



## Case Report

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# Phase 3 for COVID-19 in Italy: From a Retrospective Analysis on Deaths among Doctors in Hospitals to the Return of Children at School

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## Abstract

The cause of Coronavirus disease 2019 (COVID-19) is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is sadly well known for the dramatic loss of life it has led to; this new disease was declared a pandemic by the WHO on March 11, 2020. After the People's Republic of China, a large part of Northern Italy (the Lombardy and Veneto Regions) was the first area in Europe to be seriously affected by COVID-19, inducing the regional and central Governments to take a number of social-distancing measures to reduce the spread of the virus by adopting phase 1 of the lockdown. The pandemic has caused tens of thousands of deaths not only in the older population, but also among the doctors and health workers involved in the fight against the virus. An overview of past epidemic diffusion in Italy is reported, underlining the potential factors that could have contributed to such a large number of deaths among doctors (total 176) today, at Tzero for phase 3, September 14, 2020 with the Return of Children at school. Moreover, we make some proposals and suggestions to improve prevention for any up-surge in COVID-19, like the improve of bacterial filtration efficiency for materials designated in the production of medical-standard face-masks.

## Keywords

COVID-19, Doctors deaths, Phase 3, Medical face-masks, Bacterial filtration

## Introduction

To September 21, 2020, 30,905,162 cases of COVID-19 have been confirmed globally, including 958,703 deaths due to COVID-19 patients affected by the severe acute respiratory syndrome, coronavirus 2 (SARS-CoV-2). According to the World Health Organization as of September 21, 2020, the number of positive COVID-19 cases recorded in Europe is 5,195,853 and there have been 229,802 deaths. Comparing new cases for the pandemic, the Americas has had 15,580,622 confirmed cases, and 530,373 deaths; in the United States there have been 6,662,000 cases, and with 198,094 deaths; Brazil has had 4,495,183 confirmed cases, and with 136,532 deaths. The Western Pacific has had 581,897 cases and 12,729 deaths, (The People's Republic of) China has had 90,876 confirmed cases, and 4,744 deaths. The Eastern Mediterranean has had 2,232,748 confirmed cases, with 58,045 deaths; Israel has had 176,452 confirmed cases, with 1,176 deaths, the first country in the world that in the last week re-introduced for the second time a total lockdown. South-East Asia has had 6,167,904 confirmed cases, where India has

had 87,882 deaths. Africa has had 1,145,397 confirmed cases and 24,757 deaths [1]. Furthermore, in Europe, to September 21, 2020 UK had 390,362 cases increasing and 41,759 deaths; Spain 640,040 cases increasing and 30,495 deaths, Belgium had 100,654 cases and 9,944 deaths, France 420,855 cases with an increase of over 2,600 in the last 24 hours and 31,109 deaths, Germany had 271,415 confirmed cases and 9,386 deaths; Sweden had 88,237 cases in decrease.

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In Italy, until September 22, 2020, there have been ~300,000 confirmed incidence cases of coronavirus disease (COVID-19), with 45,489 currently active cases (including 239 patients in intensive care units - ICUs - 2,604 patients hospitalized with symptoms, 42,646 positive in home isolation), 35,738 deaths, and a number of discharged patients recovered 219,670 according to the Istituto Superiore di Sanità [2]. These latest, positive epidemiological conditions ring the start of phase 3, in Italy with the children's return at school (about 500,000) from September 14, 2020 [3]. In fact, the lockdown measures in Italy have made it possible to control the COVID-19 contagion across the national territory, although in a situation of continued as lower cluster transmission of the virus, with very different incidences in the 21 regions. The Government and the Ministry of Education worked to prepare the country towards reopening schools and reopen in the safest way possible for children, teachers and communities. These include preventive monitoring systems of temperature at home and at school, use of personnel face-mask, greater distance among child's, differentiated timely to entry and exit, use of separate doors and corridors, etc.; several strategies to foster quicker and more insightful decision making in case of suspected infection.

However, it is known that at the end of March, Italy had the highest COVID-19 fatality rate worldwide, which was higher than that of the People's Republic of China (total number of COVID-19 deaths estimated at 3,000 cases, including potential re-infections) [4]. The pandemic emergency and most of the COVID-19 cases and deaths were limited to Northern Italy, especially Lombardy, followed by the Emilia Romagna, Veneto, and Piedmont regions; in Central and Southern Italy, a limited number of cases were recorded or related to limited clusters of viral infections (in the Basilicata and Molise regions) [5]. Many hospitals in the Lombardy and Veneto regions are today included in the lists of Italian centers of excellence for many diseases, with a higher number of intensive care and resuscitation beds compared to Southern Italy. Although Lombardy could count on these facilities in the emergency, they quickly became full, necessitating both the conversion of several care hospital beds for new COVID-19 cases, and the transfer of patients to other regions and states [4].

At the end of February, the official numbers of deaths confirmed the state of emergency and later, the WHO declared the viral pandemic [6]. For many weeks, people living at home under the restrictions imposed by lockdown, waited for the sad news of the daily bulletin with its dramatic numbers of deaths [5]. Given that the fatality rate is determined by number of deaths due to COVID-19 divided by the total number of confirmed coronavirus cases, the fatality rate was 9.0% in Italy (on March 21<sup>th</sup>) which peaks in Lombardy at greater than 10%, while the fatality rate in Wuhan was 5.8% and less than 1% in the rest of the People's Republic of China [7].

On 4<sup>th</sup> June 2020, the 2<sup>nd</sup> Report "Impact of the Covid-19 epidemic on the total mortality of the resident population in the first months of 2020" was published [8]. Interesting data are presented by the Integrated National Surveillance which registered deaths from COVID-19 positive people from February 20<sup>th</sup> to April 30<sup>th</sup>, 2020 and noted that the peak was

reached (53%) on March 28<sup>th</sup> and (47%) in April. Mortality from overall causes decreases as COVID-19 cases and deaths increase. The most significant drop is observed in Lombardy and then, similarly, in the areas which are most affected by the epidemic. In Bergamo, excess mortality drops from 571% in March to 123% in April and in Lodi from 377% to 79.9%. Excess mortality in March and April, 2020, was higher for men aged 70-79 and 80-89 years and had an increase of 48% for people aged 90 and over; the increase in female mortality was lower for all age classes except for the over-90s, since it's mostly women who reach that age [8].

However, Italy was taken by surprise, having been the first among the states in Europe to face the emergency. On March 21, 2020, in coordination with the Civil Protection Agency, a call was issued for 350 doctors to fill vacancies in the northern regions [9]. Moreover, the highest initial contagiousness (with estimated R0 greater than 2.5) in a part of the Lombardy Region (including Milan) could also have been due to social phenomena that would have amplified contact and cases of infection [10]; for example, the Champions League game played on 19<sup>th</sup> February, 2020 at the San Siro football Stadium in Milan, between Atalanta (a team from Bergamo, Italy) and Valencia (from Spain), in the presence of about 45,000 fans. From this perspective, official statements from Spanish teams claimed that 35% of those infected were asymptomatic [11]. However, the confirmed number of deaths even among doctors and medical staff engaged in the fight against COVID-19, from 11<sup>th</sup> March, 2020 to date, 15<sup>th</sup> June, 2020, are so high to impose considerations. Why have so many doctors and medical staff died in Italy? In Italy, to June 22, 2020, there have been 238,720 confirmed cases of coronavirus disease (COVID-19), with 24,569 in-patients, including 127 patients in intensive care units (ICUs), 2,038 patients hospitalized with symptoms, 18,472 positive in home isolation, 34,405 deaths, a number of discharged patients recovered 183,426 and 218 newly-infected in the last 24 hours, according to the Italian Civil Protection Agency bulletin [12]. These latest, positive epidemiological conditions confirm and follow the start of phase 2, in Italy from June 3, 2020 [3]. In fact, the lockdown measures in Italy have made it possible to control the COVID-19 contagion across the national territory, although in a situation of continued widespread transmission of the virus, with very different incidences in the 21 regions.

As a support to monitor the spread of any form of viral infection in Italy, a new voluntary test of the "Immuni" contact-tracing "App" designed to help manage the 2<sup>nd</sup> phase of the coronavirus emergency is set and started for download since June 1<sup>st</sup>. Up-today, over about five million Italians, average 15%, have downloaded the app [13], but in order to be fully effective, an increasing number of people, at least 60% of the population [14], should be operating this software.

In memory of Roberto Stella (Head of the Training Area at FNOMCeO) and other doctors, the constantly-updated website provides a list of the 176 doctors, of which 11 are women, who have died during the COVID-19 epidemic in the course of their work at an average age of 66-years [16].

Why there have been so many deaths among doctors

and medical staff involved “as heroes” in the war against COVID-19 in Italy. What has caused such a large number of doctors to die?

On examining the data, it becomes noticeable that the majority of deaths occurred during the 3 10-day periods between 10<sup>th</sup> March and 10<sup>th</sup> April, 2020 (35%), peaking between 22<sup>nd</sup> March and 2<sup>nd</sup> April with 21% of the total. Among a variety of specialists, General Medical Practitioners’ deaths rose in the same period (28%), contributing to the coincident peak of 37%. Furthermore, a high number of deaths have occurred among dentists (7%) and surgeons (5%). In addition, the number of retired doctors who died early in the pandemic, in the first 20 days (17% of total) are remarkable, as a further example of their dedication to their work and their high sense of responsibility in times of national emergency.

## Discussion

Ideally, there are no acceptable reasons to expect the death of one single doctor in the fight against the biological epidemic, or viral pandemic, COVID-19. Doctors are experts and are specialized “on the front line”, fighting the war to save and cure infected people. Here, we should remember that in this time of emergency, a large number of doctors were re-assigned to new tasks, and many others who had already retired also made themselves available again despite the risks.

- An initial rationale for the higher lethality could be related to the absence of information and awareness about the dangers of novel COVID-19 and the associated symptoms of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Even before being declared as a pandemic by the WHO [6] the risks of viral contamination on first contact between doctor and patients were present. This included patients who were already displaying typical symptoms (such as a temperature over 37.5 °C and breathing difficulties from a pneumonia disease), those who were not yet displaying symptoms and those who were asymptomatic. At these preliminary stages, the adoption of guidelines and the rigorous use of personal protective equipment (PPE, such as medical masks, gloves and suits) were not so common among Generalist Medical Practitioners with consequent risk of widespread contamination for themselves and others. In short, the combination of a lack of knowledge and failings in preventative measures against viral infection.
- It is recognized that shortfalls in the supply of medical masks and PPEs in Italy and consequent shortages for healthcare personnel at the end of February 2020, often made it impossible to obtain. This situation worsened further in the weeks following the declaration of a pandemic by the WHO (March 11, 2020). In fact, the extreme demand for PPE in several European countries led to sometimes selfish, competition and even the interruption of trade. The lack of an adequate mask becomes a determining factor for the risk of contamination by droplets that spread about 1.0 meters from the infected source and by micro-droplets (aerosol) that can remain suspended in the air. If a room is not ventilated, the droplet concentration increases and without adequate PPEs, including filter FFP2 or FFP3-type which are airtight, the General Medical Practitioner breathes in the virus throughout the day. Over several days, the viral load will manifest as a symptomatic form of the disease, leading, potentially to hospitalization in intensive care and the 20% of additional deaths [17].
- The use of personal protective equipment, including medical-standard face-masks does not always ensure guaranteed protection against viral infection because adhesion to the face can be reduced during even routine work. Some documents provide standard requirements, testing methods and evaluation of materials and devices for respiration, bacterial filtration and microbial cleaning [18]. The notable technical-functional characteristics of the masks are: Type I filter out particles with diameters > 1.0 µm and have a Bacterial filtration efficiency (BFE) > 95%; Type II masks filter out particles with diameters > 0.65 µm, BFE > 95%; Type IIR masks filter out particles with diameters > 0.65 µm, BFE > 99%. It follows that total (100%) safety is not guaranteed, especially taking into account the very small size of viral particles, such as those of COVID-19 with values between 70-90 nm [19].
- Normally, salt solution (NaCl 2.0% in water) as aerosol, forcibly induced to pass through the materials, in order to verify the respirability is adopted and, under labs conditions, the average diameters of salt droplets range 50 to 800 µm; more, dolomite powder DRB 4/15 (size ranging 0.7-12 µm) is adopted to verify both the occlusion and the respiratory resistance.
- Moreover, in biological tests the EN validation method cited uses an aerosol of bacterial *Staphylococcus aureus* ATCC 6538, Biosafety Level 2 (pathogen) in an aerosol chamber [18]. The average cell-size of this pathogen is 0.8-1.0 µm and it is drawn through the mask materials to be recovered by a six-stage cascade (Andersen model) impactor and counted. Generally, bacterial spores are smaller than bacterial cells, being about 0.4 µm in size and closer to the sizes of viruses. Therefore, the use of the latter could offer notable advantages in testing the efficacy of protective materials against viral spread.
- During the COVID-19 emergency, healthcare staff have worked longer shifts (> 8h daily) while exposed to higher concentrations of viral particles, in corridors and other hospital environments and in close contact with virus patients in intensive care. The fact that these are indoor locations with increased numbers of ICU beds, where large numbers of SARS-CoV-2 patients have been treated and placed on respirators, could permit the passage of viral particles as aerosol by the forced ventilators.
- Another explanation for the higher lethality is the daily

risk of contamination while getting changed and ready in COVID-19 wards, dressing and undressing, before and after shifts.

- Furthermore, the impact of late, inadequate or, at times, deficient protective measures seeking to prevent or reduce the risk of infection cannot be overlooked. Reports of precarious working conditions, with personal safety equipment not always available, or, more frequently, not meeting safety standards, were recorded daily at the beginning of the pandemic “tsunami”.
- Finally, other factors may have influenced the increase in incidence of death among doctors (such as physical and psychological stress factors).

A large number of regions in Central and Southern Italy have now taken the decision to screen doctors and nurses even if they are asymptomatic, following evidence that asymptomatic cases transmit the virus, and could contribute to the fatality rate, in Italy.

Following this summary of potential factors that could have contributed to the high number of COVID-19 deaths among doctors in Italy, the situation in Europe as a whole, should also be considered. It is clear that collecting, updating and publishing accurate, reliable information is a complex task for Governments.

In France, SOS Médecins estimates that 16% of its doctors have been contaminated by COVID-19, while about thirty private doctors have died in France. General doctors blame the Minister of Health for betraying its promise to equip them with FFP2 filters [20]. In Spain, the official number of medical COVID-19 victims was 76, at an average of 60-years of age to May 16, 2020; in the Madrid area alone, the figure rose to 10 active doctors and five who had been retired [21]. In Britain, to April 12, 2020, the deaths of 119 NHS staff had been recorded and analyzed; the doctors who died of COVID-19 were largely from ethnic minority backgrounds, representing 44%, significantly higher than the 13 percent in the population at large [22]. In Germany, to April 16, 2020, there had been 8 COVID-19 deaths among medical staff out of more than 6,400 employees of hospitals and medical practices with infections [23].

## Proposals

What experiences gained from the initial period of the COVID-19 pandemic can we apply successfully in future phases? What considerations and proposals can we offer?

The life of every one of us is priceless and we owe a debt of gratitude to those who have already given their lives in trying to save ours. We are, of course all afraid of losing our lives, as if we were at war, yet we cannot see our enemy - this virus which is new for us but has been present on the planet since long before mankind came to inhabit it. The fear of pandemic and the loss of our pre-COVID-19 sense of security have changed a world based largely on economic power.

We are witnessing renewed confidence in scientific research, in knowledge and in the development of new inven-

tions, including vaccines and medicines, for protection against COVID-19. To show respect to all the health-care personnel and the hundreds of thousands of ordinary people who have died all around the world, we firmly believe that great care should be taken in:

- Recognize the role of Healthcare as a being an absolute priority for a country;
- Allocate significant financial resources to support and sustain scientific research, hospital facilities and well-prepared medical staff and health-care personnel;
- Rethink the organizational structure of public health, giving priority to the work carried out nationally by local doctors who must be equipped with adequate protection, favoring preventative interventions at every level, including remote medical diagnosis and surveillance on the basis of telematics transmitted data;
- Encourage manufacturers to ramp up production of life-saving equipment in the short term, guaranteeing orders into the future to support the market;
- Increase safety and personal protection procedures to reduce the risk of recurrence of infection from new viral pathogens, including the development of new devices, which offer greater protection while respecting environmental sustainability (using renewable, biodegradable materials);
- Encourage greater use of digital tracking systems (i.e. Immune or similar) to support the containment of the spread of the virus;
- Encourage a desirable influenza vaccine coverage for at-risk individuals and people over 65 years of age, so that they can support early diagnosis if symptoms occur;
- From a microbiological perspective, we would suggest urgent evaluation of the possibility of introducing new tests for BFE medical facemasks, which would replace those existing, improving standards, using safer and smaller viable microbial cells like *Bacillus* sp. and its endospores, following all our experiences with COVID-19. The adoption of adequate *Bacillus* spores would save a great deal of time in laboratory cultivation and greatly reduce costs.

Encouraging signals have come from Europe, which the allocation of significant resources through the European Stability Mechanism (MES) financial instrument, for those countries that wish to receive it, with the sole constraint being the allocation of resources to the health sector [24].

There are currently over 169 COVID-19 vaccine candidates under development, with 26 of these in the human trial phase [25], hoping that in the near future, it will be made “widely available, fairly-distributed and be non-profit”. Waiting the first vaccine against SARS-CoV-2, we must avoid what is avoidable, as recently suggested by dr. G. Parrella, medical infectiologist at the Cotugno hospital, Italy.

Finally, we believe that showing greater respect to all

those people who have been working in some of the most difficult conditions imaginable - "our heroes in the trenches" and to whom these findings are dedicated, means making a new deal for all our lives, for the environment we all live in and for greater sustainability in this, our World.

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## Author Contributions

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication. University of Molise provided funds for this work.

## Conflict of Interest

The authors have no conflict of interest to declare.

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