TITLE PAGE

Predicted effects of stopping COVID-19 lockdown on Italian hospital demand

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	Authors:			
	Jordy Bollon, MStat ¹			
6	Matteo Paganini, MD ²			
	Consuelo Rubina Nava, PhD ³			
	Nello De Vita, MD ¹			
9	Rosanna Vaschetto, MD ¹			
	Luca Ragazzoni, MD ^{1,2}			
	Francesco Della Corte, MD ^{1,2}			
12	Francesco Barone-Adesi, MD ^{1,2}			

Affiliations:

15 1) Translational Medicine Department, Università del Piemonte Orientale, Novara, Italy
2) CRIMEDIM – Research Center in Emergency and Disaster Medicine, Università del Piemonte Orientale, Novara, Italy.

18 3) Department of Economics and Political Science, University della Valle d'Aosta, Aosta, Italy;

Author Contributions :

Conceived and designed the experiments: JB, CRN, FBA; Analyzed the data: JB, CRN, FBA;

BA;
۶A

All authors approved the final version of the manuscript.

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Corresponding Author:

Francesco Barone-Adesi –Research Center in Emergency and Disaster Medicine (CRIMEDIM).
 Università del Piemonte Orientale. Via Lanino 1, 28100 Novara, Italy.
 Ph: +39 0321660620. Fax: +39 0321660620. Email: Francesco.baroneadesi@uniupo.it

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Running Title: ending covid-19 lockdown and hospital demand

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33 Abstract

Objective: Italy has been one of the first countries to implement mitigation measures to curb the COVID-19 pandemic. There is now a debate on when such measures should be loosened. Our aim

36 was to forecast the Italian hospital demand for COVID-19 during the following months, assuming different approaches in reducing the restrictions currently in place.

Methods: We used a compartmental model to evaluate two scenarios: A) an intermittent lockdown;

39 B) a gradual relaxation of the lockdown. Predicted intensive care unit (ICU) and non-ICU demand was compared with the peak in hospital bed utilization observed in April 2020.

Results: Under scenario A, while ICU demand will remain below the peak, the number of non-ICU

- 42 will substantially rise and will exceed it (132%; 95%CI: 95-174). Under scenario B, a rise in ICU and non-ICU demand will start in July and will progressively increase over the summer 2020, reaching 91% (95%CI: 70-113) and 223% (95%CI: 180-272) of the April peak.
- 45 **Conclusions**: Italian hospital demand is likely to remain high in the next months if restrictions will be reduced. Planning for next months should consider a diffuse increase in healthcare resources to maintain at least the contingency level across the country.

BACKGROUND

Since December 2019, the Coronavirus Disease 19 (COVID-19) has rapidly escalated into a

- 51 pandemic that is currently threatening most of national health systems across the world.¹ To date, with more than one hundred confirmed cases of COVID-19 and twenty thousand deaths,² Italy is one of the most affected countries, accounting for the highest death toll in Europe $(22\%)^3$ and for
- 54 15% of the Global death toll.¹ Italy has been also one of the first countries in the world to implement mitigation measures, i.e. isolation, quarantine, social distancing and community containment, in the attempt to curb the COVID-19 pandemic. On March 9th, 2020,⁴ a national
- 57 lockdown was issued, including: a) strict home confinement for the entire population; b) closure of all non-essential commercial activities; c) mobility restrictions between municipalities. Thanks to these measures, Italy is now experiencing a decrease of new COVID-19 confirmed cases and hospital admissions.² As in other countries, there is now an ongoing debate on when such measures should be loosened, and what can be the best strategy to manage this new phase of the pandemic.⁵

In particular, there are concerns on the effects that an untimely lift of the lockdown could have on 63 healthcare systems.

Pandemics are disasters characterized by a slow but exponential onset and a prolonged impact.⁶
Even though the gradual increase of cases allows governments to progressively enact mitigation
strategies and countermeasures to face an incoming wave, the sustained spread of the disease, along with a possible delayed recovery of patients, can easily lead to healthcare capacity saturation and surge capability exhaustion.⁷ In particular, the COVID-19 pandemic has been posing unique
challenges to emergency medical services (EMS), emergency departments (ED), and critical care units, in terms of stuff, staff and structures. Italian intensive care units (ICU) are currently experiencing an unprecedented and sustained demand that depleted resources on a local, regional, and national levels,⁸ thus possibly hampering a fast and further surge in capacity if a new wave of cases should occur. In this study we aim to forecast the Italian hospital demand for COVID-19

during the following months, assuming different approaches in reducing the restrictions currently in

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99 **METHODS**

Model definition

We used a compartmental model to predict hospital demand in Italy associated with the COVID-19

- 102 pandemic. The model was implemented using R software, and an overview of it is provided in Supplementary Figure 1 and Table 1. The input of the model is the number of infected individuals in each day of the simulation. Observed numbers of infected individuals were used until April 17th
- 105 (last available observation). The future number of infected under different scenarios (see hereafter) was generated using the method proposed by Tuite and colleagues.⁹ Based on the number of infected individuals, the model provided the daily number of ICU and non-ICU patients, dead and
- 108 recovered. To keep the models as simple as possible, we made a series of assumptions: i) recovered individuals remained immune from re-infection for the duration of the pandemic; ii) individuals stopped to be infectious once they were admitted to hospital (i.e. we did not model transmission
- 111 within healthcare settings).

Calibration and cross-validation of the model

- 114 The model was calibrated using the current number of infected, ICU and non-ICU patients, dead and recovered in Italy from February 24th to March 24th. These figures were obtained from the website of the Italian Civil Protection.² We used the R function *optim()* to perform a
- 117 multidimensional optimization of the model, selecting the parameters' values that minimized the mean square error between fitted and observed number of individuals in each compartment.In the final model, mean residence times in the different compartments were reasonably consistent
- 120 with those reported in the scientific literature and those observed in our University Hospital (Maggiore Hospital, Novara). Once the parameters were set, we evaluated the predictive accuracy of the model trough cross-validation, comparing the predicted number of subjects in each
- 123 compartment with the actual figures observed between March 25th and April 17th. Supplementary

figure 2 shows that predicted number of subjects in the different compartments were very close to the observed ones, suggesting a satisfactory predictive accuracy of the models.

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Scenario analysis

We then used our model to forecast the Italian hospital demand until September 1st 2020, under

129 different scenarios:

In Scenario A ("intermittent lockdown") we first assumed that from April 18th to April 30th the evolution of the pandemic follows the same trend as in the previous weeks, with a steady reduction

- of new cases of infection over time equivalent to an effective reproductive number (Rt) of 0.9.
 Then, we hypothesized that the lockdown is temporary lifted from May 1st to May 30th.
 Consequently, we assumed that two weeks after the lift the number of new cases starts to increase
- again, in a similar fashion ($R_t = 1.3$) as it was observed in Italy in the period before the lockdown entered into effect. A lag time of two weeks was included to take into account COVID-19 incubation period and the diagnostic delay after symptoms onset.¹⁰
- 138 In Scenario B ("gradual relaxation of the lockdown") we assumed that from May 1st onwards the restrictive measures are progressively reduced over time. This translates into a gradual increase of R_t, from 0.9 to 1.2 (Supplementary figure 3).
- 141 We then evaluated changes in ICU and non-ICU demand under the two scenarios. ICU and non-ICU needs were compared with the maximum hospital bed utilization for COVID-19 observed before April 17th.
- To evaluate the uncertainty of our forecasts, we run Monte Carlo simulations sampling the values of the parameters from uniform distributions (from -30% to +30% of each parameter's estimated value). We generated 95% confidence intervals [CIs] by taking the 2.5% and 97.5% percentile
- 147 estimates from 100 simulations.

Ethics committee approval

150 The study was based on publicly available aggregate data. No Ethics committee approval was necessary.

153 **RESULTS**

COVID-19 numbers in Italy, as on April 17th

On April 17th, about one month after the implementation of containment measures in Italy, the

- 156 current number of infected subjects, ICU and non-ICU patients in Italy was 106,962, 2812 and 25,786, respectively (Figure 1). The number of ICU and non-ICU admissions peaked some weeks earlier (April 3rd and 4th) and then declined, while the number of infected was still on the rise, but
- 159 approaching a plateau. The maximum recorded demand for ICU and non-ICU was 4068 and 29,010 beds, respectively.

162 <u>Scenario Analysis</u>

Under scenario A ("intermittent lockdown"), a rise in the number of infected is predicted to start in middle May, about two weeks after the end of the lockdown, followed by an increase in the demand

- 165 of ICU and non-ICU beds at the beginning of June (Figure 1). The maximum demand of ICU and non-ICU beds will occur in the first weeks of July. While ICU needs will remain below the peak levels observed in April 2020 (61%; 95%CI: 41 to 78), the number of non-ICU will substantially
- rise and will exceed the maximum demand recorded in the early phase of the pandemic (132%; 95%CI: 95 to 174). Starting from the second part of July bed demand will start to decrease, but non-ICU needs will still remain high until the end of August.
- 171 Under scenario B ("gradual relaxation of the lockdown"), a rise in the demand of ICU and non-ICU beds will start to be evident in July and will progressively increase over the summer (Figure 2). At the end of August ICU and non-ICU demand will be 91% (95%CI: 70 to113) and 223% (95%CI:
- 174 180 to 272) of the April peak. Differently from the previous scenario, no reduction in both ICU and non-ICU demand is predicted during the time frame covered by the simulation.

DISCUSSION

In this study we showed that an early reduction of the community containment measures currently

- in place in Italy could shortly translate into a substantial increase of ICU and non-ICU demand. In particular, a gradual lift of the lockdown (which is currently under discussion by Italian Government) is expected to double non-ICU admissions and to bring the number of ICU needs to
- 183 the same levels observed in the early phase of the pandemic.Our results can be useful for the Italian health system to be prepared for the next phase of theCOVID-19 pandemic. Within the hospital system, critical care services are fundamental during
- epidemics of infectious respiratory diseases,⁶ as repeatedly demonstrated during H1N1, SARS, or
 MERS outbreaks. During the early stage of an epidemic, a phased response can be useful to
 gradually increase treatment capacity while preserving critical care resilience and preventing the
- 189 collapse of the system. Similarly, a phased deactivation of resources is of paramount importance during the recovery stage of epidemics, since the risk of new outbreaks is consistent¹¹ and the scarce, remaining assets should be properly managed.
- 192 Our analysis also shows that non-ICU demand could become a rate-determining step for the health systems, because of the length of stay in the wards and the step-down of patients from the ICU. The former could be partly due to the commonly used the discharge criteria for COVID-19 cases. The
- 195 European Centre for Disease Prevention and Control (ECDC) currently recommends clinical resolution and two negative tests for the discharge.¹² However, ECDC recognizes that in the context of sustained widespread transmission (as it is currently the case in Italy), hospital discharge should
- 198 be also based on other factors such as the existing capacity of the healthcare system, laboratory diagnostic resources, and the current epidemiological situation.¹² In particular, the discharge from hospital of mild cases – if clinically appropriate – may be considered, provided that they are placed
- 201 into home care or another type of community care.¹² Telemedicine could be also useful to foster early discharge of patients, thus helping to keep non-ICU demand under control.

Our model is based on a number of assumptions and has limitations. In particular, we assumed that

- 204 the trend of non-ICU and ICU admission rates in the next months will remain similar to what we observed so far. Thus, for example, an improvement in the community-based management of COVID-19 patients would translate into a reduction of hospital demand. Moreover we did not take
- 207 into account the gradual increase in the proportion of immune individuals in the population, a phenomenon that is expected to naturally occur during the course of an epidemic. However, considering that the prevalence of infected is still low in Italy (<10%), this simplification should not</p>
- have substantially affected our results.¹³
 In conclusion, our results suggest that Italian hospital demand is likely to remain high in the next months if restrictions are reduced, which seems likely to occur. Given the cuts recently suffered by
- 213 the Italian National Health System,¹⁴ planning for next months should consider a diffuse increase in healthcare resources to maintain at least the contingency level across the country. The available assets should be deployed to the most struggling parts of the country with a certain grade of
- 216 flexibility over time, taking also into account the immunity status of the population.

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FIGURES

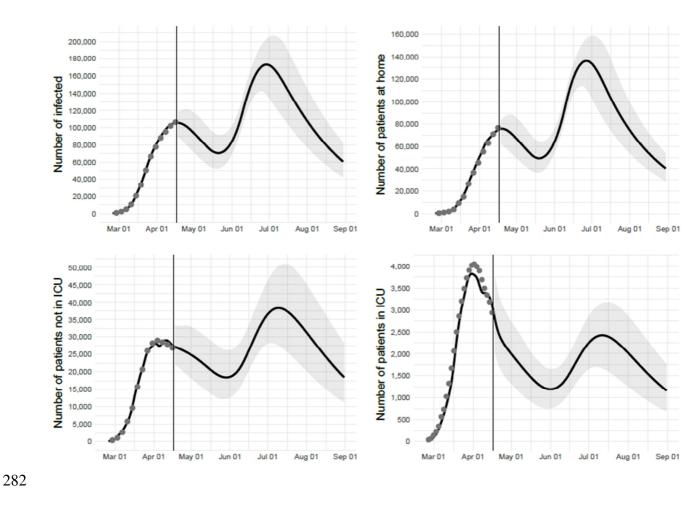
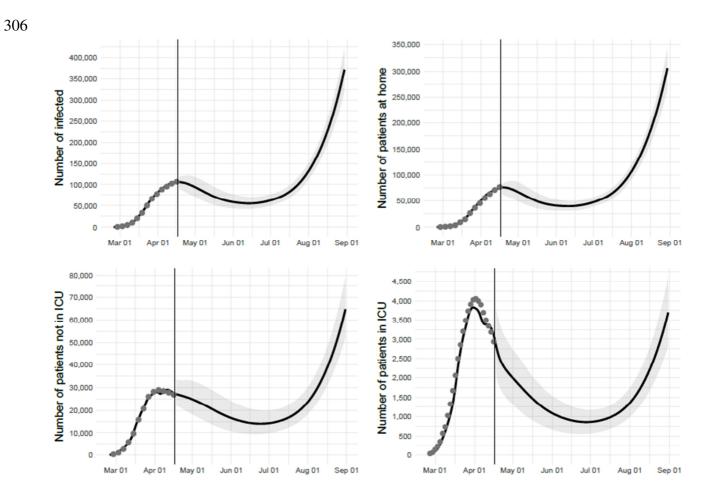


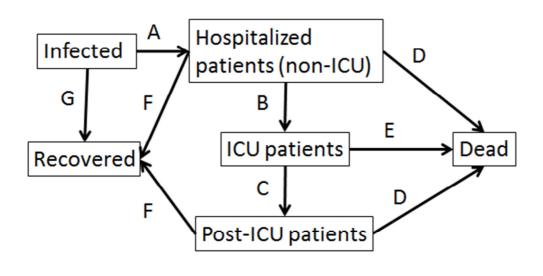
Figure 1. Observed (circles) and predicted (solid line) number of infected, patients at home, non-ICU hospitalized patients, and ICU patients over time. Scenario A (Intermittent lockdown).

Figure 2. Observed (circles) and predicted (solid line) number of infected, patients at home, nonICU hospitalized patients, and ICU patients over time. Scenario B (gradual relaxation of the lockdown).



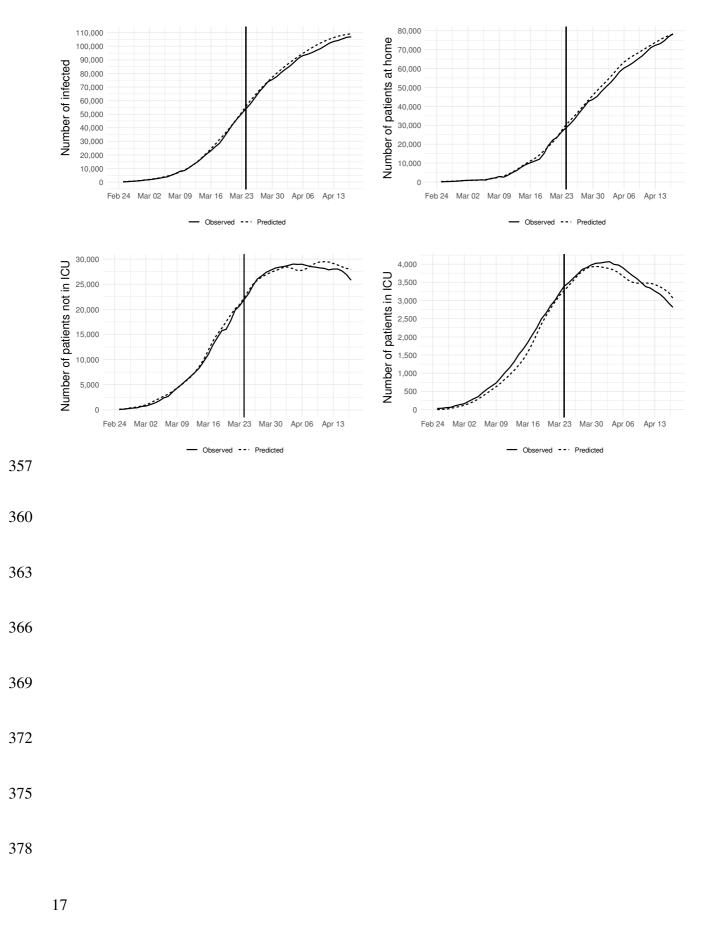
SUPPLEMENTARY MATERIAL

Suppl. figure 1. Overview of the compartmental model. Capital letters represent transition rates of the model.



Parameter	Value		
A (hospitalization rate)	Declining over time from 41% to 2.3% per day		
B (rate of ICU admission)	Declining over time from 8% to 1.5% per day		
C (discharge rate from ICU)	0% during the first 4 days of staying in ICU, then		
	22% per day		
D (mortality rate in non-ICU wards)	1.1% per day		
E (mortality rate in ICU)	13% per day		
F (hospital discharge rate)	0% during the first 6 days of hospital stay, then		
	5.3% per day		
G (recovery rate for not hospitalized	Subjects recover 29 days after the diagnosis.		
patients)			

Suppl. figure 2. Cross-validation of the model. Predicted and observed values in the different compartments.



Suppl. Figure 3. Changes of the effective reproductive number (R_t) under the assumed scenarios.

