyond. This will help physicians and researchers establish strategies to face future pandemics and develop

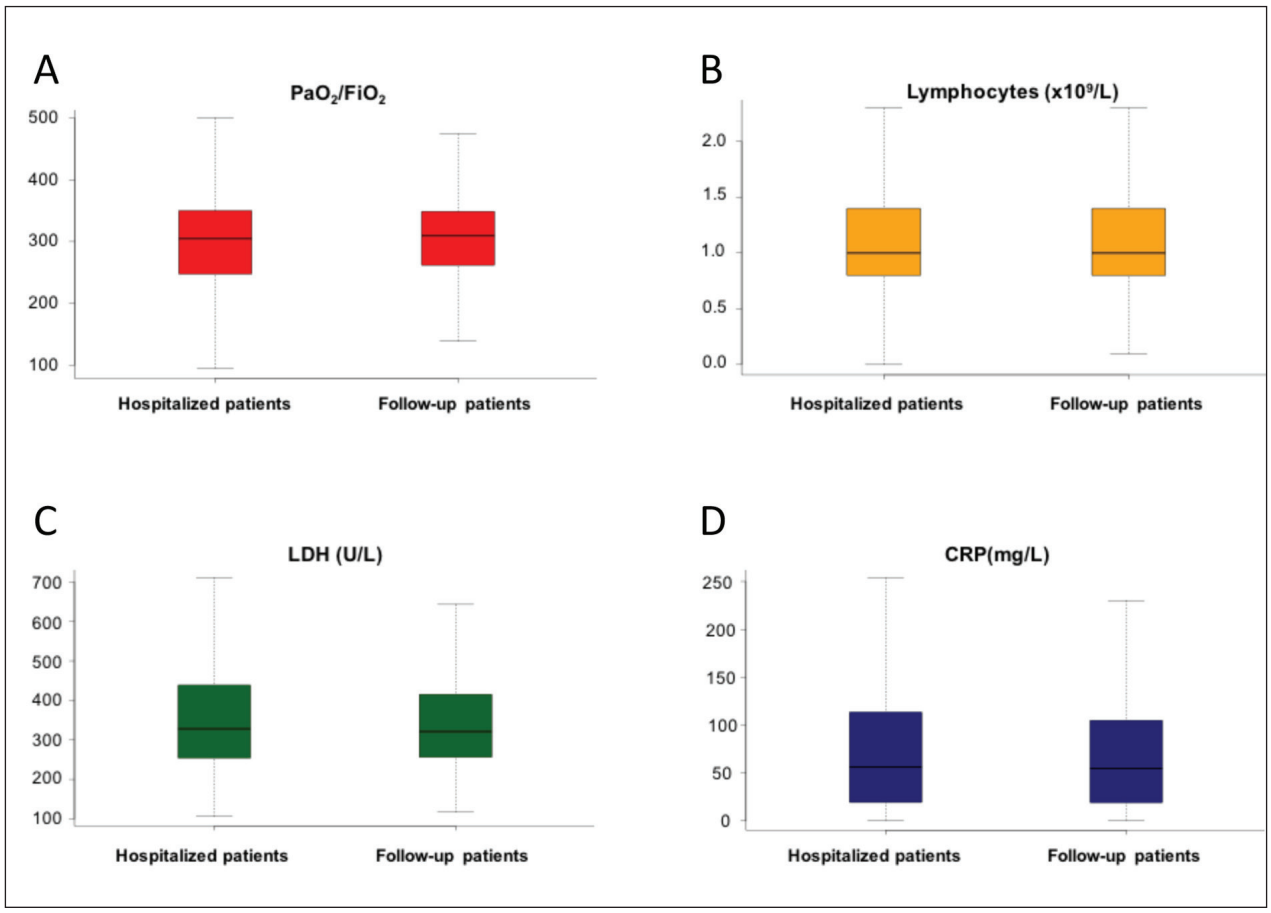

Figure 4. Comparison of markers of disease severity between hospitalized and follow-up COVID19 patients. PaO_2/FiO_2, ratio of arterial oxygen partial pressure (PaO_2) in mmHg to fractional inspired oxygen (FiO_2); CRP: C-reactive protein; LDH: lactate dehydrogenase

preventative and therapeutic strategies for similar hyperinflammatory conditions.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Original article

Monitoring emergency calls and social networks for COVID-19 surveillance. To learn for the future: The outbreak experience of the Lombardia region in Italy

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Abstract. On 18th February the first Italian case of Coronavirus Induced Disease 2019 (COVID19) due to secondary transmission outside China was identified in Codogno, Lombardia region. In the following days the number of cases started to rise not only in Lombardia but also in other Italian regions, although Lombardia remained and it is still the most affected region in Italy. At the moment, 234801 cases have been identified in Italy, out of which 90070 in Lombardia region. The (Severe Acute Respiratory Syndrome Coronavirus 2) SARS CoV 2 outbreak in Italy has been characterized by a massive spread of news coming from both official and unofficial sources leading what has been defined as infodemia, an over-abundance of information – some accurate and some not – that has made hard for people to find trustworthy sources and reliable guidance needed. Infodemia on SARS CoV 2 created the perfect field to build uncertainty in the population, which was scared and not prepared to face this outbreak. It is understandable how the rapid increase of the cases' number , the massive spread of news and the adoption of laws to face this outbreak led to a feeling of anxiety in the population whose everyday life changed very quickly. A way to assess the dynamic burden of social anxiety is a context analysis of major social networks activities over the Internet. To this aim Twitter represents a possible ideal tool since the focused role of the tweets according to the more urgent needs of information and communication rather than general aspects of social projection and debate as in the case of Facebook, which could provide slower responses for the fast individual and social context evolution dynamics. Aim of the paper is to analyse the most common reasons for calling and outcomes. Furthermore, the joint analysis with Twitter trends related to emergency services might be useful to understand possible correlations with epidemic trends and predict new outbreaks. (www.actabiomedica.it)

Key words: emergency calls and social networks for COVID-19 surveillance

Background

On 18th February the first Italian case of Coronavirus Induced Disease 2019 (COVID19) due to secondary transmission outside China was identified in Codogno, Lombardia region (1). In the following days the number of cases started to rise not only in Lombardia but also in other Italian regions, although Lombardia remained and it is still the most affected region in Italy. At the moment, 234801 cases have been identified in Italy, out of which 90070 in Lombardia region (2,3).

The (Severe Acute Respiratory Syndrome Coronavirus 2) SARS CoV 2 outbreak in Italy has been characterized by a massive spread of news coming from both official and unofficial sources leading what has been defined as infodemia, an over-abundance of information – some accurate and some not – that has made hard for people to find trustworthy sources and reliable guidance needed (4).

Infodemia on SARS CoV 2 created the perfect field to build uncertainty in the population, which was scared and not prepared to face this outbreak. It is understandable how the rapid increase of the cases' number, the massive spread of news and the adoption of laws to face this outbreak led to a feeling of anxiety in the population whose everyday life changed very quickly.

A way to assess the dynamic burden of social anxiety is a context analysis of major social networks activities over the Internet. To this aim Twitter represents a possible ideal tool since the focused role of the tweets according to the more urgent needs of information and communication rather than general aspects of social projection and debate as in the case of Facebook, which could provide slower responses for the fast individual and social context evolution dynamics (5,6).

Taking into account this specific context, it is easy to understand why the emergency number - 112 - was suddenly overwhelmed by an enormous number of calls that rapidly overcame its capacity to cope and compromised the possibility to identify those patients who needed immediate medical assistance.

As pointed out by the Scientific Italian Society for Medical Emergency (SIEMS), number of calls to 112 for the Milan province were 5086 on 16th February, before the outbreak, and rapidly increased to 6798 on 21st and 10657 on 22nd February (7).

The emergency service in Lombardia region is organized through 3 first-level PSAPs (public-safety answering points) called CUR-NUE (Unique answering operating room / point – European emergency number) that send the call to the most appropriate service, i.e. Police, Fire or medical department. After the first assessment, calls requiring medical assistance are sent to one of the four *second-level* PSAPs called SOREU (Regional Operating Rooms for Medical Emergency and Urgency), depending on the area the call is coming from in order to evaluate the patient and decide the most appropriate intervention.

To reduce the burden of calls of the first days of the outbreak to the emergency number it was necessary to redirect non urgent calls, especially those asking for information, to other services. According to European Emergency Number Association guidelines (5), Lombardia region created a regional toll-free number for COVID19, the first one in Italy. Other Italian regions created their own one in the following weeks, as well as other European countries like Spain, Germany, Croatia etc. that were facing similar issues (8).

The main goals of the regional toll-free number were:

- Reduce the burden of calls for emergency line (112)
- Give information about the outbreak and how to manage influenza-like symptoms and emphasize good behaviours to avoid the risk of infection
- Identify people who had close contacts with confirmed cases in order to isolate them at home and notify them to local health authority

The 24/24 hour toll-free number was settled on 23rd February by AREU (Regional Emergency Service Agency) in collaboration with residents in preventive medicine and public health from University of Milan. The first location was opened in Milan, but a second one was opened after some days due to the overwhelming number of calls received.

Volunteers belonging to different associations of civil society kindly provided their support in this moment of crisis and were recruited as telephone operators. Residents were in charge of training volunteers in order to prepare them to answer to most common doubts about SARS CoV 2. Flowcharts, infographics, and frequently asked questions sheets were developed to help volunteers give standardised and evidence-based answers to the population, furthermore they were provided with contacts of other public institutions like social services, medical service for continuity of care and local health authorities to guide population to refer to the right service.

Although the regional info line helped to funnel non urgent calls it was not enough because of the huge number of calls, for example on the first day it received about 400000 calls.

Each call was documented with a report containing important information such as brief anagraphic, reason for calling, and the outcome.

Aim of the paper is to analyse the most common reasons for calling and outcomes. Furthermore, the joint analysis with Twitter trends related to emergency services might be useful to understand possible correlations with epidemic trends and predict new outbreaks.

Materials and methods

We analysed all the calls made by s*econd-level* PSAP from 21st February to 11th March 2020. These calls were made to those who did not received an answer from 112 due to clogged phone line or were evaluated as non-urgent calls by a first NUE rapid assessment.

Each call had a report with time and date, municipality from which the call was coming from, brief information about the patient and the reason of the call. The final outcome was codified according to the SOREU usual system as: information, consultation, first aid or other.

As for Twitter analysis it was made collecting all tweets in Italian language with "112" or "118" in the text from 21st February to 11th March 2020. Further analysis on the text of the tweets was made in order to identify most common keywords related to the emergency bringing to the identification of 290 keywords. All tweets that did not contain any keyword in the text were excluded from the final analysis as non relevant, leading to 5989 twitters used for the purpose of this article.

Results

Table 1 shows the total number of calls and their classification for each SOREU made by *second-level PSAPs* and their classification. The most outstanding data is that only 2.89% of calls made were classified as first aid and therefore needed urgent medical assistance. shows number of calls

Concerning Twitter analysis, in Fig. 2a we reported the trends in the number of tweets produced daily and the number of replies they received. In the time series of the number of tweets we can identify two periods associated with increases in activity. The first period from 21/02 to 25/02 is associated with the days preceding the establishment of the red areas of Codogno and Vò Euganeo, while the second moment is 09/03, the day between the measures of regional and national lockdown. Concerning the number of replies, we observe a first increase in the same period indicated by the number of tweets and a peak on 02/29.

Table 1. Number of calls, their total and their classification for each SOREU

	Second-level PSAPs - SOREU				Total number of calls
	SRM	**SRA**	**SRP**	**SRL**	7436
Time period	21/02/2020 - 11/03/2020	21/02/2020 - 11/03/2020	23/02/2020 – 11/03/2020	23/02/2020 - 11/03/2020	
Number of calls	2340	2318	2029	749	
Classification					
Information	2128 (90.9%)	156 (6.7%)	108 (5.3%)	102 (13.6%)	2494 (33.54%)
Consultation	162 (6.9%)	2073 (89.4%)	1853 (91.3%)	632 (84.4%)	4720 (63.47%)
First aid	50 (2.1%)	88 (3.8%)	63 (3.1%)	14(1.9%)	215 (2.89%)
Other		1	5 (0.02%)	1 (0.1%)	7 (0.09%)

Legend
SRM: SOREU Area Metropolitana (Milan and Monza-Brianza); SRA: SOREU Area Alpina (Bergamo, Brescia and Sondrio); SRP: SOREU Area della Pianura (Lodi, Pavia, Cremona and Mantova); SRL: SOREU Area dei Laghi (Varese, Como and Lecco)

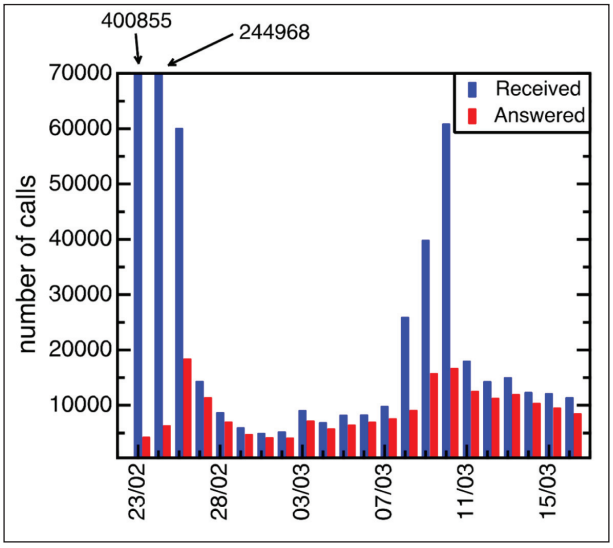

Figure 1. Number of calls received and answered by regional toll-free information number

A similar analysis was carried out for the retweet and like trends - see Fig. 2b - in which the increases in the period 21/03 - 23/03, and on 25/02, 06/03 and 09/03 are evident.

Concerning the semantic analysis of tweets, a set of 290 keywords has been identified relating to the relevant areas. In Fig. 3 a word cloud is reported relating to the set of keywords, where the word size is proportional to the frequency of the word in the bulk of tweets.

In addition to the keywords "112" and "118" which constituted the initial search set, it is rather frequent the phone number "1500" relating to the public utility service activated at the end of January 2020 to offer citizens information on COVID-19, the word "symptom" and some terms related to the emergency situation such as "emergenza" (emergency) or "soccorso" (rescue).

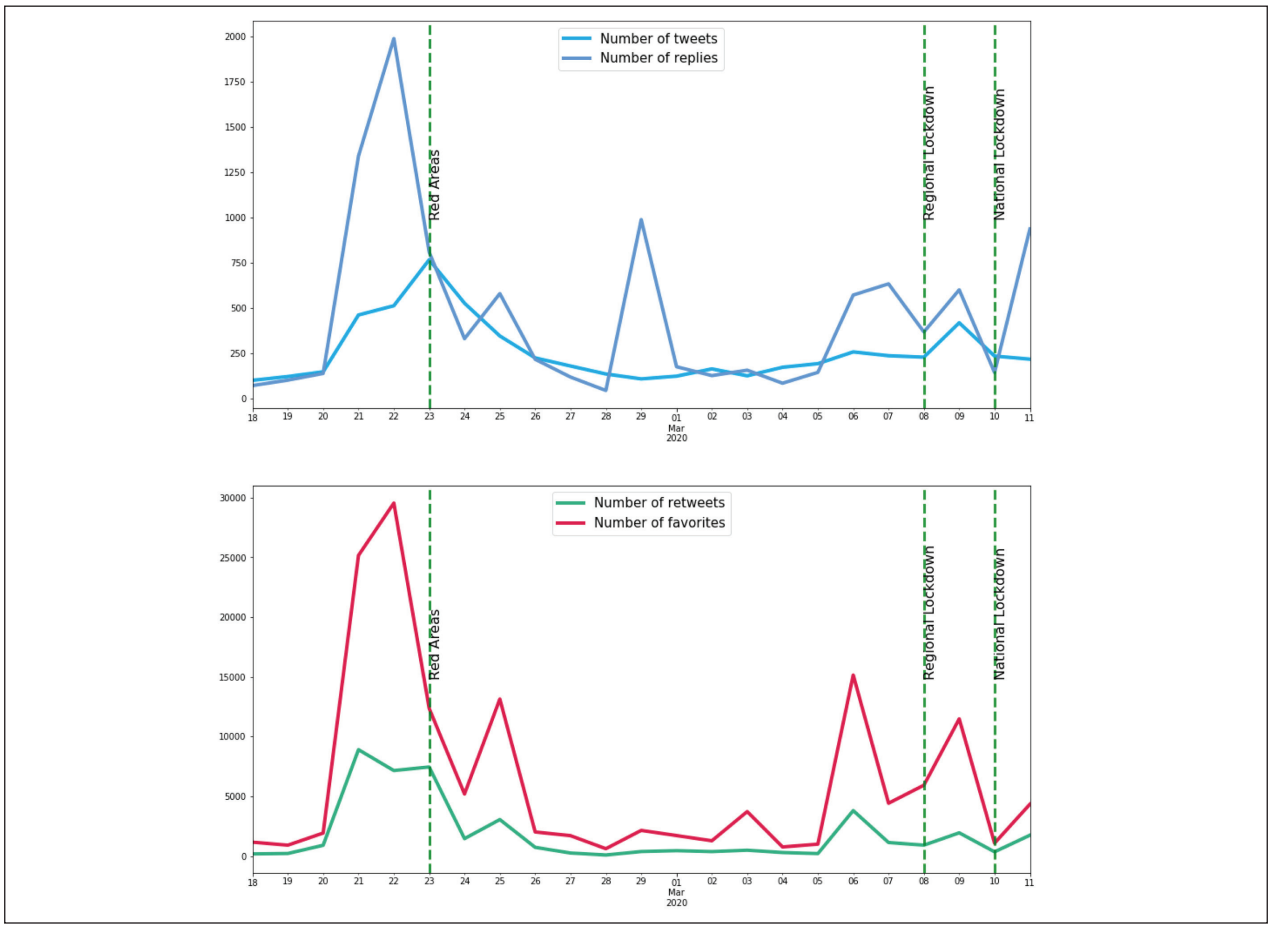

Figure 2. a) Number of daily tweets and replies; b) Number of daily retweets and likes. National and Regional lockdown events have also been reported together with the establishment of the red areas of Codogno and Vò Euganeo

Figure 3. Word Cloud of the keywords

Discussion

These data confirm that the overwhelming number of calls received to the emergency service was not due to the necessity of first aid but to the need of information or medical assistance for non urgent conditions. It's important to point out that this consideration does not apply to all the calls received by emergency service because these data are referred only to those calls that did not received an answer or were already filtered by first level PSAPs as non-urgent. Nevertheless it is remarkable how the panic induced by the increasing number of cases of COVID 19 brought a huge number of people to call the emergency service even if not necessary, seriously compromising its ability to answer to real urgent calls. This consideration is confirmed by data coming from the regional toll-free number showed in fig. 1, in fact it is possible to see how it received hundreds of thousands of calls in less than a month. Such an evidence is associated also to the dynamic patterns of the Twitter analysis showing the need of information related to the social anxiety. Further ongoing work is involving the first calls to the to the emergency service according to the predictive value over the spread of infections. Overall the joint active monitoring of the communication dynamics over emergency calls and social networks like Twitter could provide an integrated mean for the adaptive management of information delivery as well as well as the optimization of the rescue logistic and finally it could provide relevant anticipation on the outbreak. Overall these aspects appears of critical importance for COVID-19 surveillance, and for the preparedness of emergency and strategic plans (9).

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Original article

The runaway science: a bibliometric analysis of the COVID-19 scientific literature

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Abstract. *Background and aim of the work:* To reflect on content, trends and quality of scientific publishing on COVID-19. In particular, to report on the systematic screening, quantitative assessment and critical appraisal of the first 10,000 scientific papers published on COVID-19 and to compare how scientific outputs matched identified research priorities and public health needs. *Methods:* A comprehensive research strategy was developed to systematically retrieve on a daily basis all studies published on COVID-19. From included studies we extracted: bibliometric parameters, country of studies' implementation and study design. We assigned papers to 25 a priori defined COVID-19-related topics and we described scientific outputs in relation to countries' academic publishing ranking, as well as COVID-19 burden. *Results:* 10,000 scientific articles were published on COVID-19 between 20th January and 7th May 2020, accounting for 2.3% of total scientific production over the study period. One third (33%) focused on COVID-19 clinical management, with little adherence to identified research priorities. Over sixty per cent of papers were opinion pieces not reporting original data. Papers were published on 1881 different journals but with half of scientific production included in 8% of journals. The US accounted for one fourth of total scientific production, followed by China (22.2%) and Italy (9%). *Conclusions:* Never before in the history of academic publishing such a great volume of research focused on a single topic, this being likely to introduce major changes in the way science is produced and communicated, at the risk of bringing it far from its ultimate aim: informing clinical and public health practice and decision making. (www.actabiomedica.it)

Key words: COVID-19, public health, research priorities, bibliometric analysis, academic publishing, scientometric analysis

Introduction

COVID-19 pandemic is sparking an unprecedented wave of publications. The Economist positively commented on such exponential publishing trends, underlining how the virus "has changed the way scientists do their work and talk to each other" (1). Experts claim COVID-19 has accelerated much anticipated cultural shift in biomedical publishing, the question being, is it happening "for the best"? The global public health emergency context (2-4) has pushed, for example, journals in laudable efforts (5) to fast track peer reviews, and publishers to waive publication fees and provide free access to articles' content; it has pushed forward the preprints' model carrying both pro and con arguments. Do we, the scientific community, agree that "for the best" means to truly inform clinical and public health practice and decision making? In this

context we aimed to conduct a systematic screening, quantitative assessment and critical appraisal of the first 10,000 scientific papers published on COVID-19.

Methods

The "COVID-19 literature task force", was established within the Clinical Epidemiology Unit of San Raffaele Research Institute in Milan (Italy) to inform and support decision making of hospital clinical teams and regional health authorities. A comprehensive research strategy was developed to systematically retrieve, on a daily basis, all scientific papers on COVID-19 indexed on Medline. All study designs were included, and no language restrictions were set. Selected variables of interest were extracted from included studies by two researchers in blind. An *ad hoc* algorithm was developed to extract from each paper all bibliometric parameters. We assigned each paper to the country of the first author's affiliation. Retrieved records were manually classified by study type and assigned to one of 25 different *a priori* defined COVID-19 sub-topics. For clinical papers the specific clinical field of investigation was identified. Scientific journals' impact factor was obtained from the Web of Science Journal database. We conducted descriptive analysis on all parameters and variables of interest; scientific production by topic, and sub-topic was assessed over time. Research production by country was compared to the total research volume for the year 2019 reported by the Nature Index (6). Scientific outputs by country were assessed against countries' COVID-19 epidemiological burden.

Results

Our search strategy retrieved 12,201 PubMed indexed papers between December 31st 2019, and May 7th 2020. After removing duplicates and articles not related to COVID-19, 10,000 publications were selected for analysis. The first papers were indexed on PubMed on 20th January; Over the study period COVID-19-related papers accounted for 2.3% of all global scientific production, this percentage increasing over time, from 0.3% in February, to 7.1% in May. On average, 92.6 new papers on COVID-19 were indexed every day, with a peaks at 500 articles indexed per day in May. Included papers were published on 1881 different scientific journals. Less than 8% of journals published half of total COVID-19 scientific production, with two journals publishing over 200 papers on COVID in a bit more than three months (BMJ n=337, the Journal of Medical Virology n=230). On the contrary, 43.3% of journals only indexed one COVID-19 article each. Globally, scientific journals had a mean impact factor of 8.4. Half of indexed papers were published in journals with an impact factor lower than 3.5.

The largest share of papers published on COVID-19 focused on clinical aspects; in particular, 10.1% of total production was on clinical management of COVID-19 patients and 22.9% on other diseases and fields of medicine in relation to COVID-19 implications (Figure 1), with particular reference to oncology (11.4% of all specialty-specific papers) and cardiology (11.3%). 9.7% of papers reported on COVID-19 epidemiology or surveillance data in different national, regional and local settings, other explored topics included health services delivery (6.3%) and disease natural history (6.4%). Little has so far been published on new therapies and treatment evaluation (4.4%), although with increasing trends, on the contrary, data on the management and impact of containment measures decreased over the study period (Figure 2).

Table 1 reports indexed COVID-19 related papers, by country, together with countries' COVID-19 burden (COVID-19 deaths from official surveillance data) and overall scientific production ranking. The largest amount of COVID-19 papers, one-fourth of the 10,000, were published in the US, the country with the largest COVID-19 burden and ranking first in the 2019 Nature index, followed by China (22.2%). Italy was the country in Europe with the highest number of published papers on COVID (9%), followed by the UK (7.6%) and France (3.2%).

Discussion

We reflect on content, trends and quality of scientific publishing on COVID-19 since the start of the

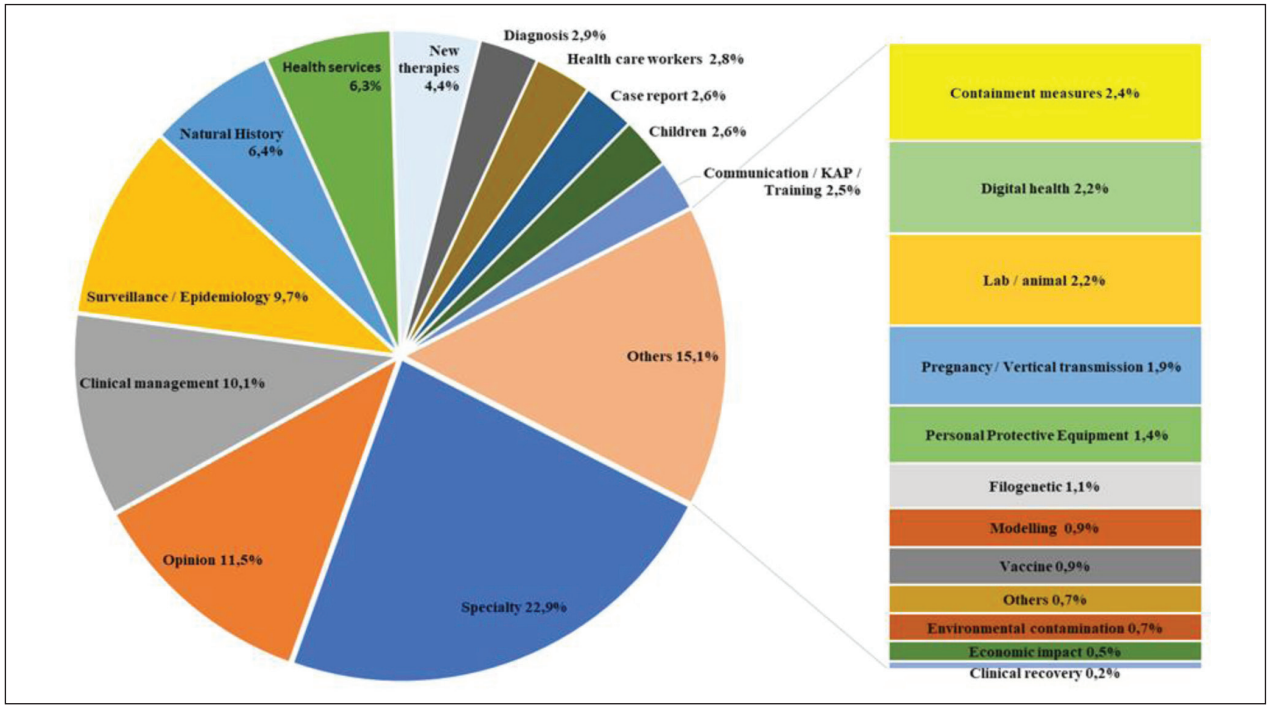

Figure 1. Distribution of total COVID-19 scientific output, by topic

Figure 2. Percentage of scientific papers published on COVID-19 containment measures and new therapies, over total COVID-19 scientific production, over time

Table 1. Country-level Covid-19 scientific production (n. of Pubmed indexed papers, 20th January-7th May)), scientific production ranking (Nature Index for the year 2019) and COVID-19 burden (n. of COVID-19 deaths on 7th May from official statistics)

Rank	Country	COVID-19 Pubmed indexed articles (n.)	COVID-19 deaths	Nature index articles count (4)	Nature Index Rank (4)
1	USA	2,647	65,197	28,403	1
2	China	2,217	4,643	18,026	2
3	Italy	903	29,684	2,638	11
4	UK	764	30,076	7,837	4
5	France	315	25,769	5,054	5
6	India	284	1,783	1,655	15
7	Canada	223	4,111	3,408	7
8	Iran	176	6,418	293	40
9	Germany	161	7,119	8,770	3
10	Singapore	157	20	1,254	19
11	Australia	145	97	2,986	9
12	Spain	138	25,857	2,767	10
13	Brazil	130	7,921	856	24
14	Korea	123	256	2,419	12
15	Switzerland	103	1,504	3,270	8
16	Taiwan	88	7	931	23
17	Japan	83	551	4,905	6
18	Netherlands	73	5,204	2,403	13
19	Turkey	68	3,584	374	37
20	Thailand	67	55	254	42
21	Belgium	54	8,339	1,176	20
22	Saudi Arabia	51	209	455	30
23	Israel	45	238	1,291	18
24	Egypt	38	69	195	46
25	Ireland	37	1,375	450	31
	Tot 25 countries	9,090	230,086	102,070	-
	Rest of the World	571	23,959	-	-
	Missing country	339	-	-	-
	World Total	10,000	254,045	-	-

pandemic. Overall, we report that a large share of total scientific production in the first months of 2020 concentrated on COVID-19, with exponentially increasing trends. COVID-19 research so far focused on selected, mostly clinical topics and more than half of scientific publications do not include analysis of original data but are opinion pieces.

Research priorities on COVID-19 have been identified over time: at the end of January 2020, two days after the first-ever paper on COVID-19 (called 2019-nCoV at the time) was indexed in Pubmed, *Nature* listed the six questions scientists were (should have been) asking on COVID-19 natural history, epidemiology, sequencing, treatment and containment measures (7). Later in March, a much detailed list of epidemiological research priorities on transmission dynamics, the severity of the disease, immunity, and impact of control and mitigation measures, among others was identified as essential to decision making (8). However, our analysis, in line with our assessments on the literature on COVID-19 (9), demonstrate that little of the research published on COVID so far matches those identified priorities, leaving many key research questions still unanswered. Although we acknowledge longer times are needed for research to be conclusive on many aspects, we notice with concern that opinion papers, speculations and personal perspectives largely surpass reporting of original data. Even prior to the retraction of two papers from The Lancet and the New England Journal of Medicine (10, 11), some scientists had warned against the risk of dissemination of inaccurate and exaggerated information (12). We fear that not only the current pandemic has introduced major changes in the approach to academic publishing but also that its drivers might be moving away from science's ultimate aims to support the pursuing of individuals' and population wellbeing. Although our study has some limitations that need to be acknowledged, including having considered only studies indexed on Pubmed and not having extracted from all included studies details on methods and finding, which was outside the scope of our analysis, we provide a clear and comprehensive overview of what has been published on COVID-19 suggesting that the strong push for scientific dissemination and visibility around COVID-19 might not be going hand in hand with the production of solid evidence much needed to inform and support clinical and public health decision making in these difficult times (13).

Conclusions

The scientific production on COVID-19 so far has the characteristics of "an epidemic in an epidemic". COVID-19 scientific output has gone viral, with both positive and negative implications. We would expect to see the current situation to bolster the value and potential of scientific research in pursuing individuals' and population wellbeing, asking the scientific community to resist the temptation of papers' inflation at the expense of scientific reputation and credibility.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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Original article

Protocols and self-checking plans for the safety of post-COVID-19 balneotherapy

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Abstract. During the COVID-19 pandemics, balneotherapic establishments were closed in Italy like in the rest of Europe. The Italian Foundation for Research in balneotherapy (FoRST) was asked to prepare a safety protocol to be proposed to the National Health Authorities to allow the establishments to restart their activity when possible, under safe conditions (the so-called *Phase-2*). The group of experts proposed the following hygienic and sanitary protocols of risk management for the initial reopening of the balneology settings in Italy. The plan aims to define the operating procedures to be implemented at the balneology establishments for the beginning of *Phase-2* and to keep them constantly updated in the different periods that will characterize *Phase-2* in relation to the trends of the disease. To this end the procedures, defined on the basis of the scientific state-of-the-art available today, will be updated and revised from time to time whenever further scientific evidence and directives from the Health Authorities make it necessary and/or useful. (www.actabiomedica.it)

Key words: balneotherapy, COVID-19, Phase-2

Introduction

Mild respiratory diseases are caused by viruses of the Coronaviridae family that circulate in the human population (1). In contrast, SARS-CoV (Severe Acute Respiratory Syndrome Coronavirus) and MERS-CoV (Middle East Respiratory Syndrome Coronavirus) are transmitted from animals to humans and cause severe respiratory diseases (SARS and MERS) (2). There are no specific vaccines or antivirals against SARS, and therefore contrast to the spreading of these viruses is based on conventional control measures like social distance and patient isolation.

SARS-CoV-2, a novel coronavirus closely related to SARS-CoV, was isolated in patients with a lung disease emerged in China in 2019 (3).

Medical Balneology is the modern, evidence-based version of the classical European thermal medicine, one of the oldest forms of western medical therapy (4-6). The "*Thermae*", as an integrated set of medical facilities and services based on a natural resource (the mineral water and its derivatives), offer therapy and rehabilitation, as well as maintenance of health conditions (7-13). At the *Thermae* people can learn a better lifestyle, exercise, reinforce their health conditions, recover and develop their physical capabilities, recover from injuries and disease, find relief from ailments. Depending on the type of water(s) and their specificities, skin (14-18), rheumatic (19-22), respiratory (23-28), inflammatory (29-31), vascular (33, 34), digestive (35), urinary (36), or metabolic (37, 38) conditions can be prevented/cured. Although natural mineral (thermal) waters have long been used as treatment for various diseases, their mechanisms of action

at the cellular and molecular levels are now becoming clear. With the huge progress of scientific medicine, the use of an apparently simple medium (mineral water) might seem unnecessary. In the age of personalized medicine, pharmacogenomics, metabolomics, lipidomics, and highly sophisticated diagnostic and surgical techniques, the role of the *Thermae* may appear at least obsolete. Instead, the explosion of chronic diseases and the increase of elderly peopleurgently pose to contemporary medicine the issue of reinforcing primary and secondary prevention, contrasting chronicity and facing polypathology that – altogether - represent nowadays the key words of the welfare systems. It is a true revolution that hits on the healthcare organization models, with the hospitals of the future exclusively focused on acute patients, and a well-organized network of not-hospitalized medical healthcare facilities that guarantee the necessary integrated approach to the patient, from prevention to rehabilitation. A great number of people in the word are taking the issues of health into their own control, at least in terms of proactive recovery and health programs, and one of the places they can do this is the contemporary *Thermae*. Medical Balneology, when done correctly under medical prescription, provide the benefit of integrated health maintenance, therapy and recovery. There is a huge overlap between proactive health maintenance and reactive sickness care. Contemporary balneology creates programs that combine proactive and reactive components of health. Often contraindicated in the acute phases of several diseases, balneological treatments – in their different applications, from hydrokinesis to aerosol and muds, integrated with classical physiotherapy, rehabilitation procedures and diet – can face several needs of low or medium intensity care of non-acute patients. Medical balneology leverages on the technical and classical know-how of medical hydrology combined, whenever necessary, with standard therapeutic treatments prescribed by medical staff and administered by appropriately trained professional and qualified operators. In line with this view for the future of the welfare systems, the World Health Organization (WHO) deemed it appropriate to include Medical Hydrology in the strategic lines for the 2014-2023 period. Reference standards for Medical Balneology can be found in the Italian Foundation for Thermal Medicine Research (FoRST), the French Association Francaise pour la Recherche Thermale (Afreth), the International Society of Medical Hydrology (ISMH), the World Federation of Hydrotherapy and Climatology (FEMTEC), and in the Hydroglobe Report (WHO).

The lockdown phase generated the suspension of all the balneological activities in Italy (like in most of the other countries in the world). However, SARSCoV- 2 prevalent transmission by breath droplets together with the structural organization of most of the balneological establishments, with several therapies administered collectively or individually but in the same space, generated the need for adequate safety rules to face the post-Covid-19 reopening and activities all over the world. Here we report the rules that the protocols and self-checking plans for the hygenic and sanitary safety of post-covid-19 balneotherapy.

Development of the protocol

Given: i) the complex situation generated by the Covid-19 epidemics in the Country (39-42); ii) that balneotherapy establishments are health settings where National Health Service therapies included in the Essential Levels of Assistance (LEA) are provided; iii) the recommendations of the World Health Organization (WHO) and the decrees of the Italian Ministry of Health aimed at limiting the risks of the so-called *Phase-2,* a specifically identified Group of Experts proposed the following operational protocols for the management of Covid-19 risk during balneology treatments. Two preliminary definitions are necessary to better understand the document: **sanitization** is the combination, in sequence, of the cleaning and disinfection procedures; **PPE (Personal Protective Equipment)** refer to the relative guidelines published by the National Health Institute (Istituto Superiore di Sanità).

Balneology treatments

The Balneology treatments for the respiratory tract and ENT are:

Irrigations

Nasal showers

The nasal showers allow the delivery of mineral water, at different pressures and temperatures, and the mineral water gases in direct contact with the mucousal surfaces of the nasal cavities.

Micronized nasal showers

Variant to the nasal shower which, instead of using the water as it gushes out at the source, conveys inside the nostrils a nebulized consisting of aqueous particles producing the dilution and elimination of secretions present in the nasal pits and in the nasopharynx, given the ability of particles to penetrate anatomical districts that are not otherwise easily accessible. **They are administered by nasal ampoules.**

Inhalation therapies

Inhalations allow the active ingredients contained in mineral waters to be sent to the mucous membranes of the upper and lower respiratory tract and to the middle ear. There are different forms and methods of delivery of inhalation therapy and the classifications take into account the technical characteristics of the appliances (single, collective, steam, compressed air), the physical characteristics of the inhaled substances (size of inhaled water particles, presence of gas, temperature and pressure) and the chemical characteristics of the mineral waters used. The most important aspect of the classification consists of the physical characteristics and in particular the

size of the particles of inhaled water. Particles with a diameter greater than 10 microns stop at the level of the upper airways (nose, pharynx and larynx), those with a diameter between 10 and 3 microns can reach the tracheobronchial mucosa, while only those of about 1 micron can reach the finest bronchial branches, down to the terminal bronchioles.

Four methods are essentially used:

- inhalations
-aerosols
-humages
-nebulizations

- Inhalations involve the use of devices capable of fragmenting mineral water into particles, forming a jet of steam which is inhaled by the patient. In direct-jet inhalations, the pressure of hot steam on mineral water generates the formation of water particles of the size of about one hundred microns. The jet is conveyed against filters or plates that eliminate larger particles obtaining a homogeneous fog. Partial cooling of the jet is also achieved, reaching an optimal temperature of 37-38 °C. The patient stands in front of the appliance, about 20-25 cm away from the spout and inhales the steam with his nose or mouth. **No masks, nasal forks or mouthpieces are used.**

- Balneological aerosols consist of fine particles of mineral water capable of reaching, based on their size, even the most distal branches of the bronchial tree. There are several devices for dispensing this method, which differ in the ways in which mineral water is fragmented and therefore in the size of the particles produced. The most common ones use compressed air at a pressure of 0.5-1 atmospheres to obtain particles of different diameters. The aerosol has a temperature corresponding to that of the water at the source and depending on the pathology to be treated, the patient can **use a mask, a nasal fork or a mouthpiece connected, through a rubber fitting, to the regulator.**

- Humages are inhalation techniques which consist in letting the patient take on the gaseous content which develops spontaneously from mineral waters. Unlike the methods described above, aqueous particles are very scarce. The most used waters are the sulphurous ones for the quality and quantity of the gas released. Direct (**individual**) and indirect (**collective**) humages are distinguished according to whether single appliances are used, or the gas is released into an environment by simple fall or by impact of the water against a solid surface.

- Nebulizations are **collective** treatments. Patients stay in an environment where mineral waters are

transformed into a mist of aqueous particles of various sizes and are mixed with any gas released by the mineral waters.

Insufflation

Insufflations use only the mineral water gases that are completely deprived of the aqueous particles in suspension. The gases are introduced both into the respiratory tree via the nasal route and, for endotympanic procedures, directly into the Eustachian tube by catheterization.

Politzer: this method which has the same purposes and characteristics as endotympanic insufflation, is used as an alternative to tubal catheterization in all situations where the introduction of the catheter into the nasal cavity is not possible or difficult, such as in children. It consists in the introduction of vaporized hydrogen sulphide in one nostril keeping the other closed. Patient rhythmical swallowing facilitates the penetration of the gas into the middle ear.

Pulmonary ventilation

Performed with an apparatus that delivers an aerosol, lung ventilation promotes, through controlled respiratory gymnastics, the improvement of respiratory function in chronic broncho-pulmonary pathologies. By law, in Italy it is the only balneo-therapy that can also include the use of drugs.

Main technical characteristics of inhalation therapy equipments

For INHALATIONS
- Stainless steel steam generator
- Misting chamber with heat and humidity regulation device
- Heat and corrosion resistant injector nozzle
- Dispenser with breaker and adjustable ceramic terminal.

For AEROSOL
- Compressor for compressed air production for medical use (oil-less, with filters)
- Mineral water flow system
- Connecting tube(s)
- Mask and / or nasal bifurcation

For MICRONIZED SHOWER
- Support for micronized shower connection pipes
- Non-toxic connection pipes for connection of compressed air and mineral water with ampoule
- Average operational temperature: 36°C
- Nasal ampoule

Other balneology treatments

Balneotherapy

It consists in the use of mineral baths, for healing purposes, of hot or artificially heated mineral waters. Among the various methods are the hydromassage, the vascular path and vascular gymnastics.

Muds

Peloids are natural or artificial products that derive from the mixing of mineral, sea, river or lake waters with inorganic, organic or mixed material of biological origin. They are used as compresses or for baths.

Mineral water drinking (Hydropinotherapy)

Hydropinotherapy consists of drinking mineral waters for therapeutic purposes. The cure consists in drinking given quantities of mineral water at a specific temperature, and according to times and modalities established by the medical prescription.

Anthrotherapy

Caves and stoves are collective balneology practices that involve exposure to variable temperatures and relative humidity rates, with prolonged stay and scarce air exchange.

Vascular path

Walkways along two pools containing mineral water, at least 80 cm deep, with a bottom suitable for vascular needs, with a temperature excursion of 5-10 °C, with a duration of 20 minutes and with the possible presence of ozone jets and lateral hydromassages at various heights.

Vaginal irrigations and rectal showers

They allow mineral waters to reach different temperatures and pressures, in direct contact with the vaginal and rectal mucous membranes. They are individual therapies, performed under medical supervision.

These definitions refer to and concern treatments envisaged, authorized and / or in some cases specifically included in the LEA (DPCM 12 January 2017).

Operative protocols

The organization chart of the persons responsible for implementing the protocol and verifying its correct execution is defined by each estabilishment and should in any case include the Property, the Prevention and Protection Service, the Occupational Doctor, the Spa Doctor and the Health Director.

The Employer defines the corporate Covid Unit, coordinated by a manager (Covid Surveyor, with a specific delegation from the Employer) in charge of collecting the evidences related to the implementation of the procedures and acting as a link between the general management, employes and users of the Balneology estabilishment. The purposes are:

- in light of the new Covid-19 prevention measures, collaborate in the definition or update of the Risk Assessment Document (RAD) and of the Prevention Plan adapted to the specifications of the balneology estabilishment by the Health Director;
- encourage the implementation of national or regional guidelines, contextualising them within the individual balneology estabilishment;
- facilitate homogeneous and coherent behaviors among the employes;
- represent a single reference figure available to all workers, avoiding uneven behaviors, while promoting staff training;
- Represent for the management the intermediate responsible for the inmplementation of operating procedures.

The General measures include:

- The Employer, through the Prevention and Protection Service and in collaboration with the Health Director and the Occupational Doctor, trains all workers (who will sign a specific training form) and implements all the applicable prevention and protection measures provided for by current legislation (including the use of specific PPE);
- The Employes, on the basis of the information and training received, will sign a commitment for a daily self-assessment of any onset of symptoms;
- The Employer, also through his delegates, defines the specific sanitisation procedures for the estabilishment, also providing periodic internal checks on the levels of sanitization;
- The Employer, also through his delegates, organizes the logistics of the changing rooms so as to guarantee the requisites of interpersonal distancing and to allow adequate and frequent sanitization interventions. To this end, he defines the maximum number of subjects present at the same time in each changing room, publicizes the rules by adequate advertizing and implements an access control system that verifies when the maximum number of people has been reached; changing rooms furnishings must be organized in such a way as to facilitate spacing (benches, lockers, chairs, etc.);
- The Employer, also through his delegates, guarantees that all subjects who access the estabilishment are subjected to body temperature measurement by means of Thermoscan; for patients, the measurement is taken before the acceptance medical examination;
- The Employer, also through his delegates, makes disinfectant gel or hydroalcoholic solution for the hands available in all environments, using in any case no-touch dispensing or non-reusable bottles;
- The Employer, also through his delegates, communicates to the patient at the time of booking to come with his own surgical mask. However, disposable surgical masks must be available both at the entrance of the structure and in

other environments to be used in case of need (damage, loss, etc.);
- The Employer, also by means of his delegates, guarantees the recirculation of the air, favoring its replacement as per current regulations and guidelines (ISS COVID-19 Report, no. 5/2020) in all patients areas of the estabilishment (waiting rooms, medical toilets, treatment departments, changing rooms, etc,);
- The Employer, also by means of his delegates, guarantees that the furnishings, the deckchairs, the tables and the seats are pre-arranged so as to allow the physical spacing of at least 2 meters;
- The Employer, also through his delegates, favors the physical distance of at least 2 meters by organizing appropriate access rounds during the working hours; however, there can be exeptions in the case of patients using the same facilities (i.e. patients sharing the same roon in the hotel);
- The Employer, also through his delegates, guarantees the individual use of the elevators and their periodic sanitization;
- The Employer, also by means of his delegates, displays signs on the rules of conduct for the public, showing the following list as a minimum:
  - ⇨ do not drink from the same bottle / flask / glass, always using disposable glasses or a nominal or personalized bottle, and do not exchange objects with other people (towels, bathrobes, etc.);
  - ⇨ prohibition to eat food in common or not specified areas;
  - ⇨ store personal items and clothing in your bags;
  - ⇨ immediately dispose the paper tissues or other used materials (patches, bandages, etc.);
  - ⇨ wash your hands thoroughly and disinfect them with antiseptic gel;
  - ⇨ do not touch your eyes, nose or mouth with unwashed / disinfected hands;
  - ⇨ maintain an interpersonal distance of at least 2 meters;
  - ⇨ wear the surgical mask correctly, ensuring coverage of the mouth and the nose;
  - ⇨ avoid staying in common areas, always guaranteeing interpersonal distance.

Specific measures for inhalation / ENT therapies and related departments

The Employer, also through his delegates, guarantees that the following services are NOT PROVIDED:

- **steam jet inhalations, as they are applied in the absence of customized dispensing devices (masks, nasal forks, mouthpieces) capable of limiting the potential viral spread from the patient to the environment. If the estabilishment has single, isolated workstations, this therapy is allowed, with complete sanitation of the environment between one patient and the next;**
- **collective therapies (collective humages, nebulizations);**
- **caves.**

The Employer, also through his delegates, also guarantees that:

- ➢ **all other inhalation therapies are carried out with respect for inter-individual distances (alternate occupation of individual workstations, with continuous and complete sanitization of unoccupied workstations);**
- ➢ the Eustachian tube catheterization stations are completely sanitized between patients, with periodic internal controls;
- ➢ the pulmonary ventilation stations are completely sanitized patients, with periodic internal controls;
- ➢ the areas are equipped with efficient air exchange, as required by current legislation in order to ensure both air circulation and appropriate spare parts.

The spa doctor, during the acceptance visit, pays particular attention to recent anamnestic data in re-

lation to the known symptomatology of COVID-19 and / or known non protected contacts and, after having detected their absence, formulates the personalized therapeutic respiratory protocol for the patient, excluding collective therapies and steam jet inhalations (unless individual), evaluating their possible replacement with other means of inhalatory administrations (e.g. sonic aerosol or nasal showers, etc.).

The spa doctor is subject to the specific prevention and protection procedures identified by the employer, as also indicated by the national Guidelines.

Measures for other balneology therapies and related departments

All individual therapies are allowed. In all procedures assisted by technical and / or health personnel, these must wear the required PPE; patients must wear the surgical mask. Disinfection of the hands between one patient and another with alcohol-based gel and replacement of gloves is mandatory. These are specific cases:

Mud-balneotherapy

The patient is allowed to remove the mask during the shower. The service staff will take this into account by increasing the distance from the patient. The treatment is carried out in a single use cabin; the operator will wear all the PPE provided, always maintaining, when possible, the established interpersonal distance.

Massage therapy

Massage without gloves is allowed. Before the massage, the operator cleans and disinfects hands and the entire forearm up to the elbow; he/she repeats the operation at the end of the treatment. During the whole treatment, the operator wears the other expected PPE.

Hydropinic therapies

Inter-personal distancing is mandatory as per general rules, also favoring people stay in open spaces. In the case of use of closed rooms for hydropinic treatment, the Employer, also by means of his delegates, indicates the maximum number of people who can be present in each room at the same time, ensuring the minimum inter-personal distance of at least 2 meters. In these rooms, however, both air circulation and appropriate spare parts are guaranteed.

Vascular paths

The Employer, also through his delegates, guarantees interpersonal distancing by adopting suitable access criteria and rounds, based on the structural characteristics of the path itself; he also guarantees the sanitization of the handrail between one patient and the next unless the patient wears disposable gloves from the beginning of the treatment or that the washing of the hands and forearms has been carried out.

Pools

The National Health Institute stated that "there is no evidence that COVID-19 can be spread to humans through the use of swimming pools or whirlpools (x). Correct operation, maintenance and adequate disinfection of swimming pools and whirlpools ensures the inactivation of the SARS-CoV-2 virus "(FAQ - ISS of 16.04.2020). The Employer, also through his delegates, guarantees that:

- the minimum interpersonal distance of 2 meters is maintained; for this purpose, the maximum number of people who can simultaneously access the pool is defined; a system is also implemented to monitor the number of visitors present and block access to the pool when the maximum allowed number of people is reached;
- an effective air extraction system is active, as per current legislation;
- the pool area is equipped with advertizing of the hygiene standards to be adopted, and with supervising personnel.

Hydrokinesitherapy

Hydrokinesitherapy is based on therapeutic exercise in water. This practice is carried out by a qualified physiotherapist who might work with the patient in water or outside the pool. If procedures requiring a reduced distance between the patient and the therapist cannot be avoided, the operator AND the patient must wear PPE.

Therefore the Employer, also through his delegates, guarantees that:

- patients shower before entering the pool;
- the hydrokinesitherapic activity takes place in dedicated pools (or in dedicated hours), allowing the physiotherapist remain out of the water;
- the operators wear the PPE required;
- in the case of rehabilitation in water of a disabled person, the presence of the therapist is allowed in water. The safety of the patient and therapist are guaranteed by PPEs that MUST be weared by both;
- at the end of each treatment the pool handrails and all tools used are sanitized.

Gyms and Rehabilitation Gyms

The employer, also through his delegates, guarantees that gym activities (such as motor rehabilitation or free attendance by users of the facility) are carried out:

- in environments where the maximum number of people who can be present at the same time has been defined;
- in environments where appropriate advertizing indicates the hygienic-sanitary behavior to be maintained;
- in environments with adequate air circulation and appropriate air exchange;
- following correct environmental sanitation of the equipment used;
- with respect for interpersonal distancing

To this end, the staff uses the PPE provided and monitors users' compliance with what is established and indicated in the signs. Users must wear masks. The spacing of at least 2 meters between patients must be ensured.

Conclusions

The recommendations collected here constitute a contribution to the recovery of activities at high interest for public health but also with a relevant economic impact. These indications, drawn from international scientific evidences, must of course be coordinated and adapted with the national and regional regulations which characterize phase 2 and which are periodically updated. In this perspective, a contribution from Italian authors appears useful not only for the long tradition in balneotherapy but also because the regions of northern Italy were the first areas of Europe to be affected by the COVID-19 pandemic and among those with the greatest number of cases and deaths (39-42).

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Original article

COVID-19 and Healthcare Facilities: a Decalogue of Design Strategies for Resilient Hospitals

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Abstract. *Background and aim:* The COVID-19 pandemic has upended the global healthcare systems. The surge in infections and sick critically ill patients has tested the resilience of healthcare infrastructures and facilities forcing organizations to quickly adapt and embrace emergency solutions. The paper proposes a decalogue of design strategies applicable both to new hospitals and to the refurbishment of existing hospitals. *Methods:* The authors conducted observations at hospitals, during public health webinars and through experts working groups from March to May 2020. *Results:* In this commentary, the authors present a list of strategies for creating critical care surge capacity and exploring design strategies for healthcare design for resilient hospital facilities. The strategies are organized into two tiers: I) design and II) operations. The (I) Design phase strategies are: 1) Strategic Site Location; 2) Typology Configuration; 3) Flexibility; 4) Functional program; 5) User-centerdness. The (II) Operation phase strategies are: 6) Healthcare network on the territory; 7) Patient safety; 8) HVAC and indoor air quality; 9) Innovative finishing materials and furniture; 10) Healthcare digital innovation. *Conclusions:* Hospitals, health care systems, and institutions urgently need to assess their resources, identify potential bottlenecks, and create strategies for increasing critical care surge capacity. The COVID-19 pandemic disrupted healthcare operations and accelerated the processes of innovation and transformation. The design and operational strategies can enable the achievement of resilient hospital facilities. Further multidisciplinary researches is needed to validate the strategies empirically. (www.actabiomedica.it)

Key words: COVID19; Hospital; Healthcare facilities; Built Environment; flexibility; resilience; evidence based design; user centerdness; digital innovation; patient safety

COVID-19 impact on healthcare systems

The coronavirus disease 2019 (COVID-19) virus is creating unprecedented stresses on healthcare facilities and critical care systems. The rate of infections and critically ill hospitalized patients reached unprecedented levels. Hospitals play a crucial role within the health system in providing essential medical care to the community, particularly during a crisis. They are complex and vulnerable institutions, dependent on critical external support and supply lines which operate with limited margin of error, at a very high rate and capacity. Even a modest rise in admission volume can overwhelm a hospital beyond its functional reserve. The COVID-19 pandemic has stressed critical support services and interrupted supply chains along with staff shortages and communications have also been challenging topics (1). Hospitals struggled to adequately respond to an unprecedented and sudden demand for emergency care and Intensive Care Unit (ICU) beds for infectious

diseases in a very short span of time. The demand for COVID-19 beds in acute care departments globally surged, forcing healthcare settings to adopt contingency capacity strategies including: adaptations to medical care spaces, staffing constraints, and supply shortages in a way that could increase capacities without significant impact on medical care delivery. The COVID-19 pandemic highlighted all the existing structural, organizational and technological challenges of worn-out and obsolete healthcare facilities. These facilities were seen to undermine flexibility and efficiency in tackling rapid epidemiological, social and economic changes that was required to address the COVID-19 surge. Additionally, in the near term, healthcare systems will face two major, "collateral" issues: the physical and mental exhaustion of the healthcare workforce and the growing "backlog" of healthcare procedures (i.e. delay in cancer procedures, operations, etc.) (2,3).

In order to overcome the saturation of spaces in existing hospitals, two main strategies have been adopted.

In order to overcome the saturation of spaces within existing hospitals, two main strategies have been adopted.

- First, in following the example of Wuhan, China, who scrambled to build an emergency hospital in 10 days, the whole world has taken the challenge to build as many temporary facilities to help support the great demand for beds for coronavirus patients. Facilities designed to support the care of 1000 patients , on a 25 thousand square meters of prefabricated blocks were undertaken as the symbol of how innovation in construction sector can impact healthcare processes. Countless temporary solutions such as containers, inflatable systems, tent structures, modules, partition panels, ships have been proposed by designers around the world such as the CURA (Connected Units for Respiratory Aliments), the open source project by Carlo Ratti Associates and colleagues or the 68 beds and 10 ICU beds at the East Meadow in Central Park in New York City.
- The second strategy regarded the transformation of non-sanitary building typologies, unused during the pandemic, such as re-tooled trade centers, airports or schools. Several studies developed by Architecture, Engineering and Construction (AEC) firms such as HKS Architects, resulted in conceptual documents to convert schools or hotels into temporary healthcare spaces in 14 days or less. In addition, a taskforce set up by the American Institute of Architects (AIA) (4) provided a planning tool to quickly identify suitable buildings for patient care. Examples can be found in the transformation of the ExCel Center in London (UK) and the Exibition Center "Fiera Milano", Milan (Italy) where also important transformations for improving the mechanical systems were done. Naturally, these examples have several limitations such as a limited capacity for surgery or high level diagnostics, lack of specialized support services and being distant from the core hospital.

The challenge of COVID-19 for healthcare facilities and the built environment

While outside the hospital pop-up structures emerged, within the existing healthcare facilities the organizations had to deal with two major aspects. The first, treating patients with severe symptoms while stemming the spread of the virus among patients, visitors and healthcare workers. In order to deal with the first aspect, there was a rapid conversion of hotels, trade centers, city parks into new hospital spaces, revealing a series of operational and safety difficulties that can be summarized in the structural impossibility of "detaching" a component such as ICUs from the rest of the hospital. Therefore, a large part of the COVID-19's related activities have been designed "on-site" with ad-hoc and extremely varied solutions according to the needs of the individual hospital, department or ward. The lack of a national or regional comprehensive strategy is not only linked to the complexity of the emergency, but especially to the high complexity and highly variable hospital infrastructures. In fact, in terms of size, number of users and volume of activity, the hospital is more similar to a city within a city characterized by stratifications of service networks distributed in internal and external areas. For example, the

state of conservation of Italian hospitals are in a critical. In fact, it is estimated that more than two thirds of the healthcare real estate has reached the end of its life cycle and more than half is not adapted to the new organizational models and epidemiological demands (3). This general state of obsolescence and rigidity has greatly contributed to the management challenges of this particular pandemic.

Hospitals were forced to adopt several cross-cutting strategies including the creation of: buffer areas between wards, the division between contaminated and non-contaminated areas, the transformation of acute care spaces (i.e. already equipped with advanced systems such suction, oxygen, negative pressure, etc.) starting from operating theatres; creating dedicated spaces for donning and doffing of personal protective equipment (PPE) decontamination areas for healthcare workers; new spaces with prefabricated technologies; core and shell empty environments at disposal (so-called "lung" spaces) to be equipped for emergencies or also unused area, gyms, car parks or congress centers.

The second challenge faced by hospitals is the virus containment. The lack of scientifically validated data and evidence-based protocols forced each hospital to develop ad hoc solutions sometimes based on models of prior epidemics caused by viruses such as Ebola (2013) and SARS (2003) or bacterial epidemics such as Tuberculosis. Coping with these highly contagious events required applying strict infection control protocols in the corridors, at key thresholds such as entrances to better manage the flows of staff who can infect themselves, colleagues and patients.

The aim is to propose strategies for hospitals to meet the needs for critical care capacity applicable both to new hospitals and to the refurbishment of existing hospitals to support a response for future health emergencies. What are the bottlenecks in critical care resources that might create a mismatch with the projected demand posed by the COVID-19 pandemic?

A decalogue for resilient hospital design

The aim of this commentary is to suggest a decalogue of strategies that are applicable both to new hospitals and to the re-furburishment of existing hospitals in order to respond rapidly and in the best possible way to the emergent needs that future health emergencies may bring to light. The hospitals of the future will have to be resilient to changes and capable of protecting different users' health and tackle the transforming social, economic, environmental and epidemiological needs of the context in which they are located. We made a series of observation from March to May 2020 during public health webinars and through experts working groups. In particular, we built on the extensive expertise of the author's in healthcare design and research. The observations were conducted in the following settings:

- Participation in webinars organized by Public Health and Healthcare Design Associations at national and international level (Accademia Lombarda di Sanità Pubblica, Società Italiana di Igiene e Medicina Preventiva, Centro Nazionale Edilizia e Tecnica Ospedaliera, Design in Mental Health Network, Center for Health Design, International Academy for Design & Health);
- Participation in institutional working groups such as Department of Architecture Built environment Construction engineering Observatories (Osservatori DABC) founded in response to need for institutional best practices formulation to face the so-called "Phase 2" in Italy;
- Data was collected and reviewed from the gray literature and technical website, combining the following keywords: *hospital; COVID-19; hospital planning; hospital refurbishment; design strategies;*
- Interaction with keynote speakers at the XI edition of the postgraduate Master "Planning, Programming Design of Healthcare and Socio-sanitary systems" Politecnico di Milano, Università degli Studi di Milano and Università Cattolica del Sacro Cuore di Roma.

According to previous statement and scenario a comparative matrix has been structured in order to merge the strategies derived from the data and case studies collection. Two areas of improvement have been highlighted: (I) strategies that can be implemented during the design phase and (II) strategies that can instead be achieved during the operation phase. We present a decalogue (5+5) of healthcare design strategies for resilient hospital facilities (Figure 1).

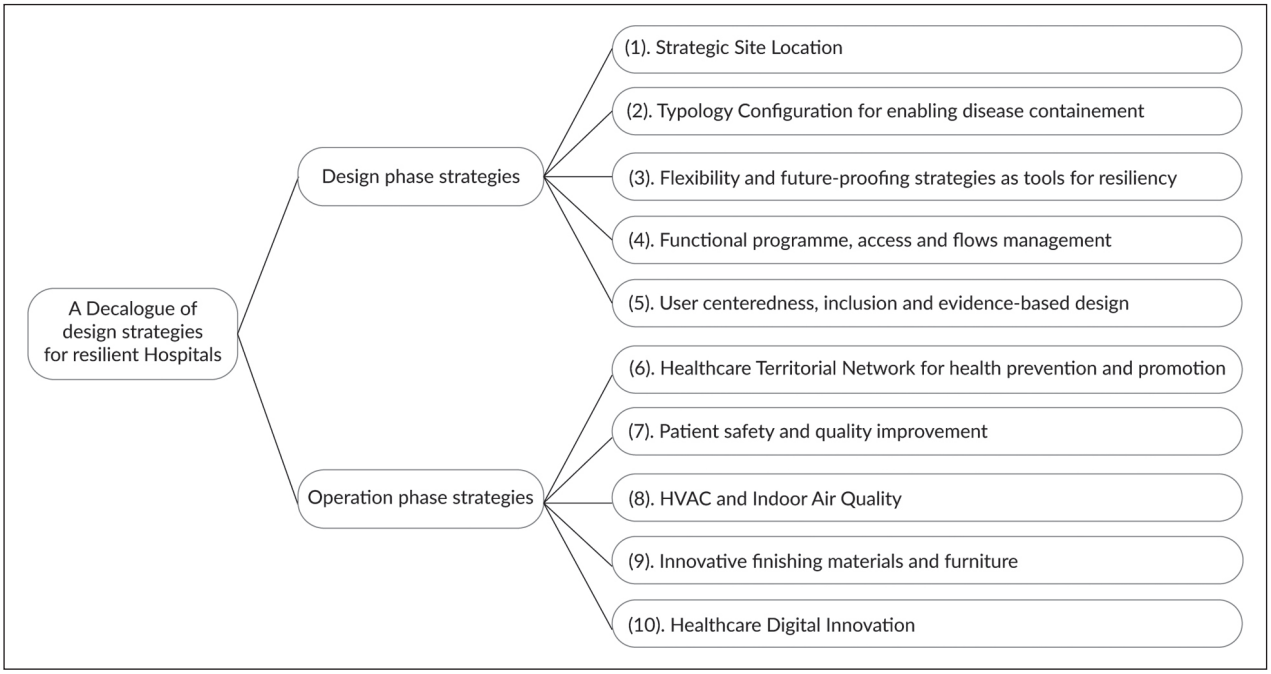

Figure 1. Flowchart of the decalogue of design strategies for resilient hospitals

(I) Design Phase strategies

1. Strategic Site Location

In the urban context, the hospital represents an important element for different factors, such as: the accommodation of a wide amount of users and visitors, the relevant building dimension and the economic supply chain. For this reason, hospitals' site selection is a crucial topic in planning decision processes that affects the environmental, social and economic sustainability of healthcare structures and the efficiency of the health service (5,6)

In recent years, hospital trends have highlighted the importance of localization in central areas of the city, however past and ongoing experiences, especially in relation to an infectious epidemic, are challenging this tendence. Indeed, the capability of changing hospital's areas or spreading them outside, has been often limited due to the lack of flexibility expansion related to the facilities' location in dense city center. Learning from the management of previous pandemics, the localization of the post-COVID hospital to the city boundaries, can guarantee both the limitation of flows outside urban areas, containing possible risks of contagion in large high density city centers and the accessibility from the urban areas (7). At the same time, a correct strategic location represents an opportunity for spreading in areas close to the healthcare facility. On the other hand, central areas must host territorial facilities able to provide: health services at the first level, prevention and health promotion at the neighborhood scale(8).

2. Typology Configuration for Enabling Disease Containement

Currently, trends of hospital design typology are mainly characterized by horizontal configurations. This setting ensures, in emergency situations, the possibility to organize areas of the facility without constraining the entire flows and routes system (9). In order to provide an effective emergency management, treatment areas for infectious patients should be isolated through a clear routes separations, limiting cross-contaminations by avoiding the use of vertical and horizontal connections for multiple areas. Therefore, a hybrid typological configuration, characterized by a main body

connected to support pavilions, might represent a strategic solution, with dedicated accesses for emergency and logistics vehicles. In case of infectious emergency, the independence of the buildings or the availability of autonomous internal units, allow to separate different functional areas from the rest of the hospital system, without ordinary activities interruption. Providing outdoor spaces around the hospital area is also suitable for hosting possible temporary structures such as tents, tensile structures or other modular solutions, which guarantee the connection to the hospital and the relationship to driveways for ambulances and logistics vehicles.

3. Flexibility and Future-Proofing Strategies as Tools for Resiliency

Resilience is one of the most important challenges that hospital structures must tackle according to healthcare emergency needs that might arise or disappear at a very fast rate. In order to ensure effective emergency management, flexibility represents a fundamental aspect to consider in the hospital design process, from the overall building system to the single functional and environmental units (10). The Rush University Medical Center in Chicago was a relevant example during COVID-19 pandemic. The hospital can expand both the emergency department capacity and the number of isolation rooms when needed. During ordinary operations, the Rush hospital has 40 negative pressure rooms that help prevent the spread of potentially infectious diseases in the air. Each room has a negative pressure with respect to the external corridor, in order to let the air flow from the corridor into the room, leaving the hospital through the introduction of HEPA filters. All the interventions that can guarantee a fast reconfiguration are therefore strategic in emergency situations, such as:

- o the presence of "lung" spaces, empty and support areas among different lots and departments to accommodate expansions, reconfigurations or isolation areas;
- o non-sanitary hospitals areas easily transformable and to be equipped with low investments. For instance, the underground parking of the Rambam hospital in Haifa (Israel) can be converted into a hospital with 2.000 beds in wartime or flexible sports facilities ca be reconfigured. Therefore, these areas must be supported by direct internal connections with the rest of the hospital and outside for ambulances;
- o functional areas that can be easily reconverted, such as common hospital ward that are provided of the proper amount of technical installations.

4. Functional Programme, Access and Flows Management

Functional program is fundamental in complex facilities such as hospital. In case of emergency the design should consider some transversal issues:

- o Distribution is one of the main aspects to consider within the functional programme in relation to emergencies. The access for staff must be unique, as well as that one for visitors who are not directed to the emergency department. In case of an infectious emergency, flows that are normally differentiated between users and health workers, must be able to be further separated, in order to divide the flows of patients with suspected or known infection by other users. In this regard, recognizable signage must effectively indicate temporary changes in hospital routes.
- o The strong relation between the emergency department and infectious wards requires a fast connection for the movement of patients and healthcare workers. These spaces should be therefore placed at the same level promoting short and horizontal connections.
- o The presence of storage areas is also required, which in case of infective emergency can host the wide amount of sanitary material, PPE and contaminated waste. Furthermore, there is a need of solutions for the extraordinary placement of corpses in low temperature environments, in close communication with the external driveways for their transport.
- o In order to decrease the risk of nosocomial diffusion of any infectious agent, all ordinary hospital wards must maximize the number of single rooms. This can be reached with a set of bed head beams and engineering plant equip-

ment that allow to transform rooms into double rooms in case of hyper flow of patients.

In addition, a resilient hospital design must consider some organizational aspects of both high and low care areas mostly interested by the infectious emergency, such as:

- The intensive care department results as the one of the most affected, so additional filter areas are needed for the dressing/undressing of the healthcare workers. Separated working areas from the main care area are suggested, in order to reduce the staff exposure and the use of mobile diagnostic equipment (i.e. mobile ultrasound scanner, Point-Of-Care Testing POCT machines, X-ray diagnostics and mobile Computed Tomography CT).
- The emergency department must at the same time host patients with suspected infection and continue to manage all non-infectious cases, separating them from their entrance. Therefore two separate entrances are recommended to distinguish sick people through dedicated triage, with separate paths and waiting and treatment spaces. External multiple decontamination areas for ambulances and areas for the preparation of pre-triage tents must be provided.
- The sanitary hotel, which usually welcomes outpatients, relatives or visitors, in emergency conditions must have a flexible configuration that allows to accommodate ordinary and additional healthcare workers, reducing the infectious risk for their families and ensuring them an effective rest in situations of high work stress. Similarly, it could be transformed to accommodate infectious patients of lower gravity or patient who need rehabilitation.

5. User Centerdness. Inclusion and Evidence Based Design

Studies on *User-Centered Design* and more in general *Universal Design* (11), confirm that during all the different phases of the design process, attention must be focused to the physical, psychological and social needs of all users to avoid future disabling situations generated due to COVID-like overwhelming conditions (12). This is especially true in hospital environments, where aspects as accessibility, wayfinding and comfort, directly impact on different users (patients, healthcare workers, visitors) during emergency situations. In particular, healthcare workers show symptoms of anxiety, depression, insomnia and stress higher than normal within hospital facilities. In this regard, during the COVID-19 pandemic, the design firm Studio Elsewhere develops "recharge rooms" for hospitals characterized by natural design elements that support medical workers recover from a physically and mentally taxing shift. These spaces are designed to be customized according to the users' needs, such as sounds, sights, and smells. The rooms use bringing the outdoors into built environments - to create spaces with nature (real and on a screen) out of underused hospital spaces near intensive care departments. Researches, in fact, have demonstrated that looking at nature can improve recovery patient time and reduce nursing stress levels (13-15).

Evidence Based Design (EBD) studies demonstrate that the presence of spaces for the physical and psychological well-being is strategic for all users and it also positively influence the work performance of the healthcare staff. Such spaces, in fact, in case of emergency, could guarantee users environments to relax from psychological stress and daily pressures. They can be both areas inside the structure - close to the functional areas - or green areas of the hospital (i.e. garden and terraces), preferably with a variety of spaces, different seats and isolation points to ensure user's privacy (17).

(II) Operation phase strategies

6. Healthcare Territorial Network for Health Prevention and Promotion

The synergy between territorial services and hospital organizations plays a crucial role for health promotion (18,19). In particular, starting from the recent experience, the adoption of Hub & Spoke model could turn out particularly efficient in cases of high emergencies, avoiding the overflow of users in the hospital thanks to health home care management or low and medium-care facilities (20).

The creation of community health centers in the territory for guaranteeing the primary care services and triage activities could ensure a better management of low and medium-care services, as well as to favor the use of smart diagnostics and to support the outpatients management on the territory (21). This capillary model encourages access to care for the population (6), reducing the patients' transfer across the territory, decreasing the overcrowding of the emergency departments, and minimizing hospital-based cross-contamination among users and healthcare staff. These healthcare facilities should be configured as integrated hub between healthcare professionals and healthcare and social services, also for NGOs and voluntary associations for addressing fragile users needs (22-24). In addition, the use and application of healthcare devices for the smart hospital, as well as telemedicine programs, can easily support and strengthen the health network and the monitoring of the users' health status, even in the presence of healthcare emergencies (18,25).

7. Patient Safety and Quality Improvement

It is well-known that healthcare organizations regularly give rise to protocols for risk control and patient safety in hospital settings. In particular, during the pandemic, the healthcare leadership need to reorganized the users' behaviors and healthcare protocols in line with the best practices for the COVID-19 control. Healthcare design should give rise to physical environments that support providers to act in a professional, trustful and respectful manner for all the community (26). Facility design affects how people work, and what processes, systems and technologies they will require to support the functioning of a learning work environment. In addition it is necessary to take into consideration design strategies aimed at responding to possible emergencies and medical needs for guaranteeing patient safety. For example, among them, several healthcare facilities have included visual cues for visitors and users for highlighting the proximity of risk functional areas and infectious impatient wards. Others have adopted protocols for bringing healthcare devices and materials, as well as the medical waste, through dedicated elevators in an attempt to minimize cross-contamination. Moreover, for guaranteeing the regular disinfection activities, some hospitals adopted spaces called "pods" for low-acuity patients. They were designed to reduce possible infection by separating the patient from the equipment to be cleaned, thus reducing the possibility of contaminating them (27). Several hospitals adopted strategies, such as adhesive tape on the floor, signage and signs boards on door used for annotations with special markers, intentionally positioned. Stations for accessing the PPE were provided in key positions, which in turn influenced the way and the place in which the hospital staff used the equipment. The ability to interpret and understand the configuration of the space can be a powerful tool to support healthcare professionals within unfamiliar and rapidly evolving COVID-19 care environments. Simple visual devices, wayfinding strategies and design-nudges can help to mitigate the transmission of infections by clearly defining risk areas, creating "mental anchors" for specific activities (28,29) and consequently reducing mental fatigue and helping to align the behavior with the protocols to be followed.

8. HVAC and Indoor Air Quality

It is well known that air quality in confined spaces plays a direct or indirect leading role in prevention, especially in environments with vulnerable users. The quality of the indoor air (IAQ) depends not only on the outdoor air but also on the presence of indoor sources that emit pollutants that can affect its composition (30,31). It is therefore necessary to ensure adequate air exchange in all environments through mechanical and, where possible, mixed ventilation. To ensure efficient management in case of emergency, such as infectious epidemics the ventilation systems have a strategic role, but its functioning must be able to respond to different healthcare needs, in all the conditions and especially in emergency situations where air could be a possible means of infection diffusions (32,33). The heating, ventilation, and air conditioning (HVAC) must be flexible and their operation must be able to be modified in terms of the air used, from recirculation to all-air systems, and pressure, from positive to negative (34,35). In addition, their regular and constant maintenance, cleaning and disinfection also become strategic through the use of innovative materi-

als. As a consequence new generation systems must be designed with solutions that guarantee easy inspection, and the possibility of intervention (36).

9. Innovative Finishing Materials and Furniture

Healthcare Acquired Infections (HAIs) have a relevant strategic role in the light of the management of the COVID pandemic. In synergy with monitoring and risk management activities, it is necessary to use high-performance, long-lasting and easy to clean materials in relation to the medical needs. In particular, innovative materials must be introduced to reduce the bacterial (and viral) load on the finishing surfaces (37) among which also eco-active ones and photocatalytic paints (30,38), as well as characterized by high performances and flexibility-in-use. It is necessary to investigate and take into consideration, also, solutions used in emergency contexts such as, for example, washable textile materials (39). Their application could be extended in different sanitary areas for social distancing, and which in case of need can be easily clean and replaced, and/or removed for guaranteeing the adaptability and resilience of the spaces (40,41). Together with the application of best practices of ventilation, the choice of cleaning products must be defined in relation to the finishing materials and furnishings in the environmental unit, considering the peculiarities and features of each surface (42). In addition, detergents (such as hydrogen peroxide, alcohols, sodium hypochlorite or benzenzonium chloride) have chemical compositions that kill the bacterial and antiviral load but, at the same time, they can present volatile organic compounds (VOCs) toxic to humans (30), and require paying attention to environmental sustainability (43).

10. Healthcare Digital Innovation

The new digital technologies can support the patients' treatment and care processes both in the hospital and on the territorial healthcare network (20). It can be considered not only for ordinary medical activities, but also in case of emergency. In fact, the continuous control of the health status and vital parameters through IT systems, such as smartphone or wearable devices, can guarantee a better management of hospitalization, and consequently an efficient organization of hospital settings (44). Moreover, the modular planning and forecasting of the occupation of Intensive Care Unit (ICU) and ordinary beds, both in the same hospital and within the territorial hospital network, can support - in real time - the possible directing of the ambulances to the more appropriate healthcare facility. In addition, the constant monitoring and technological advancement allows the use of some electro-medical equipment remotely, decreasing the contacts between (infected) patients and hospital staff, and guaranteeing an overall control and a more efficient use of the resources (45). As well the use of sensors and devices through the Internet of Things allows the hospital to guarantee a personalized and dedicated experience for each user, monitoring the degree of comfort and satisfaction (27). In conclusion, the substantial reduction of paper-based health and administrative documentation through the digital innovation allows the reuse of storage spaces and archives for other functions, including server rooms (41). In the close future all medical procedures that can be treated without physical presence, will be carried out through digital systems and healthcare organizations will also be able to better manage patients' clinical information and therefore users at risk will be more protected through tailored medical paths. Nowadays more than ever, digital healthcare system represents a 'life saver', an accelerator of health and an evident reduction in the costs of healthcare services.

Preliminary conclusions and future perspectives

As in many other spheres and economic activities, this pandemic has accelerated all those processes of innovation and digitization that had somehow already been activated. The home care issue, the use of smart devices for a dialogue between the healthcare professionals and the pervasive use of apps to monitor certain health parameters, are just some of the megatrends that were being observed and which have now necessarily entered into everyday life. In the same way, the hospital, which in the face of this gradual process of dematerialization and relocation of 'softer' clinical-diagnostic activities, reaffirms itself as a centre of the

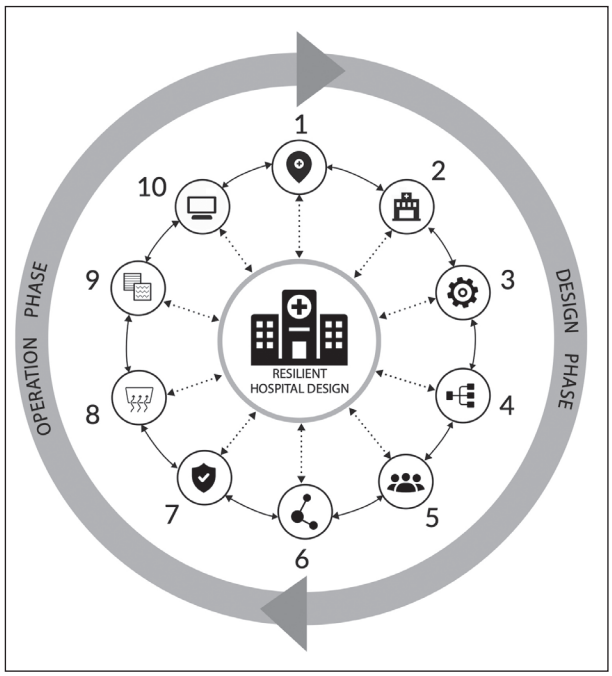

Figure 2. A graphical diagram that describe the 10 strategies proposed in the commentary

highest specialty for the treatment and care of acute patients, for high-level clinical and experimental research, for diagnostics and more complex operations (Figure 2).

Antimicrobial resistance has been recently highlighted by several institutions due to the mis-use and/or overuse of antibiotics in human medicine, specific facilities for infectious diseases treatment and containments emerged (46-51). The COVID pandemic highlighted that a post-antibiotic era can be very difficult to tackle and the role of built environment is of increasing importance. Indeed, due to the high diffusion and infectious rates of COVID and in the absence of reliable drugs or specific vaccinations, the pandemic containment has been mainly performed through physical and social tool such as the confinement practices and hand washing. The hospital will have to increasingly reflect on its role of health promotion and protection, especially towards the most fragile users.

It is essential to promote multidisciplinary actions and monitoring programs for quality improvement through evidence-based evaluation tools in order to develop a new design for the hospital of the near future (52). Further multidisciplinary researches is encouraged to validate the presented strategies in case studies and in empirical settings.

The decalogue of strategie aims to briefly indicate the key strategies to be considered in the design of new resilient hospitals and in the re-functionalization of existing structures.

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Original article

COVID-19 and Living space challenge. Well-being and Public Health recommendations for a healthy, safe, and sustainable housing

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Abstract. *Background and aim of the work:* The ongoing pandemic of COVID-19 is a strong reminder that the lockdown period has changed the way that people and communities live, work, and interact, and it's necessary to make resilient the built environment, both outdoor and mainly the indoor spaces: housing, workplaces, public buildings, and entertainment facilities. How can we re-design the concept of Well-being and Public Health in relation to the living places of the future? *Methods:* According to the previous statements and scenario, this paper aims to integrate the building hygiene and well-being, focusing the possible responses, both existing and for the new buildings, taking home a strong message from this "period" of physical distancing. *Results:* The Well-being and Public Health recommendations for a healthy, safe, and sustainable housing are framed into the following key points: 1. Visible and accessible green elements and spaces; 2. Flexibility, adaptability, sharing, and crowding of living spaces, and compliant functions located into the buildings; 3. Re-appropriation of the basic principles and archetypes of sustainable architecture, thermal comfort and Indoor Air Quality (IAQ); 4. Water consumption and Wastewater Management; 5. Urban Solid Waste Management; 6. Housing automation and electromagnetic fields; 7. Indoor building and finishing materials. *Conclusions:* The Well-being and Public Health recommendations for a healthy, safe and sustainable housing may provide a useful basis for Designers, Policy Makers (fostering tax incentives for building renewal), Public Health experts and Local Health Agencies, in promoting actions and policies aimed to transform living places in healthier and *Salutogenic* spaces. (www.actabiomedica.it)

Key words: COVID-19 Living Spaces; COVID-19 Housing; COVID-19 Built Environment; Public Health Recommendations; Healthy Living Spaces; Safe and Sustainable Housing; Sustainable Architecture; Indoor Air Quality; Water Consumption; Wastewater Management; Urban Solid Waste Management; Housing Automation

Was the Italian housing context ready to face the pandemic impact?

Prior to the COVID-19 pandemic, the Italian population spent roughly 60% of their time in the home (1). However, following the imposition of lockdown measures nationwide, this increased to 100% for most members of the 25.7 million Italian families [Istat, 2019] for a period of up to 2-3 months.

What are the characteristics of Italian homes? A recent survey by the Italian Fiscal Authority [Agenzia delle Entrate, 2019 - report *Gli immobili in Italia*]

discovered that average apartment size is 117 m^2, but with a very large range. Milan, the second largest in size of the 14 metropolitan cities, has the smallest average apartment size, just 88 m^2. According to the most recent Italian census of people and homes [Istat, 2011 - Censimento popolazione e abitazioni], more than one third of apartments (3,232,000) are below 60 m^2. The crowding index shows that 20.7% of the apartments housing more than 4 people measure less than 80 m^2. In 2018, 28.8% of the population (16.8 million) lived in overcrowded apartments [Istat, 2019 - 2nd report *SDGs*]. In addition to overcrowding, Italian apartments in general suffer from a limitation of primary services and a serious inadequacy in terms of structural requirements. Despite improvements in the previous 4 years, in 2018 almost 8 million people (13.2% of the total population) were living in apartments with damp on the walls. According to the 2011 census, up to 415,400 apartments had no running water, 250,600 no water heating, 2,081,000 no central heating, 35,900 no toilet, 138,100 no shower/bathtub, and up to 6,458,400 had no separate kitchen. Lastly – but very critical in the lockdown period – in 2018, 11.4% of the apartments, corresponding to 2,650,000 families, were lacking balconies, terraces or gardens [Istat, 2018 - report *Aspetti di vita quotidiana*]. It must be said that apartments provided with such benefits can reach an extra monetary value of up to 8%.

Considering the above situation, it is easy to understand that the "individual isolation" of people within their living spaces, to avoid reciprocal viral shedding via air (2), contact or fomites (3), was particularly difficult in overcrowded apartments, inhabited by the poorest people, including children, the elderly and the most fragile. During the lockdown period the in-house transmission of the virus became a problem, aggravated by the frequent inadequacy of the apartments (1-2).

Such a situation prompted the researchers to retrieve some chapters of the classic environmental hygiene, in particular those applying to civil constructions (2-4), often neglected in the last few years, such as the need for an optimal air exchange, for sufficient natural lighting, the latter having been found an effective means to reduce the half-life of the coronavirus in the environment (5-6).

The lockdown and the consequent confinement of people inside their homes has contributed to the worsening of Non-Communicable Diseases, such as some chronic diseases (e.g. cardivascular diseases and diabetes) and mental disorders such as anxiety, insomnia, depression, and learning problems in children. This was mainly due to overcrowding, sedentarity, an increased intake of food and beverages (both often of an unhealthy nature), and supposedly also an increase of tobacco smoking and consumption of drugs (7-10).

The lockdown, which has undoubtedly had the merit of having reduced the impact of the pandemic, has however been detrimental to the physical and Mental Health of the population, weighing particularly on the most vulnerable (11); and has brought to everybody's attention the housing crisis of the whole country. This housing crisis is due to a progressive deterioration of both public and private real estate assets, which has been insufficiently (or not at all) contrasted by renovation efforts from politicians which have proven too bland and unsystematic (12).

The consequences of the pandemic, and the imminent risk of its repetition, highlight the need to apply a new concept of health, in terms of indoor well-being, to housing policy. The present paper, taking the above considerations as a starting point, will aim to give practical ideas and key-solutions for a rethinking of the living spaces, focusing on some elements necessary for protecting the health and indoor well-being of the inhabitants. An attempt will be made to compile a list of meaningful recommendations for a safe, healthy and sustainable housing. Our goal is to provide Planners, Architects and Public Health officers with a series of practical indications for their future efforts in the field of housing.

Which strategies are required for both existing and for new buildings?
The well-being and Public Health recommendations for a healthy, safe and sustainable housing

1. Visible and accessible green elements and spaces

Numerous studies have documented how the level of exposure to natural environments affects physical

and Mental Health. The presence of green elements, in addition to having an important role in mitigating the impacts of the built environment on the climate and improving the ecological-climatic conditions of the cities, brings a wide range of health benefits for all age groups (13-14).

One of its main effects is the mitigation of the urban climate, helping to reduce the health impacts of heat waves, to increase the humidity content in the air and to lower the temperature in the hottest periods. In the absence of greenery, depending on the morphological characteristics of the city, the average maximum summer temperatures can be 1-3 time higher than in the countryside, with possible higher variations, especially at night (15). This entails an inevitable increase in the demand for energy for cooling indoor environments in summer. In rethinking the living space, it is therefore necessary to ensure the use of suitable materials to control the albedo of the ground in open spaces and to maximize the summer shading of the buildings in order to reduce surface temperatures with positive effects on external comfort, on the reduction of solar loads and, consequently, on the need for air-conditioning in closed spaces. Furthermore, providing for the installation of green walls and roofs, in addition to urban microclimatic control, could favor evaporation, the absorption of polluting agents, the reduction of fine dust, the limiting of noise pollution, the protection of the natural environment local and urban bio-diversity.

Numerous international experiences put forward the creation of green roofs as a possible solution to the problem and as an opportunity to increase green areas in urban contexts. Chicago, Toronto, Seattle, as well as Paris and other EU cities have recently carried out significant redevelopment projects at urban scale, based on increasing the number of green roofs to improve the quality of life (16) and to reduce the urban heat island. The interest focuses on the recently published *"Roadmap for green roofs, walls and facades in Australia's urban landscapes 2020-2030"* which calls for strong government leadership, policies combining incentives and regulation, and education and advocacy to ensure standards in design, installation and maintenance.

In addition, green elements offer greater opportunities to practice physical and leisure/recreational activities thus helping to promote well-being and social relationships, as well as reducing the frequency of various pathologies such as coronary heart disease, skeletal disorders, anxiety, depression, diabetes, etc. (17).

One of the most widely studied effects of greenery is the psychological effect. Some studies highlight its contribution in reducing stress and mental fatigue, in mitigating emotional states such as anger, anxiety, sadness and depression, acting on various levels- promoting physical activity, providing meeting places for residents, encouraging social ties (18). Introducing vegetation into the courtyards of buildings or in the immediate vicinity provides spaces useful for socializing and relaxing. It also helps to produce a greater sense of belonging and to reduce crime rates (19).

Following the COVID-19 pandemic, confinement at home has also revealed that it is necessary to understand if being able to view greenery from their homes or even the possibility of growing plants in their home could contribute to the well-being and health of the residents. The lockdown period has underlined the importance of increasing greenery within both existing and new buildings, by measuring the quality and quantity of green infrastructures, such as green roofs, walls, and common gardens.

The interest stems from the fact that most of the research exploring the psychological benefits of the natural environment has focused on direct exposure to the outside. However, people spend most of their time indoors, especially in office buildings and, in this particular period, in their home. On this specific topic, some studies highlight how viewing greenery from the windows of a building can have beneficial effects in reducing stress especially if natural elements or landscapes are visible (20) and this can even contribute to accelerating the healing process of hospitalized patients (21-22).

An experience-based study conducted by the authors from the Polytechnic University of Milan relating to exposure to nature (balcony, terrace, private garden, shared garden, etc.) for the population and health personnel has shown how 20-25 minutes spent in a natural environment, can positively influence the well-being of users, especially for those under 30 and those over 60 years of age. It has also been observed that in a period of great stress for healthcare workers, a break of 20-25 minutes spent in a green area can

positively affect the operator's energy and performance levels. Similarly, several studies in recent years have highlighted different strategies for implementing the performance and perceptual aspects of confined environments, including the *Biophilic Design,* a scientific approach aimed to improve occupant connectivity to the natural environment through the use of direct or indirect natural elements, and conditions of space and place (23).

In addition to psychological and perceptive benefits, with positive influences on housing quality and the population's quality of life , the benefits of environmental sustainability (e.g. reduction of noise pollution, absorption of electro-smog, mitigation of the microclimate and curtailment of fine particles) should be taken into consideration. Within a large scale urban redevelopment project, green roofs bring economic benefits, including a reduction of peak water demand and saving of energy costs, since green roofs provide good heat insulation in winter and cooling in summer, allowing significant savings in the costs of heating and cooling buildings.

Equally interesting is the role of gardening, both in educational terms and in terms of well-being. This activity appears to increase life satisfaction, vigor, psychological well-being, positive personal intra-personal relationships, sense of community, and cognitive function of the individual, especially in certain age groups (24). It also contributes to reducing stress, anger, fatigue, depression, and anxiety (25). Consequently, the commitment to gardening is increasingly recognized not only as a profitable health intervention (26), but also as a therapy for people with psychological health problems, the so-called "horticultural therapy" (27).

In this regard, a recent meta-analysis highlights how a regular engagement in gardening and the care dedicated to it, already considered an effective therapy for people with psychological health problems, could today become an efficient design strategy to improve public health (24).

For the aforementioned reasons, it of utmost importance to consider these elements for the purpose of creating new settlements and, where possible, in the recovery of existing ones.

2. Flexibility, adaptability, sharing, and crowding of living spaces, and compliant functions located within the buildings

According to World Health Organization (WHO), living space must be such as to guarantee adequate privacy in order to meet the needs of the occupants, be accessible and usable for extended users and be large enough to comfortably accommodate people of different ages (28).

It must therefore meet ergonomic requirements, so as to safeguard the safety of users, without requiring special protective measures and it must meet the need for privacy and have characteristics that enable it to be used to carry out daily activities in total safety and well-being.

The housing units must satisfy different needs that have expanded over time, also in light of the current situation linked to COVID-19, including not only the increased life expectancy of the population, climate changes, immigration - topics which have already been widely discussed in the literature (9-12) - but also other aspects such as adequate and flexible spaces for possible isolation or for working from home, are examples of problems to which today's homes must respond, both in qualitative and quantitative terms (29).

In fact, having an adequate space in the home is a fundamental aspect of well-being and health, because interpersonal distance and spatial relationships between people and the environment play a fundamental role in feeling comfortable or uncomfortable in a certain situation.

From a dimensional point of view, Istat reports that more than a quarter of the Italian resident population lives in overcrowded conditions (30) and 20% of housing shows problems of degradation from damp and significant structural problems (31). These problems are much more prevalent with regards to the immigrant population (32). Similar situations are also found in other countries, as described, for example, by the CABE study, which highlighted how many individuals consider the space available in the home to be insufficient or inadequate for carrying out the basic activities of daily life (33).

The non-compliance of the living space with the physical characteristics and needs of the user can pose obstacles to the full use of the rooms and, in some

cases, may even represent a real source of danger. The health impacts of an inadequate living space are varied: several are associated with overcrowding, others with accessibility (28).

The overcrowding of a home does not only depend on the number of people sharing it, but is also conditioned by their age, relationship and gender. Several studies have shown a direct association between crowding and certain negative health outcomes, such as infectious diseases (including tuberculosis and now COVID-19) (2,9,11) and Mental Health problems (psychological distress, alcohol abuse, depression and unhappiness, social isolation, reduced school performance in children) (8-9,34).

It is therefore necessary to adopt targeted strategies and appropriate design solutions for living spaces, paying particular attention to room size, to ensure their health, accessibility, and internal flexibility, in order to allow adaptability to any changes in distribution structure, both in the short and long term (33,35).

Space affects how and where people prepare and consume food; how they socialize; how they manage domestic waste and recycling; how they store goods; how much privacy they have for studying, working, relaxing or free time; how much and how they can adapt to new needs (e.g. isolation, disability), etc. (36).

In a situation such as the one in which we currently find ourselves, inadequate spaces in terms of size and lack of flexibility, not only accentuate health risks, but also interfere with productivity in remote working and school performances (37).

Finally, it is necessary to ensure in co-housing situations or in condominium areas, the maximum flexibility of the spaces (ground floors, basements, free floors) (38-39) in order to be able to easily adapt them in the case of a necessity to increase the areas available to the inhabitants (for example in order to have a temporary quiet work station) and to maintain social distancing, always taking into account the specific regulatory requirements (40).

Moreover, the lockdown emphasized the functional inconsistencies and interferences within the same building and, at the same time, highlighted the need to have common spaces for collective use such as sport and recreational activities. Looking both at the outdoor spaces close to the building and at the ground floors, it is crucial to plan and program the neighborhood functional mix, as already described in a previous article (29). These proposals have attempted to offer an adequate level of quality of life at a short distance, taking into account some essential urban social functions such as living, working, supplying goods and services, providing care and assistance, learning, and enjoying recreational facilities.

At the same time, as regards the indoor common spaces of the dwellings, to guarantee the safety and privacy of residential units and working spaces, it would be appropriate to evaluate in advance the possible impact of the simultaneous presence, in the same building, of units and spaces with incoherent functional use, with particular attention to the sources of noise and atmospheric pollution. The design criteria should, among other things, favor the choice of activities that are complementary and compatible with the health and well-being of the occupants, limit interference through a careful study of the ways in which the spaces are used, and define such distribution layouts to minimize the negative impacts that the presence of different activities can generate.

3. Re-appropriation of the basic principles and archetypes of sustainable architecture, thermal comfort and Indoor Air Quality (IAQ)

Starting from the recent pandemic, the importance and the need to re-appropriate the architecture sustainability archetypes related to the building shape and orientation become a priority for investigation. The housing units and living spaces, even if small when located in densely built-up areas, should be designed in accordance with at least the minimum, basic principles of building hygiene.

Strategies include requirements for correct orientation, to make best use of sunlight and natural heat and light, thus in temperate climates like Italy's, the following orientations are favored: southeast-, south- and southwest-facing for the living spaces; east-facing for the bedrooms; and the north-facing for the working areas to ensure diffused natural lighting and avoid the glare effect.

Moreover, it is important to take into account the natural lighting through glass surfaces for an adequate

level of illumination in the room, considering also the external view and, at the same time, to use light colors for internal surfaces to increase reflection and also to ensure, where possible, an adequate view of the neighborhood, and possibly of green areas (23).

Finally, it would be appropriate to move from a merely prescriptive-based approach of the buildings codes to a performance-based design approach that takes into consideration - at least - the Daylight Factor (DF) in defining the quality objectives of natural daylighting (41).

Another strategic topic is thermal comfort and Indoor Air Quality (IAQ), of particular relevance during the lockdown when the population was confined to the home. However, as in periods of high pollution rates in cities, residents must not make the mistake of keeping the windows closed, in order to guarantee regular natural air change rates (42). In fact, it is known that the quality of the air in confined spaces plays a direct or indirect leading role in health prevention. In addition to the quality of the outdoor air, IAQ also depends on the presence of internal sources of emission and diffusion of contaminants, with the concentration of chemical and biological pollutants that can influence their features (43).

Starting from the issue of indoor air conditioning systems, mainly during the summer season and the possible increase of the risk of COVID-19 transmission among occupants (44), it is preferable to suspend mechanical systems, guaranteeing natural ventilation through more frequent window opening, especially if some rooms have been adapted as remote working and homework stations (44-45).

The necessity and frequency of opening windows may vary according to the number of people and the activities carried out in the rooms. It is advisable, especially in winter, to open the windows even for few minutes several times a day, and in the spring and summer seasons to keep them open, or at least ajar, to ensure a regular air flow from outdoors, according to solar exposure and the absence of possible noise sources.

Environmental units without windows (such as bathrooms, closets, etc.) must be equipped with air extractors. However, it should be remembered that during the SARS epidemic of 2003 in Hong Kong, virus transmission was demonstrated through engineering plants from toilets equipped with extractors; therefore, it is necessary to clean them regularly (44).

In the presence of ventilation, cooling and/or heating systems, it is appropriate to maintain suitable microclimatic conditions by avoiding air which is too dry and ensuring an adequate level of relative humidity (35). In any case, constant cleaning of the components and grids is necessary to eliminate all the dust and compounds where favorable conditions to the development and survival of bacteria and mold can occur, and air filters should be replaced regularly (46).

In addition, to ensure proper thermo-hygrometric well-being, natural and/or mechanical ventilation, and adequate IAQ, home automation systems (smart homes) could play a strategic role with suitable and programmed actions, also supported by on-site detectors, which can guarantee optimal conditions for the living environments with the automatic opening of windows for regular air changes.

4. Water consumption and Wastewater Management

The recent lockdown measures were the consequence of the absolute necessity of ensuring health by avoiding the contagion, but keeping people confined to the home for weeks also requires that the sanitary conditions of the dwellings be maintained at their best (32). In particular, the co-presence of sick individuals during home isolation represented the biggest challenge, as the other family members must be protected: therefore rethinking dwellings as places that comply with safety recommendations is essential.

In this context, if, on the one hand, the availability of properly treated and distributed drinking water is decisive to guarantee a source of a safe supply for consumption (47-48), on the other hand, the management of both liquid and solid municipal wastes becomes an additional critical point.

In particular, liquid waste is currently being studied by the international scientific community, given its possible role as a vehicle for infection.

Recently, the Italian Institute of Health (ISS) has documented the presence of genetic material of SARS-CoV-2 in urban wastewater, confirming the epidemiological opportunity of using wastewater as an indicator of the presence of the virus in the area (48-49). The US

Centers for Disease Control and Prevention (CDC) have confirmed this evidence (50). It must be said that the technique employed merely demonstrates the presence of one or more sequences of the genetic material – not infectious - of the virus, and not necessarily the presence of the infectious particle. However, it has been recently hypothesized (51-52) that the virus could survive in stools and, therefore, that droplets of wastewater could transport infectious particles, exposing the individuals (both sewage workers and also inhabitants) to contagion. At the moment, the situation is still uncertain and constantly under debate. In any case, the ISS is activating an environmental surveillance network on the national territory of Italy, to acquire useful knowledge for the assessment of the real role of wastewaters in viral transmission or, at least, to demonstrate the availability of a useful monitoring indicator (53).

As far as drinking water is concerned, according to the World Health Organization (WHO) "Interim Guidance on Water, Sanitation, Hygiene, and Waste Management for the COVID-19 virus" (54), the most important practices to be implemented in places where centralized water treatment and safe piped-water supplies are not available, regard the safe management of water, which should be safely collected and stored at home in regularly cleaned and covered containers. In addition, when the available water is not safe, household water treatment technologies (such as boiling, solar irradiation, UV irradiation and appropriately dosed free chlorine) must be made available and effective in removing or destroying the virus.

Furthermore, on ascertaining the drinking water quality, which depends on proper treatment and disinfection processes, it is desirable to undertake an adequate communication to the citizens, aimed at emphasizing the safety and security of the resource, to contrast the well-known distrust that the population has towards this precious asset (55-59). The current epidemic could offer further inspiration to underline the positive aspects of tap water which, we recall, is constantly monitored, unlike other alternative sources of supply (i.e., wells, springs, etc.). For the latter, an important recommendation regards the need to always implement appropriate water disinfection before using it for human consumption.

On the other hand, particular attention should be paid to the treatment of liquid waste, especially when the recovery of such water is envisaged. Monitoring and constant disinfection are strongly recommended, especially in light of the studies currently in progress, aimed at deciphering the role of possible sources of viral diffusion, in addition to the due technical-plant engineering measures (i.e. well-maintained plumbing, sealed bathroom drains, backflow valves on sprayers and faucets), necessary to avoid possible exposures in domestic environments. Finally, as far as wastewaters are concerned, it would be desirable for individuals with suspected (or confirmed) COVID-19 to be provided with separate bathrooms to be cleaned and disinfected at least once a day, using personal protective equipment. If home toilets are not connected to sewers, hygienic on-site treatment systems should be provided.

5. Urban Solid Waste Management

The quarantine policies, imposed in most countries, have brought about a series of behavioural and environmental consequences that have to be taken into consideration in future solid waste management policies.

First of all, consumers modified their habits, with an increased demand for online shopping for food or other products with home delivery, all shipped or distributed packed, causing an increase in both organic and unorganic waste production. Furthermore, medical waste rose with an increase in the use of personal protective equipment such as masks and gloves (29). As a result of the pandemic, some US and European cities have suspended recycling programs, as authorities have been concerned about the risk of COVID-19 spreading in recycling centers.

Italy has prohibited infected residents from sorting their waste (60): in buildings with SARS-Cov-2 positive or suspected subjects, under isolation or in mandatory quarantine, the recycling program has been stopped and all domestic waste, including organic waste, glass, metal, plastics, paper tissues, paper rolls, disposable sheets, masks and gloves, has been treated as "unsorted" (54,61).

Although the "*23 Global Cities and Regions Advance Towards Zero Waste*" (62) stated the commitment

to avoid, by 2030, the disposal of - at least - 87 million tons of waste, the new worldwide situation created by the lockdown period has underlined the high topicality of the urban solid waste (USW) problem, especially in densely built-up contexts, where sanitation has taken on a crucial role in tackling the spread of COVID-19.

Therefore practical, feasible, repeatable strategies and actions are crucial and include:

- programming innovative digital and smart devices, capable of facilitating differentiated waste collection and making citizens conscious and active participants in the processes of reporting anomalous situations, thus obtaining a capillary control over the whole city, increasing the efficiency of the system;
- disseminating "returnable" practice like the Milan and Stockholm experiences, which allow an immediate and significant reduction of waste;
- replacing regular bins with smart bins, which could allow a careful and continuous monitoring of waste collection, especially in public spaces, which are neglected on numerous occasions;
- increasing pneumatic networks like the Automated Vacuum Waste Collection System (Oslo and Stockholm).

Starting from the recent pandemic, the presence of an adequate garbage area, protected from rodents and pests, within the condominium spaces with a flexible configuration enables a response to various uses over time.

6. Housing automation and electromagnetic fields

In the face of the COVID-19 epidemic, the role of home automation, better known as smart home, becomes strategic: the larger the housing unit, the more a smart home system is necessary. In fact, computer systems, supported by detectors and sensors inside the environment and by mobile interface devices, can guarantee an easy control and management of the home, improving comfort (air quality, temperature and humidity, air changes, etc.), planning various activities in advance (watering gardens/terraces, activating washing machine, dishwasher, oven, portable vacuum cleaners, etc.), increasing security (anti-theft systems, fire prevention systems, remote environmental video control, systems for opening and closing windows, doors and shutters, etc.), as well as generating economic and energy savings by monitoring consumption, activating and deactivating systems when they are not needed (lighting system, space heating and/or cooling, etc.) (32), although the system itself requires minimal consumption for 24/7 monitoring. However, it is not excluded that the presence of home automation (sensors, detectors, cameras, technological equipment for lifting the user and/or stair lifts, etc.), in housing units with elderly and/or sick people, who live alone, could guarantee their greater safety and immediate assistance in case of need.

It is therefore clear that these systems require the presence of internet and Wi-Fi networks for their operation and remote control.

In addition, with the onset of the COVID-19 pandemic, the population, confined to their homes, transformed their living environments into places for recreation, work, study, physical activity, etc. putting the flexibility, versatility and resilience of spaces to the test (44). Responding to a series of different needs, but above all for smart working or online lessons for students, and in the face of the mandatory social distancing due to the health emergency, the presence of Internet and Wi-Fi connections becomes strategic and fundamental (11-12).

The presence of IT systems in each housing unit and, given the restrictions due to COVID-19, the excessive use of this network from morning to evening (from smart-working and online lessons to video calls, streaming movies, etc.), used by several family members at the same time, has resulted in and entails the need for ever better performing IT systems in new homes.

This measure to ensure an adequate computer connection is fully part of the current scientific debate relating to electromagnetic fields and the introduction of new, increasingly high-performing computer networks (5G). This mobile phone technology will give rise to new scenarios of exposure of the population to radio frequency electromagnetic fields which will be emitted in different frequency bands from those currently used for mobile telephony. One of the particularly novel aspects of 5G consists in the fact that various wireless devices communicate directly with

each other, in particular using electromagnetic waves, known as "millimeter waves", although the latter correspond more precisely to frequencies between 30 and 300 GHz (wavelengths between 1 and 10 mm) (63).

Nowadays, the evidence regarding health effects linked with exposure to wireless technologies are not conclusive. WHO and several international institutions will review scientific evidence related to potential health risks from 5G exposure as the new technology is deployed, and as more public health-related data become available (64).

7. Indoor building and finishing materials

Following the experience of the COVID-19 pandemic, designers and users have observed starting with their own living environments, that building materials, and in particular the finishing materials and furnishings, have a strategic role for health promotion and for the cleanliness of domestic environments.

Finishing materials of the floors, walls and ceilings are very varied, and for example the same house can have very different flooring among the environmental units, each different properties, treatments and compositions (65). Among these, it must be underlined that several finishing and furnishing materials emit VOCs, and in the presence of high temperatures and/or due to the solar exposure of the environments, their emissions increase (66).

Currently the market offers innovative materials to reduce the bacterial load on the finishing surfaces also with eco-active materials and photocatalytic paints, but with no demonstration on the viral load.

In fact, although it has not yet been shown that the transmission of viral loads derives directly from contact with commonly used objects, evidence shows that viruses belonging to the same group (Coronavirus, SARS virus and MERS virus) can persist on inanimate surfaces for up to several days depending on the material, the quantity of biological fluid and the initial viral concentration, the air temperature and relative humidity, even though their infectious capacity has not been proven (35).

More recent data relating to the SARS-CoV-2 virus (67) confirm that on plastic and stainless steel, under experimental conditions (therefore with microclimatic conditions in the laboratory), the ability of the virus to persist is similar to that of the SARS virus (SARS-CoV-1), however, it showed an exponential decay of viral capacity over time (half of the viral particles were no longer infectious after a few hours). Indeed, from the laboratory data, van Doremalen et Al. (67) observe that copper and cardboard have a complete reduction of the viral load in reduced times (respectively about 4 hours and 24 hours).

However, the absence of antibacterial and antiviral materials can be easily overcome by careful, regular and constant disinfection of spaces (35). It is clear that particular attention must be paid to the surfaces most frequently touched (e.g. doors, door handles, windows, tables, light switches, toilets, taps, sinks, desks, chairs, cell phones, keyboard, etc.) (68), and that not all detergents can be used on all surfaces and materials (44). In fact, in homes we also find materials and/or furnishings that cannot be washed (e.g. rugs, carpets and mattresses), and therefore it is necessary to use steam appliances (35).

In general, as evidenced by the Scientific Community, airing the environments both during and after the use of cleaning products is optimal to ensure healthy environments.

Take-Home Messages and Research Outlooks: Challenges and Opportunities

The lockdown due to the COVID-19 pandemic forcefully put on display again the importance of housing conditions on people's health and well-being, underlining the vast inequalities in housing registered in Italy, particularly in metropolitan areas. The lack of adequate space, terraces and gardens have contributed to increased stress and aggressivity, especially among the disadvantaged.

Therefore, the policymakers should consider housing as a major priority for the potential relapses in public health related to it.

The issues previously described regarding overcrowding and the quality of dwellings underlines some, as yet unresolved, past problems (69). First of all, it is necessary to provide updated and rigorous requirements for the built environment and in particular

for residences (1,11), taking into account that in Italy the demand for public housing is increasing, as is the demand for buildings with high energy efficiency.

Table 1 summarizes some recommendations prompted by the quarantine imposed during the COVID-19 pandemic which should be taken into ac-

Table 1. Indications for a healthy, safe and sustainable housing

Investigated areas	Pre-existing constructions	New constructions
1. Visible and accessible green elements and spaces.	• use of suitable material to control the albedo of the flooring of open spaces • implement the building with green roofs and walls, or small balconies, where possible	• use of vegetation for the summer shading of buildings • use of suitable material to control the albedo of the flooring of open spaces • provision of green roofs and walls • emphasize the presence of balconies and/or terraces • view of greenery from windows
2. Flexibility, adaptability, sharing and crowding of living spaces, and compliant functions located within the buildings.	• usability and accessibility at least in terms of adaptability of living spaces • flexibility of the indoor spaces • quality of living spaces: furniture, dimensional standards • compatibility between different functions in the building • flexibility of the condominium spaces (ground floors, basements, free floors)	• usability and accessibility of living spaces • flexibility of the indoor spaces • quality of spaces: furniture, dimensional standards, views • compatibility between different functions in the building • flexibility of the building common spaces (ground floors, basements, free floors)
3. Re-appropriation of the basic principles and archetypes of sustainable architecture, thermal comfort and Indoor Air Quality (IAQ).	• adequate orientation of the living spaces • regular natural air change rates • regular maintenance of ventilation, cooling and/or heating systems, where present	• correct orientation of living spaces, according to the solar radiation and to the natural heat and lighting supplies • regular natural air change rates • regular maintenance of ventilation, cooling and/or heating systems, where present
4. Water consumption and Wastewater Management.	• ease of access to household water storage • implementation of household water treatment technologies • installation of backflow valves on sprayers and faucets	• ease of access to household water storage • implementation of household water treatment technologies • implementation of technical-plant engineering measures (i.e. well-maintained plumbing, sealed bathroom drains, backflow valves on sprayers and faucets) • installation of more than one bathroom
5. Urban Waste Management.	• flexibility of the garbage area or specific spaces in the courtyard or common spaces • differentiation of access to the waste collector area • application of "returnable" practice which allow an immediate and significant reduction of waste • replacement of regular bins with smart bins	• presence of a garbage area • flexibility of the garbage room • more than one access to the garbage room to respond to various uses over time • development of innovative digital and smart devices, to facilitate differentiated waste collection • replacement of regular bins with smart bins • development of pneumatic networks where possible

(continued on next page)

Table 1. Indications for a healthy, safe and sustainable housing

Investigated areas	Pre-existing constructions	New constructions
6. Housing automation and electromagnetic fields.	• introduction of smart home systems with detectors and sensors • control and management of indoor air quality, temperature and relative humidity, air change rates, etc. • mechanical window opening and closing, where possible • control systems for elderly and/or sick people, in case of need	• introduction of housing automation and smart home systems with detectors and sensors • control and management of indoor air quality, temperature and relative humidity, air change rates, etc. • mechanical window opening and closing • control systems for elderly and/or sick people, in case of need
7. Indoor building and finishing materials.	• introduction of high performance furnishing materials • use of adequate detergent and cleaning products • regular cleaning activities	• introduction of high performance finishing and furnishing materials • selection of low VOC materials • use of adequate detergent and cleaning products • regular cleaning activities

count both for the renovation of pre-existing constructions and for the construction of new buildings.

What emerges from the scientific literature (01,12,35,70-72) is that, in order to guarantee good health standards, nowadays it is indispensable to direct political and administrative choices to improve the overall conditions of the neighborhood and of the buildings within. Therefore, evaluating a healthy living environment implies taking into account, not only the single housing unit, but also the environmental context within which it is inserted, paying particular attention to the solutions adopted regarding environmental sustainability and adaptation to climate changes. We have addressed several of these topics related to the COVID-19 pandemic in a previous paper (29).

Many aspects included in Table 1 are considered essential by WHO (72) and are accounted for in many European building codes (73). In Italy, the introduction in 2016 of the National Building Code (74), already adopted by some Italian Regions, attempted to bridge this gap by integrating several regulations into a single one. However, regarding health standards related to housing, it refers to a previous ministerial decree (11), which requires updating, given that 45 years have passed since it was approved. Therefore, without a clear national legislation on hygienic requirements, it is easy to understand how difficult the daily practice for both designers and Public Health Officers is (11). To these latter, in particular, the current legislation attributes a limited role regarding the design and construction choices for new buildings and restorations, Consequently, the relevance attributed to health in the design solutions proposed mainly depends on the competence of designers and on the responsibility of the builders (29).

The COVID-19 pandemic also underlined the crucial need for a strong interdisciplinary and transdisciplinary approach between researchers and practitioners, from both technical and health backgrounds, in order to address the main Public Health issues related to the built environment (35,75-77) and to the housing demands.

For this reason, taking into account the previous work of the authors (29) involved in the Building Hygiene Working Group of the Italian Society of Hygiene (SItI) it becomes important to improve stakeholders' awareness of the factors affecting health in living spaces, and to inform both the citizens and the policymakers - both building code legislators and tax incentive providers - about the design strategies for people's psychophysical and social well-being, for the protection of the environment and for the safety of the occupants of the dwellings.

It is also important to consider there is little shared vocabulary among disciplines (78), which poses a problem since cities are multi-dimensional systems influenced by trends and processes operating at local, national or supranational levels, e.g. global initiatives

(79) that address urban issues, such as the Sustainable Development Goals (SDGs).

It is necessary to pool the knowledge from the technical field and Public Health expertise, identifying exportable and scalable best practices: in order to reach this goal, the professional figure of the previously defined Health City Manager (75), who may be included in the team of Public Administrators, could bring together the competences of the Municipal Department of Construction and the Public Health experts (80) working in the Local Health Agencies, to make the building and hygiene regulations, although sometimes still conflicting, work more cohesively, taking into account both local and global trends .

In conclusion, as underlined by WHO (9), building healthy housing is a complex issue and a multisectoral responsibility, achievable only if a contribution is made by all relevant players and the COVID-19 pandemic has placed the country's profound housing crisis under the spotlight, and further highlighted the need to address it in a systematic way.

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Original article

Detection of SARS-CoV-2 on hospital surfaces

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Abstract. The COVID-19 pandemic, affecting 213 countries, with more than 10 million cases and over 500,000 deaths is still causing serious health, social and economic emergency worldwide. Italian Northern regions are among the most badly affected areas. Surfaces represent matrices to which particular attention should be paid for prevention and control of SARS-CoV-2 transmission. A few studies have highlighted virus presence on surfaces. We report the evidence of its presence on hospital surfaces, in a single room hosting a patient whose nose-pharyngeal swab resulted positive for SARS-CoV-2 RNA at the admission. The surfaces sampling was carried out using pre-wetted swabs followed by extraction and amplification of viral RNA by reverse Real-Time Polymerase Chain Reaction (rRT-PCR). A total of 4/15 (26.66%) surfaces were positive for SARS-CoV-2 RNA: the right bed rail, the call button, the bed trapeze bar, the stethoscope; moreover, the patient's inner surgical mask was positive, showing the emission of the virus from the patient. This study is a further confirmation that the surfaces represent a potential vehicle of transmission. This supports the need for strict adherence to hand and environmental hygiene. (www.actabiomedica.it)

Key words: SARS-CoV-2, hospital environment, surface contamination, surface sampling

Introduction

The COVID-19 pandemic caused by the new coronavirus SARS-CoV-2, affecting 213 countries, with more than 10 million cases and over 500,000 deaths, is still causing serious health, social and economic emergency (1). Italy is among the most badly affected countries, with a higher incidence and mortality in the Northern regions (2).

The mechanisms of transmission of the disease are not yet fully known, even if close contact through droplets, which can reach, directly or through contaminated surfaces, susceptible subjects, is considered determinant (3). Experimental studies have shown the presence for hours of infectious virus in droplets and for hours or days on surfaces, according to the type of material, the humidity and temperature (4). Air and surfaces therefore represent matrices to which particular attention should be paid for the prevention and control of SARS-CoV-2 transmission. Identifying the presence of viable SARS-CoV-2 and knowing the degree of environmental viral contamination, through an appropriate monitoring of air and surfaces, is fundamental to the understanding of transmission mechanisms (5). World Health Organization underlines the importance of accessing the extent and persistence of surface contamination of SARS-CoV-2 and identifying environmental surfaces which may play a role in onwards transmission, and provides specific indications for surface sampling (6).

A few studies, in most cases performed in China, have highlighted the presence of the virus on surfaces. This study reports evidence of its presence on hospital room surfaces.

Materials and Methods

The study was carried out in a single room hosting an elderly patient with fever, dyspnea and pneumonia, diagnosed by High Resolution Computerized Tomography, with nose-pharyngeal swab resulted positive for SARS-CoV-2 RNA (Cycle threshold value, Ct 20) at the admission. The surfaces sampling was carried out two days after the patient's second positive swab (Ct 24), seven days after hospitalization. The surfaces sampling was carried out two hours after cleaning and disinfection procedures using a FLOQSwab(R) pre-wetted with molecular water and stored in the eNAT(TM) medium (code 608CS01R Copan Italia S.p.A.). The following surfaces were sampled the two bed rails, the bedside table, the floor near the patient's bed, the head and the foot of the bed, the door handle, the call button, the chair, the wall behind the bed head, the side table, the bed trapeze bar, the air intake grille, the head of the patient's wheelchair, the diaphragm of the stethoscope dedicated to the patient. Moreover, the patient's inner surgical mask was sampled to verify the emission of the virus from the patient. The SARS-CoV-2 research included extraction and amplification of the viral RNA performed by reverse Real-Time Polymerase Chain Reaction (rRT-PCR) using primers and probes related to the E gene, with a detection limit of 5.2 copies of RNA/reaction (7).

Results

A total of 4/15 (26.66%) of surfaces were positive for SARS-CoV-2 RNA: the right bed rail (Ct 31), the call button (Ct 31), the bed trapeze bar (Ct 31), the stethoscope (Ct 33). The surgical mask showed a Ct value of 35 registering the virus emission. Our results show the presence of viral RNA on some of the examined surfaces with Ct values slightly lower than that detected in the patient's nose-pharyngeal swab two days before.

Conclusions

In this study SARS-CoV-2 RNA was identified on hospital surfaces; to our knowledge, in Italy, only two studies have shown the presence of the virus on surfaces. In the first study, the virus was found on surfaces closely related to the patients (CPAP helmet) (8); in the second it was found on several inanimate surfaces, but the Ct values where not reported (9).

Our study is a further confirmation that surfaces are a potential vehicle of transmission. It is interesting to note that the surfaces tested positive were only those in the immediate vicinity of the patient, more frequently touched by hands, more probably by the patient. This supports the need to pay particular attention to adherence to hand and environmental hygiene. It should be considered that surfaces like the ones we found contaminated, can become contaminated very quickly, even though a cleaning and disinfecting procedure has been performed. Therefore, it is essential to educate also the patient to the behaviour contributing to the reduction of environmental contamination. Enforcement of hand hygiene in healthcare workers is also essential. The stethoscope has also been shown to harbour SARS-CoV-2 suggesting it to be a possible vehicle of infection.

The limitation of our study is to have conducted it in only one room with only a single sampling, without assessing its potential infectivity. This aspect, together with the verification of the homology between the environmental and patient viral strains, needs to be considered. Moreover, for a global understanding of the role of the environment in the virus transmission it will be also necessary to verify its presence in the air. A lot of efforts will be needed to standardize the sampling methods and the interpretation of data, in order to understand the role of the environment in the transmission of SARS-CoV-2 and to manage the infectious risk in healthcare settings.

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Original article

Correct management and low rate of contagiousness of healthcare workers in a University Hospital in Southern Italy: from contact tracing to serological investigation

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Abstract. The COVID-19 epidemic, which began in Wuhan in December 2019, quickly spread all over the world, leading in a few months to a high number of deaths also in healthcare workers. The purpose of the study is to a) describe the importance of a correct management of SARS-CoV-2 infections; b) report the number of positive healthcare workers after the epidemic phase and to describe their socio-characteristics data, the main methods of transmission and the symptoms; c) to report the seroconversion rate of healthcare workers (HCWs). The study was conducted from March 9, 2020 to June 19, 2020 in three phases:1) in a first phase, we implemented the guidelines to be followed for patient care in our hospital; 2) in a second phase, we provided the epidemiological investigation/contact tracing of HCWs; 3) we collected swabs on all healthcare workers and we also performed serological investigation. The number of healthcare workers under surveillance is of 2611 subjects and, of these, only 0.65% contracted COVID-19. In particular, 70.6% of these have been infected in the healthcare setting, 11, 8% in the family and 17.6% returning from high risk areas. Ultimately, only 0.1% of HCWs dedicated to the treatment of COVID-19 patients contracted the infection (one was asymptomatic). Only 2% of HCWS were positive for serological investigation. (www.actabiomedica.it)

Key words: management, healthcare workers, COVID-19, SARS-CoV-2, symptoms

Introduction

The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) epidemic, which began in Wuhan, China in December 2019, quickly spread all over the world, leading in a few months to a high number of deaths and 8,986,016 infected (last update June 22) (1).

Many initial cases reported outside of China were imported or were linked to travellers from China (2). However, as community transmission has become widespread, the source of cases of COronaVIrus Disease 19 (COVID-19) in several countries has not been established (3).

In Italy, the first cases have been described in Rome on January 29 involving two Chinese tourists referring to the Spallanzani Institute, representing imported cases (4). Subsequently, unfortunately, on February 21 the first autochthonous Italian case of COVID 19 was identified, in Lombardy (Codogno),

the region that first struck by this invisible infection paid the highest price in terms of mortality and morbidity (5,6).

The epidemiological nature of the disease, with its long incubation period, has given time to the health systems of other regions, thanks also to the lockdown measures undertaken, to get ready by setting up proper COVID hospitals or wards (7). At the same time, the continuous updating of international and national guidelines, also allowed a further limitation of the contagions, as far as well applied.

In particular, on January 30 2020, after the second meeting of the Security Committee, the General Director of the World Health Organization (WHO) has declared the international outbreak of COVID-19 as a public health emergency of international relevance (Public Health Emergency of International Concern - PHEIC), as established in the International Health Regulations (8).

In Italy, on February 21, the Ministry of Health enforced the quarantine measure with active surveillance for fourteen days for individuals who have had close contacts with confirmed COVID-19 positive subjects, or in the last fourteen days had returned from high risk areas of China, by the means of the territorially competent health authorities which had the obligation to notify the Local Health Units (9).

The definition of close contact and the indications related to laboratory diagnosis were established by the Ministry of Health (10).

Contact tracing, in combination with the early detection of cases and in synergy with other measures such as physical distancing, are essential actions to combat the ongoing epidemic, as well as for preventive purposes. The purpose of identifying and managing the contacts of probable or confirmed cases of COVID-19 is to quickly identify and isolate the secondary cases, in order to intervene and interrupt the transmission chain. It is also worth remembering the role of asymptomatic in the dynamics of the epidemic spread of COVID-19 (11).

In healthcare workers (HCWs) "the provision referred to in article 1, paragraph 2, letter h), of the decree-law of 23 February 2020, no. 6 (quarantine) does not apply and they must instead have supervised. The same HCWs must suspend their work activity only in the case of respiratory symptoms or a positive test for SARS-CoV-2 (12). Additionally, in Sicily, the local government introduced as mandatory the search for SARS-CoV-2 on all HCWs using a nasopharyngeal swab, thus testing also asymptomatic subjects (13).

The molecular diagnostic protocols for SARS-CoV-2 drawn by WHO are based on the identification of viral RNA by Real-Time reverse transcription polymerase chain reaction (Real Time RT-PCR) (14-16). In Italy, Annex 4 of the circular of the Ministry of Health dated February 22 (17) establishes the guidelines for laboratory protocols and all details on the collection and sending of biological samples for diagnosis. From that time on SARS-CoV-2 detection could be performed only by certified laboratories and main hospitals identified by regional health departments on the basis of the afore mentioned protocols. For specimen collection in clinical settings samples were taken from the lower respiratory tract using sputum, endotracheal aspiration, or bronchoalveolar lavages. In the event that patients do not show signs of lower respiratory tract disease, or if the specimen collection was not possible, even if clinically indicated, samples taken from the upper respiratory tract such as nasopharyngeal aspirate or nasopharyngeal swabs was recommended.

In this context, serological testing can have a crucial role in identifying convalescent cases or people with milder symptoms who might have been missed by other surveillance methods. The preliminary observations, available from the initial outbreaks in China, quantified in about 85% the total number of infected people from high risk areas (18). It should be emphasized that the presence of antibodies does not necessarily translate into immunity, since not all antibodies are able to neutralize the virus. Serological tests can provide a qualitative (yes/no) or quantitative measurement of antibodies relative to a specific viral antigen. However, the ability of antibodies to prevent viral replication and clear infection is determined through neutralization assays. To date, it appears that the truly neutralizing antibodies are those specific to the spike protein (S) and nucleocapsid protein (N) of SARS-CoV-2 (19). It should be emphasized that one of the most important limits for the extension of serological test to the entire population is represented by the

sensitivity and specificity values of the test, but thanks to a Bayesian method, it is possible to build a range of credibility values of the prevalence when the sensitivity and the specificities are unknown (20).

The purpose of this study is to a) describe the importance of a correct management of SARS-CoV-2 infections and of a correct organization b) report the number of positive HCWs after the epidemic phase and to describe their socio-characteristics data, the main methods of transmission and the symptoms c) report the seroconversion rate of HCWs.

Materials and methods

The University Hospital "G.Martino" of Messina includes 14 pavilions, indicated with the letters of the alphabet which have four to six raised floors with a total of about 570 beds. Following the COVID-19 epidemic, an entire pavilion was dedicated to the care of these patients (70 places) and other 90 have been added at a later stage, also creating a "surgical area" for the exclusive use of positive patients. The number of healthcare workers in the entire structure is of 2311 units plus 330 postgraduate medical doctors for a total of 2611 HCWs.

The study was conducted from March 9, 2020 to June 19, 2020 in three phases:

1) In a first phase, the guidelines to be followed in patient care, the indications on a correct and rational use of individual protection devices and sanitizers were implemented in the University Hospital by the Hospital Hygiene Unit and the Health Department;

2) In a second phase, a plan was adopted for the epidemiological investigation and contact tracing of HCWs who for clinical or epidemiological reasons (confirmed / probable case contacts or individuals coming from city at high risk or foreign countries) required the start of the protocol. The pharyngeal swab was then performed on symptomatic subjects for the detection of SARS-CoV-2.

In particular, the epidemiological investigation was carried out by adapting the model provided by the superior health institution (SHI) and implemented with the European Center of Disease Control (ECDC) guidelines, by collecting the socio-personal information (gender, age, job, hospital unit), the date of onset of symptoms and the type of symptoms (by monitoring the subjects twice a day on a daily bases), the possible return from areas at high risk, the way of contact with any suspected/ confirmed case or with subjects with flu-like symptoms and the adherence during the patient's approach of the company guidelines on the use of personal protective equipment (PPE) and on hand sanitization measures (as indicated in the document provided by ECDC), the vaccination status for influenza, any contact with other individuals and compliance with isolation measures.

3) The third phase, in accordance with the indications of the regional decree, was represented by the performing of the swabs on all the healthcare workers and moreover, at a later time, from the start of the serological investigation.

We collected nnasopharyngeal swabs by all HCWs and they were immediately processed for molecular SARS-CoV-2 detection using Allplex™ 2019-nCoV Assay (Seegene, Korea). Briefly, viral RNA was extracted using a Nuclisens Easymag platform (Bio-Mérieux), which can process 24 samples per run. A total of 200 µl of each sample was extracted and eluted with 100 µl of elution buffer, according to manufacturer's recommendations with minor modifications. Briefly, to enhance the recovery of viral RNA, 10 µL of poly (A) RNA carrier (Qiagen) were added, after the lysis incubation step, to each sample before the addition of magnetic silica. Amplification and identification of 2 target genes specific for COVID-19 and an E gene specific for all of Sarbecovirus including SARS-CoV-2, were performed using the Allplex™ 2019-nCoV, a multiplex RT PCR assay, according to the manufacturer's instructions, on a CFX96 Instrument (Bio-Rad Laboratories). Single RT-PCR was performed in a 25-µL reaction mixture for each sample. The threshold cycle (C_t) from the following fluorogenic probes: FAM (E gene), Cal Red 610 (RdRp gene), Quasar 670 (N gene) and HEX (internal control) were acquired. Samples were considered positive with a $C_{t\ value} < 40$ for any gene. The samples must be considered negative when the internal control, but not the viral genes, are amplified. When there was no amplification of the internal control the samples must always be considered invalid.

Later, according with the Document of the Ministry of Health titled "Patient cured for Covid-19" (21), concerning the screening of the asymptomatic HCWs; and the Circular of the Ministry of Health of May 9, 2020 (22) concerning the interpretation of serology, we proceed to serological investigation as follows:

1) If the HCW is positive for IgM (with or without IgG) serum, he/she must remain in home isolation as long as it is negative for the presence of SARS-CoV-2 ribonucleic acid (RNA) on nasopharyngeal swab, repeated twice for 2 consecutive days, and only on this case the HCW will be able to return to work. However, for prudential purposes, serological test was carried out again after 7 days together with nasopharyngeal swab for SARS-CoV-2 RNA detection.

2) If the HCW is positive for serum IgG only, he/she will have to remain in close home isolation until it is negative for the presence of SARS-CoV-2 RNA on nasopharyngeal swab, repeated twice for 2 consecutive days. At that point the HCW will be able to return to work.

For the assessment of IgG and IgM antibodies against SARS-CoV-2 we used MAGLUMI 2019-nCoV IgG and IgM (two indirect CLIAs) in human serum or plasma samples, on the fully automated MAGLUMI analyser (SNIBE–Shenzhen New Industries Biomedical Engineering Co., Ltd, Shenzhen, China). According to the manufacturer's declarations, the antibodies used in these assays are directed against both CoV-S (spike) and CoV-N (nucleocapsid). A value ≥1.10AU/mLis considered reactive, whilst the overall reproducibility declared by the manufacturer is between 6.8% and 8.7%.

Results

The number of healthcare workers under surveillance was equal to 2611 units and of these only 0.65% (17) contracted SARS-CoV-2 infection.

In particular, 43 epidemiological investigations were carried out for the presence of SARS-CoV-2 like symptoms or for the exposure to suspected/confirmed cases of COVID-19 disease with the detection of 17 positive cases among HCWs. The average age of the subjects interviewed was 47 ± 11 years, equally distributed by gender. The socio-personal and working characteristics of the positive subjects and of all the interviewees are summarized in Table 1.

The type of exposure was most represented by the workplace (67.4%; n = 29), followed by contacts with suspected/confirmed cases in the family environment, or outside the work area, or the onset of flu like symptoms (23.3%; n = 10: of these 33.3% lived in the same house of COVID-19 positive subject) and, finally, from the return from high risk areas/foreign states (11.6%; n = 4).

The most frequent type of contact in the healthcare area was represented by permanency in the same room of a confirmed case of COVID 19 at a distance of less than 2 meters and for over 15 minutes (58.6%); while the least frequent was contact with secretions (6.9%). The types of contacts are shown in Figure 1. Only in one case the subject performed aerosol-generating procedures. Only in 3 cases the patient wore the surgical mask. All healthcare workers wore PPE, although the surgical mask and gloves were the most worn. All healthcare workers have stated that they always wear all PPE as recommended and disposed of it

Table 1. Socio-personal and working characteristics of the positive subjects and of all the interviewees

Characteristics	Interviewed HCWs (n=43) %(n)	Positive HCWs (n=17) %(n)
Gender females	51 (22)	58,8 (10)
Mean Age ±SD	47 ± 11 years	46 ± 13 years
Hospital ward^		
-COVID Hospital	18,4 (8)	17,6 (3)
-Medicine	44,2 (19)	52, 9 (9)
-Surgery	23,3(10)	5,9 (1)
-Pediatric	11,6 (5)	23,5 (4)
-Emergency room	2,3 (1)	0 (0)
HCWs type		
- physicians	52,5 (21)	58,8 (10)
- nurses	40 (16)	23,5 (4)
- social healthcare workers	12,5 (5)	17,6 (3)
- other	2,5 (1)	0 (0)

^hospital driver = 1

as per hospital guidelines. This lead, except in few cases, in a reduction of the intra-hospital infection rate.

76.5% of COVID-19 positive HCWs developed symptoms (23.5% of asymptomatic subjects) and in particular cough (29%) and fever (47%) (see Figure 2). In two cases, antibiotic or antiviral therapy had to be started.

In two cases the subject required hospitalization which resulted in clinical recovery without complications. None of the subjects had ever been vaccinated for flu.

The swabs gave a positive result in 0.67% (17) of healthcare workers whose socio-personal and working characteristics are described in Table 1. In particular, 70.6% of these contracted infection in the healthcare setting, 11,8% in the family environment and 17.6% returning from high risk areas before the onset of epidemic in Italy. Among those who contracted the disease in the healthcare area, 83.3% worked in the internal medicine operating unit, where the arrival of a patient then confirmed positive for COVID-19 (first two swabs were negative) seems to be related to transmission in the HCWs. The other transmission cases (17.7%) derived from close contacts with cases confirmed in two healthcare workers of the COVID Hospital. Ultimately, only 0.1% (2) of the healthcare workers dedicated to the treatment of COVID-19 patients acquired the infection (1 of which in asymptomatic form).

With regard to the serological survey, 2% (n = 53) of the healthcare workers were positive, of which 41.5% (n = 22) male and 58.5% (n = 31) female. The average age of the subjects who tested positive was 50.12 ±12.09 years. 74% of the subjects tested for Ig G/Ig M positive for Ig G, 20% for Ig M and 6% for both. The data are represented in figure 3.

None of the serological positive subjects were positive for SARS-CoV-2 RNA (no asymptomatic HCWs were detected after the first step of nasopharyngeal swabs). The detection performed after one week of distance, as described in the materials and methods, revealed similar values to those described above.

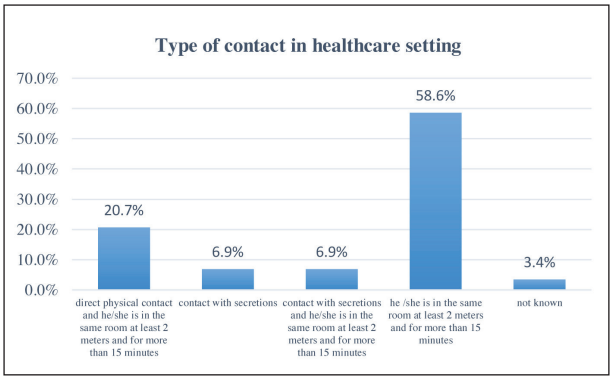

Figure 1. Type of contact in healthcare setting

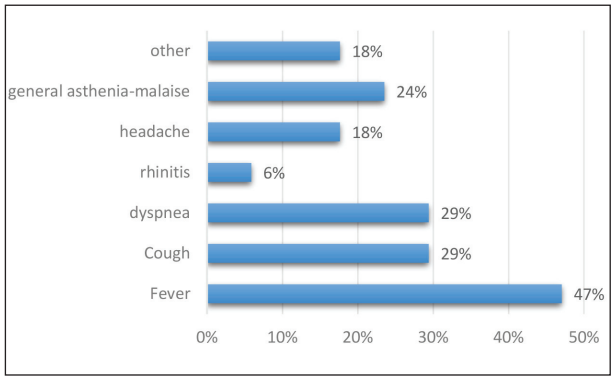

Figure 2. Type of symptoms in HCWs infected

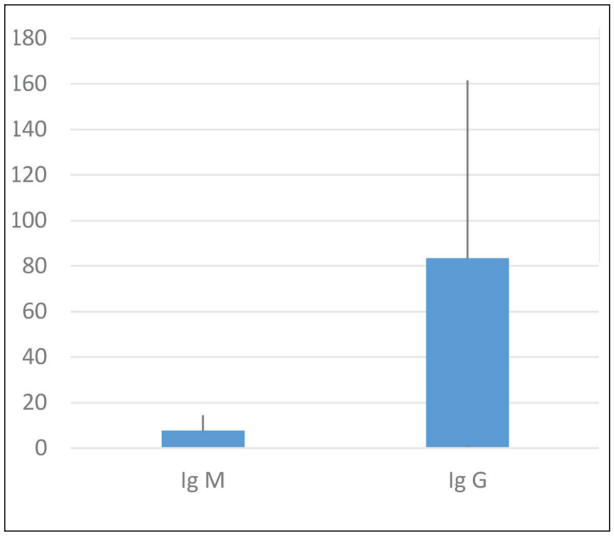

Figure 3. Box plot of Ig M and Ig G of HCWs

Discussion and conclusion

The SARS-CoV-2 epidemic has led to a great impact on all social and healthcare systems all over the world, with a high number of victims even among the healthcare workers (23).

Until June 21, 2020 38,901 cases of COVID-19 were registered in Italy, of which 33,369 died; and 29,174 healthcare workers have been infected (24). This data does not refer to the number of subjects infected during healthcare assistance but only to the type of professional role.

Healthcare workers face an elevated risk of exposure to infectious diseases, including COVID-19, thus, it is imperative to ensure the safety of healthcare workers not only to safeguard continuous patient care but also to ensure they do not transmit the virus. COVID-19 can spread via cough or respiratory droplets, contact with bodily fluids, or from contaminated surfaces and so hospital environment is a potential source of infection both of HCWs and of patients (25).

Our study finds that a correct adherence to the guidelines and the correct use and disposal of PPE are fundamental measures to reduce the risk of contagion, which however cannot be completely eliminated (26).

The greatest risk of transmission occurred in addition to the nosocomial context in the family as previously described in the literature (26,27). In our study, most of the COVID-19 cases among healthcare workers were mild and were managed at home with self-isolation measures, however two infected healthcare workers (11.8%) were hospitalized, despite this no one died. The serological investigation confirmed the previous infection of the positive subjects, but the positivity for IgM and/or Ig G did not lead to new diagnoses, unlike other studies described (28-30).

The availability of serological tests for the assay of anti-SARS-CoV-2 antibodies is however fundamental both for studying the humoral response in infected subjects and for conducting seroprevalence studies in the general population. In this phase 2 that we are addressing the need to identify those who are still susceptible to infections, those who are undergoing acute infection, and those who are cured and, therefore, potentially immune to reinfection remains of paramount importance. Serological tests, suitably validated, could prove useful for acquiring information on the real extent of the pandemic, especially in relation to asymptomatic, and for contributing to the management of the population in the SARS-CoV-2 pandemic. However, it is believed that, at the moment, it is necessary to acquire data that demonstrate the real effectiveness of the immunity conferred by the antibodies. Furthermore, a factor that could complicate the strategy of testing SARS-CoV-2 antibodies on a large scale could be the difficulty of identifying all those who actually present the antibodies, as tests should be repeated at regular intervals to identify new infections through the seroconversion (positivity for IgM and/or IgG).

In fact, considering the nonnegligible percentage of false positives and false negatives, the results provided by the serological methods are less accurate than the RT-PCR performed on samples taken with nasopharyngeal swabs, which remains the most reliable and detect method for diagnosis of COVID-19 even before the onset of symptoms.

In our study, none of the subjects interviewed were vaccinated for the flu and this not only made the differential diagnosis difficult, but led to a reduction in staff (even if negligible) in the emergency phase (31). In addition, a recent study in the literature has hypothesized a protective role of influenza vaccination: the influenza virus would seem to lead to an amplification of the expression of ACE-2, used as the gateway receptor by the SARS-CoV-2 virus (32). In light of this, as with other diseases, vaccination in healthcare workers is essential both to reduce absenteeism and to prevent healthcare professionals from becoming potential greasers (33-38).

In conclusion, according to our results, the best strategy to reduce the possibility of intra-hospital and intrafamily contagion, and to immunize all HCWs, is to test, track and treat SARS-CoV-2 positive subjects. In this perspective, the correct application of guidelines, the role of public health and prevention represent are fundamental points in the health system of each country and their importance should be highlighted also into account of the recent epidemic that hit the world (39-47).

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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COVID-19 lockdown impact on lifestyle habits of Italian adults

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Abstract. In March 2020, when the Government imposed nation-wide lockdown measures to contrast the COVID-19 outbreak, the life of Italians suddenly changed. In order to evaluate the impact of lockdown on lifestyle habits and behavioral risk factors of the general adult population in Italy, we set up the *Lost in Italy* (LOckdown and lifeSTyles IN ITALY) project. Within this project, the online panel of Doxa was used to conduct a web-based cross-sectional study during the first phase of the lockdown, on a large representative sample of adults aged 18-74 years (N=6003). The self-administered questionnaire included information on lifestyle habits and perceived physical and mental health, through the use of validated scales. As we are working within the *Lost in Italy* project, we got two additional grants to further research on the medium-term impact of lockdown, a topic of great interest and with anticipated large socio-economic and public health implications. In details: we obtained by the AXA Research Fund support to evaluate the impact of COVID-19 lockdown on physical, mental, and social wellbeing of elderly and fragile populations in the Lombardy region, the area most heavily hit by the pandemic in the country. Moreover, as a fruitful integration, we obtained support by the Directorate General for Welfare of the region to assess health services delivery and access to healthcare in the same study population, combining an analysis of administrative databases with an economic analysis. We are confident that the solid background of our partners, the multi-disciplinary competencies they bring, together with appropriate funding and access to rich data sources will allow us to fulfill our research objectives. (www.actabiomedica.it)

Key words: COVID-19; lockdown; lifestyles; Italy; cross-sectional study

Italy has been within the European countries with the earliest and heaviest coronavirus disease 2019 (COVID-19) burden (1). To contrast the COVID-19 outbreak, since 9 March 2020 Italians have been under lockdown, with most workplaces and public places, including schools, shops, bars, and restaurants, closed,

and nation-wide stay-at-home order imposed by the Government through 17 May (2). The life of millions of Italians has suddenly changed (3) and lifestyle habits have been substantially modified, with possible short-term consequences on health. The restrictions likely resulted in reduced physical activity, modified dietary habits, smoking and alcohol consumption, as well as altered family relationships and working routine, with ultimate impact on quality of life and psychological well-being (5). In addition, long-term and unequally distributed socio-economic effects of COVID-19 response are anticipated. Evaluating population-level health impact of the current public health emergency is a complex task with distal determinants, laying within health systems, welfare, and economy, and proximal determinants still far from being quantified and explored.

We established a multi-disciplinary consortium with the aim of evaluating the short and medium-term impact of lockdown measures on lifestyle habits and behavioral risk factors of the adult general population in Italy. The consortium comprises representatives of the Italian National Institute of Health, the National and Regional Health Service, research institutes and the academia with expertise in the field of economics, social sciences, epidemiology, public health, and clinical medicine (i.e., internal medicine and mental health). The consortium set up the *Lost in Italy* (LOckdown and lifeSTyles IN ITALY) project. Within this project, a cross-sectional investigation has been conducted during the first phase of the lockdown (i.e., from 27 April to 3 May 2020) on a large representative sample of Italian adults aged 18-74 years. Six-thousand-three subjects were recruited through the online panel of Doxa - the Italian branch of the Worldwide Independent Network/Gallup International Association - and filled in an online self-administered questionnaire. Information has been collected on demographic and socio-economic characteristics, selected lifestyle habits, including tobacco smoking, use of e-cigarettes and heated tobacco products (HTP), alcohol consumption, addictions and gambling, social relationships, and perceived physical, and mental health. The survey tool was developed through experts' consensus, combining and integrating, when available, previously used tools and validated scales. The questionnaire pre-post design allowed us to explore how characteristics of interest had been modified by lockdown measures. The protocol of the study was approved by the ethics committee (EC) of the coordinating center (EC of Istituto Besta, file number: 71-73, April 2020). After data collection completion, we have now defined a list of priority research questions which will be answered in the weeks and months to come. The research outputs will offer insight on the impact of the COVID-19 lockdown in Italy on selected behavioral risk factors, their determinants, and their distribution in different socio-economic strata.

Preliminary results - presented by the National Institute of Health on World No Tobacco Day 2020 - showed decreased smoking prevalence (from 23.3% to 21.9%) but increased number of cigarettes per day among smokers (from 10.9 to 12.7 cigarettes per day), resulting in an overall percent increase by 9.1% during the lockdown in Italy. An increase has been also observed in the prevalence of e-cigarette (from 8.1% to 9.1%) and HTP users (from 4.0% to 4.5%) (6). As soon as evidence from the *Lost in Italy* study accumulates, we will have elements to build a comprehensive and detailed picture of societal, household, and individual-level changes introduced by lockdown measures in Italy.

Building on the outputs from the *Lost in Italy* study, we plan to further investigate the medium-term impact of COVID-19 public health emergency and response on elderly and fragile populations, which represents a sub-group of the general population at higher risk of: i) developing more severe and deadly COVID-19, ii) being negatively impacted by decreased demand and supply of non-COVID-19 healthcare services in time of crisis, and – last but not least – iii) suffering disproportionate socioeconomic consequences of confinement and social distancing measures. In this context, part of our consortium submitted a successful grant proposal to the AXA Research Fund and will work during the next 18 months to conduct an impact evaluation of COVID-19 on physical, mental, and social wellbeing of this high-risk population in the Lombardy region, the area most heavily hit by the pandemic in the country (7). The protocol includes the conduction of a cross-sectional study on a representative sample of the elderly population (≥65 years) in Lombardy. We also obtained by the Directorate General for Welfare of the

Lombardy Region the financial support for a companion project aimed at evaluating health services delivery and access to healthcare in this high-risk population, combining an analysis of administrative databases with an economic analysis in Lombardy region.

We have an ambitious research plan and a considerable amount of work ahead of us; still we are confident that the solid background of our partners, the multi-disciplinary competencies they bring, together with appropriate funding and access to rich data sources will allow us to fulfill our research objectives. We will be able to timely provide solid evidence on the effects of COVID-19 containment measures on behavioral risk factors, physical and mental health in Italy and in Lombardy, so as to identify subjects at higher risk, inform the planning and implementation of targeted mitigation interventions, as well as strengthen preparedness for future public health crisis.

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COVID-19: new scenario old problems

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Abstract. The short paper present the problem of hospital acquired infection in subintensive units of a research and teaching hospital. (www.actabiomedica.it)

Key words: COVID 19 epidemic hospital acquired infection

The Corona Virus 19 (COVID-19) epidemic is an infectious disease which was declared as a pandemic and hit all the Countries, all over the world, from the beginning of the year 2020 (1).

In Italy the epidemic started in Lombardia Region and then it circulated all over the Country and at the moment (30.06.2020) there are 239.709 confirmed cases, 33.542 deaths with 14% as case fatality rate (2,3).

As it was recorded from the beginning of this epidemic up to now almost 10% of patients with COVID-19 experiments an hospital admission and 9% of them needs to stay in intensive care units but the numbers were very different at the beginning of the epidemic when the patients with critical conditions were much more (2).

In a research and teaching hospital located in the centre of Milan to face the sudden flow of critical ill COVID 19 patients many beds were turned in intensive and sub intensive care ones, in particular 84 subintensive beds out of the active 716 beds were set up to admit patients who needed less intensive care than in the intensive care units. In total from March 9th to June 6th 2020, 246 patients were admitted to these 84 beds for sub intensive care and 80 of whom perished (data from the hospital administrative records).

During their stay in hospital these patients, as all the others, faced also a considerable threat for their safety caused by healthcare associated infections (HAIs) which might have determined adverse clinical outcomes (4-8).

All these 246 patients were routinely followed with the usual local infection control surveillance program to detect colonization by multidrug-resistant bacteria, namely MRSA (Methicillin-resistant Staphylococcus aureus), multidrug-resistant Gram-negative bacteria and VRE (Vancomycin-resistant enterococci) in addiction received all the microbiological investigation in case of infectious symptoms.

Globally, 751 swabs for surveillance program were performed and 90 were found positive in 73 patients. Among these, 14 patients had more than one positive swab in different body sites (namely nose and rectum) with different bacteria species. In particular 35 swabs were positive for VRE and 16 for an extended spectrum beta-lactamase (ESBL) Escherichia coli.

Of the 938 cultures performed for clinical purposes in symptomatic patients, 186 resulted positive belonging to 74 patients. Thirty eight patients were diagnosed with an infective episode during hospitalization, 13 with 2 and 12 with 3. The most common isolated pathogens were Enterococcus faecalis, Staphylococcus epidermidis (29 cases each) and Escherichia coli (22 cases).

These first results showed how management of COVID-19 can often be complicated with the emer-

gence of colonization with drug-resistant bacteria and with nosocomial infections, which can lead to aggressive antimicrobial therapies with further resistance selection (9,10).

In our hospital the medical team for HAIs prevention decided against implementing an antibiotic empirical approach for COVID patients, however it must be considered that most of these patients were hospitalized in intensive care units where the odd to receive an antimicrobical therapy is high.

Currently, an universal, safe, effective and targeted treatment for COVID-19 is lacking. More over COVID-19 patients are at high risk of HAIs so their care must be transversal and multidisciplinary and the use and selection of antibiotics should be weighed to prevent resistance selection (10).

In any case these patients must considered very frail and must be protect with a very high standard of environmental hygiene and clinical performance (10).

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Letter to the editor

The homes in the COVID-19 era. How their use and values are changing

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The long lockdown, the frequent adoption of smart working, the online lessons for both school and university students, and the home isolation of many people in order to stop the spread of the SARS-CoV-2, have changed the way millions of people lived their home spaces in the last few months. This also led to a backlash on real estate values, enhancing some characteristics and penalizing others.

This brief contribution comes from a group of university researchers expert in public health and in architecture & health who have been engaging from many years in addressing together the health problems arising from the life in today's cities and homes. This aim could be a stimulus for closer and wider scientific relationship between the components of medicine and architecture for better well-being of people in living environments, with particular reference to urban settings (1, 2).

The COVID-19 pandemic found most of the systems unprepared to this challenge, made worse by the unavailability of a specific vaccine and even of effective drugs (3, 4), and forced the Health Authorities to rely for the containment on traditional public health strategies, such as quarantine, phisical distancing, passive protection by masks, Semmelweis-era hygiene practices such as hand washing and general cleaning of surfaces and furnishings. Due to the SARS-CoV-2 high diffusion rate, the fight against the pandemic has been mainly managed through containment and mitigation measures. Although with different degrees of rigidity, the home lockdown has been one of the most common strategies implemented worldwide by national and regional governments. This situation provided unexpected and prompt changes in the lifestyle of several people, but with the most serious effects to appear progressively only in a long-time period. Several basic concepts emerge as important in tackling the relationship between the home built environment and the occupants' health (5, 6). Let us discuss here a couple of them.

Point one. As the sudden lockdown to contain the spread of the COVID-19 pandemic has been launched, the homes of millions of people have been riorganized in several ways: bedrooms transformed into workstations, kitchens into web-meeting rooms, living rooms into web-classrooms, and balconies (if any) into the only break spaces. By the way, also staying at home was not risk-free: if one member of the family had been infected before the lockdown, the home was to become the starting place of a significant number of contagions (up to 30% during the lockdown), due to the close and continuous contacts between the occupants.

Recent trends in home design and lifestyles have been completely disrupted by this new challenge. Homes, that until a few months ago were used mainly as dormitories, are now hosting several and multiple daytime functions. If this could not be a problem in one-room apartments inhabited by a single, the situation becomes dramatic for small and medium-size apartments inhabited by many people. In such cases, the possibility of "digging" spaces for individual activity does not exist: impossible to have father and mother engaged separately in smart working, and the children attending their online lesson.

The average apartment size in Italy is 117 m^2, but with a very large range: Milan, the second-largest in size of the metropolitan cities, has only 88 m^2, but more than one-third of the Italian apartments is below 60 m^2. The crowding index nationwide shows that 20.7% of the apartments, housing more than 4 people, measure less than 80 m^2. In 2018, 28.8% of the population (16.8 million) lived in overcrowded apartments. A third of the Italian homes do not have even a balcony, 60% has a single bathroom and only 8% of the entire stock has been built in the XXI century (7). Although it is estimated that a contraction of the real estate values by 1.1-3.1% will take place in 2020-2021, homes with high-quality features will instead count on effective market leverages. These features include wider spaces, balconies with good quality views, green areas and separation of common settings (8). Usually, the above features are easier to obtain by building one-family houses with garden; but, contrary to what happens in the suburbs of US or UK cities, including the large ones, this is not the rule for the metropolitan cities of Italy, where – both downtown and in the residential peripheries, due to the cost of land - the building philosophy and the traditions are prone to realize apartment buildings. Then, the defy for our architects and city planners will be, shortly, to find solutions for housing projects which should offer the possibility for the members of the family to practice smart work, to attend digital classes, to have leisure time, to be physically active, in addition to all the tasks of modern family life in modern homes; and this, maintaining a reasonable size of the apartment and squeezing the costs! We believe that some of the activities could be moved to some common spaces of the building: an open space substituting the roof, or a green area around the building, for adult physical activities and/or children playground; a common laundry in the basement to save space in the home; and so on.

Point two. During the epidemic peak, domestic spaces hosted up to 100,000 infected or suspected people under isolation on a trust basis. Creating a true isolation area within individual homes is not an easy task and several points of attention must be considered, such as space and flow separation, cleaning provision, double bathrooms, waste disposal, and support for family members. In this direction, telemedicine can provide important improvements. Lastly, it is renowned that the living condition is an important factor to decide between health or developing diseases, and also to create social inequalities (9, 10, 11). Additionally, several studies agree in showing that, albeit the undiscussable benefits of mandatory mass quarantine, home lockdown might have some negative effects on individual psycho-physical status such as fears of infection, frustration, and boredom, inadequate supplies and information, financial loss and stigma, along with a daily physical activity decay. Considering that built environment features such as dimension, views, natural lights, balconies, and indoor qualities can mediate mental health issues, the characteristics of homes assume an increasingly important role (12).

In conclusion, we can say that, despite the tragedy caused, the COVID-19 pandemic could be an opportunity to accelerate the process of promoting healthier, safer and more resilient homes and for improving the living conditions and favoring the use of homes that improve the well-being of the occupants, reduce the risk of contagion and allow uses consistent with the recent UN and WHO *Sustainable Development Goals* recommendations (13, 14).

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COVID-19 pandemic impact on mental health of vulnerable populations

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Since the World Health Organization (WHO) declared the 2019 coronavirus disease (COVID-19) outbreak first a Public Health Emergency of International Concern, and then a pandemic (1), rapid and severe public policies have been adopted to restrict population movements in order to help curb the epidemic (2). These include so-called 'lockdown' measures, with school closures, border restrictions, quarantine of confirmed or suspected patients and 'stay-at-home' or confinement policies.

These most severe social distancing and confinement measures were pursued both to contain infection transmission at the population level, and to protect high risk and vulnerable groups, including the elderly and people with chronic long-term health conditions (3).

Indeed, the elderly and people with chronic long-term health conditions are those paying the highest price for the COVID-19 emergency: they hold the highest risk of developing severe and deadly forms of COVID-19, with 25% case fatality rate in subjects aged >80 years, as compared <1% in subjects younger than 50 years (4), and the risk of death increasing with increasing number of concomitant chronic diseases (5).

The elderly and people with chronic long-term health conditions are also likely to have experienced unmet non-COVID-19 healthcare needs during the acute phase of the outbreak when health services were stretched to capacity with COVID-19 clinical management. In fact, due to the rapid spread of COVID-19 pandemic, many hospitals witnessed large numbers of unexpected patients with consequent shortages of hospital beds, medical and nursing staff, and medical equipment for chronic conditions care (6). As the COVID-19 pandemic focuses medical attention on treating COVID-19 positive patients and protecting others from infection, elderly and patients with chronic non–COVID-19 related diseases are faced reconsideration of usual standards of care and protocol modifications (7).

Last, but not least, the elderly and people with chronic long-term health conditions are at higher risk of negative mental health consequences of confinement and social distancing. The rapid COVID-19 transmission, as well as, the higher case-fatality in vulnerable groups may enhance the risk of psychopathological decompensation and exacerbate existing psychiatric disorders (8).

The COVID-19 health emergency and associated-social distancing imposed measures can promote feelings of loneliness, hopelessness, despair, death anxiety (9), which are independent predictors of suicide, and enhance difficulties to access regular outpatient visits for clinical evaluations and prescriptions (10).

Moreover, in pandemic times, prejudices and stigma towards vulnerable individuals may be further reinforced by social deprivation, uncertainty, inadequate supplies and information, and could lead to marginali-

zation, segregation, and increased institutionalization of these people, reducing individual autonomy and self-dignity that play a key role in resilience for any age group (11).

As hospital care is restricted by COVID-19, telemental health services could promote continuity of care for at-risk populations at the community-level, remotely supporting them to cope with loneliness and hopelessness during quarantine and self-isolation, reducing the current pressure on health services' capacity and the risk of viral transmission in hospital settings (12). In turn, ensuring continuity of care via teleconsultation might lower the risk of psychopathological decompensation and consequent need of hospitalization for those patients.

The protection of the mental health status of this vulnerable segment of population needs to be recognized as a real public health priority. A careful and comprehensive analysis of risk and protective factors in the individual and environmental context should be performed in order to early detect peculiar needs of care as well as plan and implement appropriate and targeted interventions centred on vulnerable population health.

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The Covid-19 pandemic: looking ahead

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Over the last 100 years, the epidemiological transition in Europe brought progressive decrease in the burden of infectious diseases and concomitant increase in non-communicable degenerative conditions (1). A century has passed since the last serious epidemic in our Continent, the "Spanish" flu; after the second World War, even more, the feeling of safety and success for having defeated one of the most dramatic threat for humanity – an epidemic – became integral part of societal thinking, and object of numerous scientific outputs (2). Health and well-being improved after Europe recovered from the Spanish Flu, thanks to multiple factors, including improved hygiene, living and working conditions, antibiotic use and mass immunization programmes.

Since the 1950s, the way of living in Europe has been evolving around this new epidemiological scenario. Housing, transportation, food, the built environment (hospitals, schools, hotels, restaurants, prisons, nursing homes etc.) have been built and organized to cope with an ageing population and high chronic diseases prevalence in a world where physical proximity and social contact were not considered risk factor, rather an opportunity to socialize and make an efficient use of spaces. The current outbreak brings us back to the past with a disease whose risk of airborne transmission increases with proximity and obliges us to rethink the whole system where we live and work and to re-design the space around us. In this context, society faces new needs (3-5) that can be roughly divided in two different phases, in the short, medium and long-run.

In the short run, control efforts focus on the enforcement of behavioral preventive measures (individual protection, distancing, sanitation, quarantine), whose implementation at the population-level has large socio-economic impacts (6, 7). In addition to preventive measures, the initial phase of the COVID-19 epidemic came with massive pressure on health systems, with particular reference to hospital services having to handle massive and unexpected healthcare needs of COVID-19 patients. This first phase – especially if adopted preventive measures are effective - is relatively short in time and is followed by endemic-epidemic trends with possible isolated clustered infection outbreaks, this until a vaccine will become available. However, other epidemics will eventually come in the future, this raising challenges in a second phase, and in the long-run.

The epidemiological, psychological (8), social and economic (9) impact of the COVID-19 epidemic is likely to generate solid and long-lasting awareness of the epidemic risk at the societal level, this supporting the implementation of structural interventions to modify the urban, architectural and functional characteristics of the world in which we live, so as design safe houses, schools, public transports and other public pleases, nursing homes and, of course, safe hospitals and healthcare facilities. As done in past centuries when we designed and built aqueducts and sewers, monitored food production and distribution so as to ensure safety, likewise now we need to design and build a world that protect us from epidemics. All this, both first and second phase actions requires money and resources. It will be therefore important that all stakeholders, starting from healthcare workers, develop a strong design thinking, proposing solid ideas to gather economic resources that need to be efficiently used, also taking into consideration their management at the European level.

The healthcare sector, where we, and our associations authoritatively belong, has to raise its voice (10) and contribute to the debate. We have a unique opportunity to help to create a resilient word, protected against future epidemics, and we can do that starting with:

1. Strengthening scientific research
2. Building safe spaces and facilities with limited biological hazards
3. Identifying and secting technologies supporting environmental safety in high-risk settings, including hospitals
4. Promote the digitalization of processes and procedures
5. Develop and implement of telemedicine services
6. Improvement monitoring and evaluations systems
7. Improve diagnostic capacities, with particular reference to rapid testing
8. Develop new treatments' protocols
9. Promote staff training and education

This, and much more, will contribute to the general aim of having a safer word, prepared to tackle new challenges related to infectious diseases spread. To lead the change we all need, without further due, to enter a new dimension, and be ready with strong ideas when, in the months to come, the European Commission will start to invest in this important new programme.

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