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## Forecasting the burden of COVID-19 hospitalized patients during the SARS-CoV-2 second wave in Lombardy, Italy

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Reliable forecasting of the incidence of SARS-CoV-2 infections and of symptomatic COVID-19 patients can help plan strategic choices for the healthcare system (e.g., remodeling of and/or building of hospitals) (1), although the epidemiological dynamics of SARS-CoV-2 infection are highly dependent on political, environmental, and social determinants. In Lombardy, the estimation of hospital beds at different levels of care for COVID-19 patients is key, since it is the Italian region with the highest COVID-19 cases and deaths.

Several studies showed the mortality and infection diffusion trend in different settings (1-3). During the first wave of SARS-CoV-2 pandemic, we reported trend curves of virus-related deaths in Italy, European and non-European countries. A 3rd-grade polynomial curve with a growth up to the daily peak, and, then, a five-parameter logistic (5PL) asymmetrical sigmoidal curve following a parametric growth described the temporal evolution of the deaths (4).

Aim of the present study was to model official data on hospitalizations collected in Lombardy (Real-time data on COVID-19 infection in Italy from Protezione Civile

<http://opendatadpc.maps.arcgis.com/apps/opsdashboard/index.html#/b0c68bce2cce478eaac82fe38d4138b1>) to estimate the number of COVID-19 hospitalized cases until the end of 2020, taking into account the impact of strict measures to tackle the SARS-CoV-2 diffusion.

The predicted number of hospitalized cases in Lombardy was determined using the following formula:  $\text{Hospitalized (t0)} = \text{Hospitalized (t-1)} - \text{Deaths (t-1)} - \text{ICU transferred (t-1)} - \text{Recovered (t-1)} + \text{new hospitalized (t0)}$ . The estimation relies on the time period between 4 October, the first day after which the number of hospitalized patients began to grow daily (305 hospitalizations) and 13 October 2020 (546 hospitalizations). Importantly, we considered data of the confinement rules implementation, since the estimation of COVID-19 patients is strictly related to the containment measure. The new model describes the expected number of COVID-19 related hospitalized patients, and we drew two curves (figure 1), based on the strengthening measures implemented on 24 October and on 5 November 2020 (Gazzetta Ufficiale della Repubblica Italiana. Available from: <https://www.gazzettaufficiale.it/eli/id/2020/11/04/20A06109/sg>), respectively, with the purpose to identify the impact of the containment measures implementation on the number of hospitalized patients in Lombardy.

Each curve is characterized by three distinctive phases:

1. Growth: the trend maintains the same growth rate up to the effect of strict measures adoption, occurring 9 days after its start. This time frame is coherent with an average of seven days of incubation, plus two days for symptoms occurrence before hospitalization. This phase is in keep with 4-PL symmetric sigmoidal curve showing estimated values weighed on  $1/y^2$  (4).
2. Peak: the turning point is calculated 23 days after the containment measures implementation, as we previously described for COVID-19 death trends (2). The curve follows a 4-PL parametric symmetric sigmoidal, assuming a peak of 60% can be reached nine days after the adoption of the control rules.
3. Decrease: 4-PL parametric symmetric sigmoidal interpolated using the following data: i) -30% of cases during the following 23 days after the peak; ii) -50% of cases in double the time needed to reach the peak; iii) -100% of cases which occurs in a number of days equal to four times to reach the turning point.

The curve grows up to 23 days after the adoption of the strict measures, becoming flat for a few days and, then, decreasing, even if more slowly than during the growth phase. Although calculated using local data, we surmise that these trends can be inferred to other settings, keeping into consideration the different public health restrictions.

Figure 2 shows the potential peak of hospitalized COVID-19 patients in Lombardy, calculated after 23 days from the day of implementation of the containment measures. In x-axis are indicated the turning points, and by this curve, it is possible to estimate the effect of the delay of strict containment measures on the number of hospitalized patients. If there had not been any containment measures taken until November 15, the number of hospitalizations would have reached 32,900, 23 days after

their implementation. If we consider the beginning of the restrictions starting from October 24, we estimate about 8000 by the 26 of November. Finally, if we consider the beginning of the containment from 5 November, the estimate is 15,000 by 28 November.

To estimate the reliability of our model, we calculated the accuracy curve, by plotting real data of Lombardy (grey bars) with the expected cases. The accuracy curve was achieved by plotting real data until November 7 (grey bars) with expected hospitalized COVID-19 cases, considering the impact of the strengthening measures of 24 October and 5 November 2020.  $R^2$  values are 0.997 and 0.998 considering November 5 and October 24, respectively; while calculated delta for the same dates are 17.8% and 1.5%, respectively. Taken together these findings suggest the reliability of the model. It can be also inferred that the trend has started flattening after October 24, suggesting that also less restrictive measure can have an impact on SARS-CoV-2 spreading.

Although considering the limitations of forecasting data, we surmise that it crucial to identify the trend the dynamics of disease for the second COVID-19. Recently, Cacciapaglia et al (5) used the Renormalization Group (eRG) approach to efficiently simulate the trend of pandemic transmission and spreading across different European countries. Although with a different modeling method, they also used in the simulation data, the information from the first wave.

We are aware that our findings are strongly influenced by several factors, such as the number of non-hospitalized symptomatic patients, the proportion of past and current asymptomatic or mildly symptomatic cases in the population, the potential lack of homogeneous treatment protocols, and the inaccuracy of reporting of hospitalized cases. In addition, our model did not consider stratification for the main confounding variables (e.g., age, sex, and pre-existing comorbidities), which can affect outcomes of the SARS-CoV-2 infection.

Even if intrinsic limitations of forecasting data are considered, the rapid growth of new COVID-19 hospitalizations requires rapid public health action.

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*Authors' contributions.*— AG designed the model, performed the computational framework and data mining; MM, LF wrote the manuscript with input from all authors; SC, DC supervised and encourage the study; GS, CLV supervised the findings of the study and contributed to the interpretation of the results. All authors discussed the results and approved the final version of the manuscript.

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## FIGURES

Figure 1. Model describing expected hospitalized COVID-19 patients in Lombardy (Italy) until the end of 2020, considering the containment measures of 24 October and 5 November 5 2020.

Figure 2. Trend showing the different peaks of hospitalized COVID-19 patients in Lombardy (Italy) after 23 days from the strict measures implementation (dates indicated in x-axis).

Figure 3. The accuracy curve of our model was achieved by plotting real data until 7 November 2020 (grey bars) with expected hospitalized COVID-19 cases in Lombardy (Italy), considering the impact of the strict measures of 24 October 2020 and 5 November 2020.





