Impact of a Nationwide Lockdown on SARS-CoV-2 Transmissibility, Italy

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On March 11, 2020, Italy imposed a national lockdown to curtail the spread of severe acute respiratory syndrome coronavirus 2. We estimate that, 14 days after lockdown, the net reproduction number had dropped below 1 and remained stable at ≈0.76 (95% CI 0.67–0.85) in all regions for ≥3 of the following weeks.

On February 21, 2020, the earliest known case of locally transmitted severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) infection was reported in Italy (*1*; D. Cereda et al., unpub. data, https://arxiv.org/abs/2003.09320). Since then, several interventions have been deployed to control disease spread in regions with sustained transmission, including quarantine of most-affected municipalities, ban of mass gatherings, and local school closures. School closure at the national level was mandated on March 5, and a national lockdown (stay-home mandate and closure of all nonessential productive activities) was issued on March 11 (*2,3*), then eased after May 4, 2020 (Appendix, https://wwwnc.cdc.gov/EID/article/27/1/20-2114-App1.pdf). The aim of this study is to evaluate the impact of these interventions on SARS-CoV-2 transmissibility in Italy.

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The Study

We measured SARS-CoV-2 transmissibility in terms of the basic (R_0) and net (R_t) reproduction numbers. These quantities represent the mean number of secondary infections generated by 1 primary infector in a fully susceptible population (R_0) and in the presence of control interventions and human behavioral adaptations (R_t). When R_t decreases below the threshold of 1, the number of new infections begins to decline. Estimates were obtained through a Bayesian approach applied to case-based surveillance data collected by regional health authorities (Appendix).

To account for the geographic heterogeneity in contacts, healthcare organization, and timelines of interventions, R_t was estimated separately for different provinces and regions. We considered all 19 regions in Italy plus the 2 autonomous provinces of Trento and Bolzano. Moreover, we considered 100 of the remaining 105 provinces for which the data were sufficiently complete. The selected provinces covered 99.1% of the population of Italy and, as of May 3, 2020, accounted for 153,558 symptomatic cases (97.9% of the total recorded in the surveillance database). To evaluate the progressive decrease of transmission, we computed R_t at 3 dates: the day before lockdown (March 10) and 1 and 2 weeks after lockdown (March 18 and 25). In addition, we considered the average value of R_t over the successive 3 weeks (March 26–April 15). These choices were suggested by the trend of the national R_t (Appendix).

The R_0 range was 2.83–3.10 (Figure 1) in the 8 regions for which the estimate was possible

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(Appendix). On March 10, R_t range was 1.79–3.36 across regions; Basilicata and Molise had an insufficient number of symptomatic cases (Figure 1). One week into lockdown, on March 18, R_t had decreased consistently, but no region or autonomous province was yet below the epidemic threshold (Figure 1). As of March 25, R_t was <1 in most regions and autonomous provinces (12/21) and <1 in the successive 3 weeks for all regions except Molise and Piedmont (Figure 1). The mean value of R_t across the regions and autonomous provinces, weighted by the number of reported cases at the corresponding date, fell from an average of 2.03 (95% CI 1.94–2.13) on March 10 to 1.28 (95% CI 1.23–1.33) on March 18, to 0.88 (95% CI 0.84–0.91) on March 25, corresponding to an overall 62.6% reduction (range across regions 45.6%–85.0%). In the 3 weeks of March 26–April 15, R_t remained stable in all regions, showing a further slight reduction at an average value of 0.76 (95% CI 0.67–0.85).

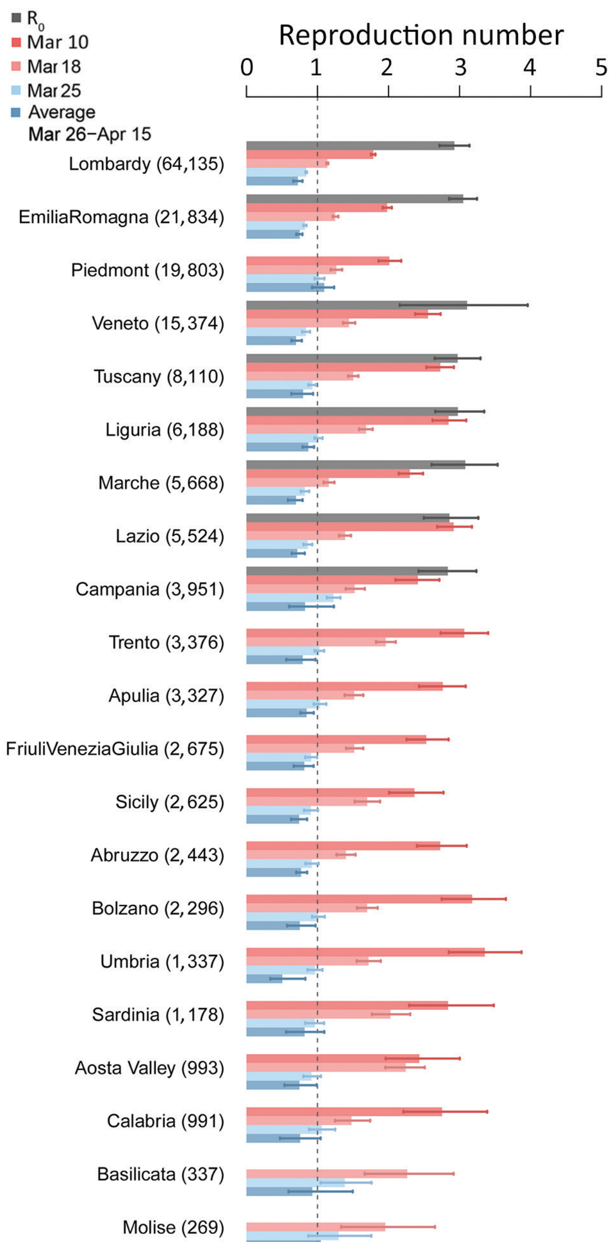

Figure 1. Basic (R_0) and net reproduction numbers for severe acute respiratory syndrome coronavirus 2 for all regions and autonomous provinces in Italy. Regions are sorted by decreasing number of cases (numbers in parentheses) on April 17. Bars indicate mean numbers; error bars indicate 95% CIs.

Results were consistent when analyzing estimates from the 100 selected provinces (Figure 2). As of March 10, no province had a mean estimated value of R_t <1 (n = 75; the number of symptomatic cases was insufficient for the estimate in 25 provinces). One week after lockdown, on March 18, 5/93 provinces (5.4%) had an average R_t <1, whereas on March 25 this figure increased to 49/96 provinces (51.0%). The fraction of provinces with R_t below 1 rose to 84/100 (84.0%) when considering the average over the following 3 weeks. The mean value of the reproduction number across the provinces, weighted by the province's number of reported cases at the corresponding date, was 2.01 (95% CI 1.83–2.22) on March 10, 1.26 (95%CI 1.15–1.38) on March 18, 0.88 (95% CI 0.79–0.97) on March 25, and 0.77 (95% CI 0.63–0.95) for the period March 26–April 15.

Conclusions

Our results suggest that the national lockdown put in place as of March 11 to limit the spread of SARS-CoV-2 in Italy brought R_t below 1 in most regions and provinces within 2 weeks. Although R_t had been declining steeply even before the national lockdown (*3*) in regions with intense interventions, we estimated that the epidemic was brought under control only after the implementation of the lockdown. Lockdown was fundamental to prevent an explosion in the number of cases in other regions in which transmission had started weeks later compared with the outbreak epicenter (Lombardy, Veneto, Emilia Romagna). The range of estimates of R_0 in 8 regions was 2.8–3.1, within the range of estimates obtained for other countries (*4–6*).

A massive and sustained scale-up of testing capacity was set up in all regions of Italy during the course of the epidemic (*7*); it was not accompanied by a corresponding increase of confirmed incident cases in the weeks following March 25, as indicated by the declining proportion of positive tests (Appendix). This finding suggests an increase of notification rates and thus a possible overestimation of R_t (*8*). To compensate for possible biases, we supplemented our results by computing alternative estimates based on the

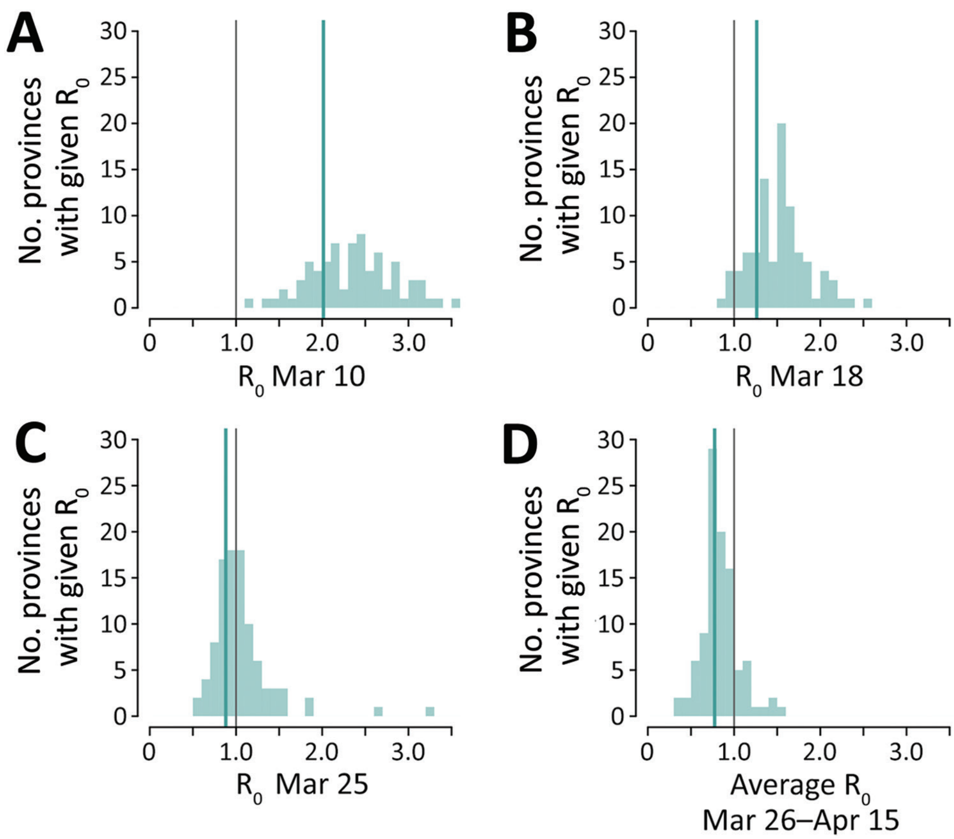

Figure 2. Distribution of the mean net reproduction numbers for severe acute respiratory syndrome coronavirus 2 in 100 selected provinces in Italy. Green lines indicate average value of R_t, weighted by the number of reported cases by each province. Gray line indicates epidemic threshold.

time series of hospitalized cases. Criteria for hospitalization are more homogeneous across local health systems and over time than testing criteria because they are grounded in the patient's need for medical assistance. Furthermore, the hospitalization date is an easier piece of information to collect with respect to the symptom onset date, which requires an epidemiologic investigation and may be subject to recall bias. Results obtained with this additional method were consistent with our conclusions (Appendix).

We did not consider asymptomatic cases in our analysis. The adopted methodology is robust even in the presence of large underdetection rates, provided that these rates are constant over time or even slightly fluctuating (*8*,*9*). We did not consider imported cases either, due to the lack of data; imported cases are potential infectors, but do not contribute to the number of transmitted cases, thereby lowering estimates of reproduction numbers. In Italy, most cases were probably locally transmitted. After March 11, the ban of movement across provinces imposed by the lockdown made the role of imported cases negligible. Reproduction numbers were computed using the distribution of serial interval for Italy (*10*; D. Cereda et al.), which is an acceptable approximation of the generation interval (*11*; S. Hu et al., unpub. data, https://10.1101/2020.07.23.20160317). Both distributions are strongly influenced by country-dependent variables, such as behavior of infected persons and the adopted interventions. Estimates of the generation interval distribution are still unavailable for Italy as of October 2020.

Italy was the first country outside of Asia to impose a nationwide lockdown, rapidly followed by many countries worldwide. The effectiveness of lockdown had been proven in China, where the reproduction number was estimated to fall to ≈0.3 in Wuhan (*12*) and 0.5 in other provinces (*8*); Western countries had enforced a comparatively softer version of restrictions. We have shown that these measures enabled rapid reversal of the epidemic trend within 2 weeks, although probably at higher values of the reproduction number.

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Dr. Guzzetta is a researcher at the Bruno Kessler Foundation in Trento, Italy. His primary research interests are mathematical models of infectious disease transmission dynamics with a focus on public health applications, assessments of potential risks, and evaluation of effectiveness of interventions.

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Appendix

Timeline of Interventions

The interventions performed in Italy to control the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were initially localized in the 3 regions in which the large majority of cases had been detected (Lombardy, Veneto, Emilia Romagna), and included the creation of red zones in areas with sustained transmission, the ban of mass gatherings, and the closure of schools. School closure at the national level was mandated on March 5. On March 8, the red zone was extended to the entire region of Lombardy, and to several provinces in the regions of Emilia-Romagna, Piedmont, Veneto, and Marche. Finally, the national lockdown (stay-home mandate and closure of all nonessential productive activities) was issued on March 11, 2020. The timeline of interventions performed over the period February 23, 2020−May 4, 2020 is summarized (Appendix Table 1).

Changes in Infection Ascertainment Rates

Temporal changes in the ascertainment rate of SARS-CoV-2 infections can be indirectly evaluated by observing changes in the proportion of positive tests, given by the ratio between the number of new confirmed cases and the number of performed tests (*1*). A declining proportion of positive tests may derive from the combined effect of a nondecreasing prevalence of infection and an increasing number of tests being administered, thereby resulting in higher rates of cases being ascertained. A massive scale-up of the testing capacity was implemented during the course of the epidemic, resulting in a declining proportion of positive tests after March 25; however, the decline of positive tests needs to be interpreted in the context of a likely declining incidence (R_t <1) (Appendix Figure 1).

Bayesian Methods for Estimating the Basic and Net Reproduction Number

Case-based surveillance data were collected by regional health authorities and collated by the Istituto Superiore di Sanità using a secure online platform, according to a progressively harmonized track record. Data include, among other information, the place of residence, the date of symptom onset and the date of first hospital admission for laboratory-confirmed COVID-19 cases (*3*). In the early phase of the epidemics, the Italian regions did not report the number of cases that were imported from abroad or from other regions in the country. However, it is likely that the large majority of cases were locally transmitted, given that the epidemic was already widespread by the time of detection on February 1, 2020. After March 11, the national lockdown imposed a ban on movement across provinces except for well-documented special cases (health- or work-related), and thus the role of imported cases was probably negligible.

The distribution of the net reproduction number R_t was estimated by applying a well-established statistical method (*4*), which is based on the knowledge of the distribution of the generation time and on the time series of cases. In particular, the posterior distribution of R_t for any time point t was estimated by applying the Metropolis-Hastings Markov chain Monte Carlo sampling to a likelihood function defined as follows:

$$\mathcal{L} = \prod_{t=1}^{T} P\left(C(t);\ R_t \sum_{s=1}^{T} \varphi(s) C(t-s) \right)$$

where

• $P(k; \lambda)$ is the probability mass function of a Poisson distribution (i.e., the probability of observing k events if these events occur with rate λ)

• $C(t)$ is the daily number of new cases having symptom onset at time t

• R_t is the net reproduction number at time t to be estimated

• $\varphi(s)$ is the probability distribution density of the generation time evaluated at time s.

As a proxy for the distribution of the generation time, we used the distribution of the serial interval, estimated from the analysis of contact tracing data in Lombardy (D. Cereda et al., unpub. data, https://arxiv.org/abs/2003.09320), i.e., a gamma function with shape 1.87 and rate 0.28, having a mean of 6.6 days. This estimate was later confirmed by independent study on a village (Vo' Euganeo) in the region of Veneto (*5*) and is within the range estimated for other countries (*6*–*9*; S. Hu et al., unpub. data, https://10.1101/2020.07.23.20160317).

To estimate R_0, we estimated a constant daily reproduction number $R_t = R_0$ over a time window, defined as a period of exponential growth in the early phase of the outbreak preceding the implementation of interventions (Appendix Table 2).

Regions that were not considered for the estimation of R_0 did not have a clearly identifiable exponential growth window of $\geq$1 week before the implementation of any interventions and $\geq$5 symptomatic cases per day. In the early phase of the epidemic, the region of Piedmont was not able to track the date of symptom onset for a large number of cases, resulting in an epidemic curve that cannot be used to provide a reliable estimate of R_0.

Trends in Country-Level Net Reproduction Number

We estimated the net reproduction number R_t from the time series of cases occurring in the whole country by date of symptom onset (Appendix Figure 2). Darker gray lines indicate the dates of March 10, 18, and 25, at which we sampled the regional and provincial estimates in the main analysis. A declining trend was visible before the lockdown (March 11), but lockdown enhanced the negative slope of the decline and brought R_t below threshold. After March 25, the R_t for Italy oscillated slightly around a stable value.

Comparison of Results with Hospitalization-Derived Reproduction Number

We performed a sensitivity analysis in which we adopted the same methodology used to estimate R_t, but applied to the time series of hospitalized cases (by date of hospitalization) instead of date of symptom onset (Appendix Figure 3). In particular, we estimated the reproduction number at March 25, using 2 different datasets: the time series of COVID-19 cases by date of symptom onset C(t) (estimate denoted by R^{symp}), as shown in Figure 1; and the time series of hospitalized cases by date of hospital admission, H(t) (estimate denoted by R^{hosp}). Because case-patients are admitted to the hospital at delayed time D from their symptom onset, we computed R^{hosp} using the shifted time series of hospitalized cases, H(t+D). The median value of D was estimated at 7 days from surveillance data, using 32,893 cases for which both the date of symptom onset and the date of hospital admission were available. Overall, H(t) includes

60,439 hospitalized cases recorded in the surveillance dataset as of April 1. Estimates of R^{hosp} for Piedmont could not be computed because the hospitalization data was incomplete.

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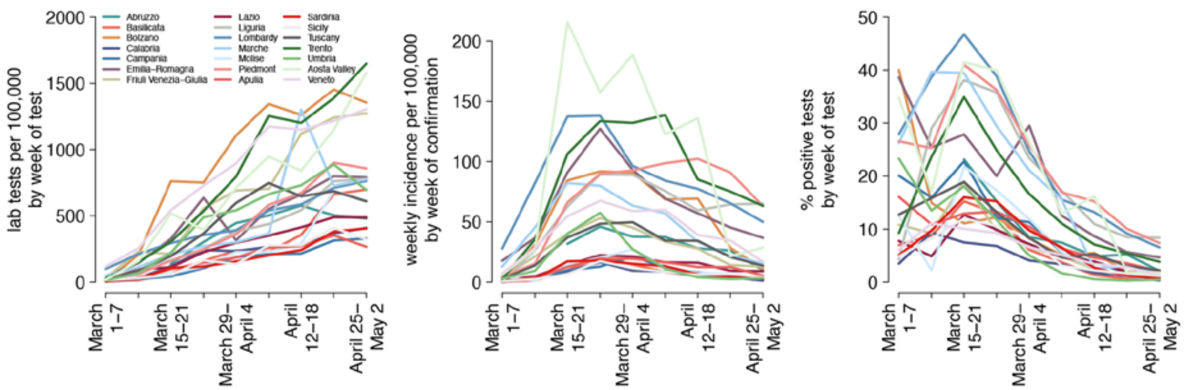
Appendix Table 1. Interventions performed in Italy to prevent transmission of severe acute respiratory syndrome coronavirus 2 during February 21−May 4, 2020

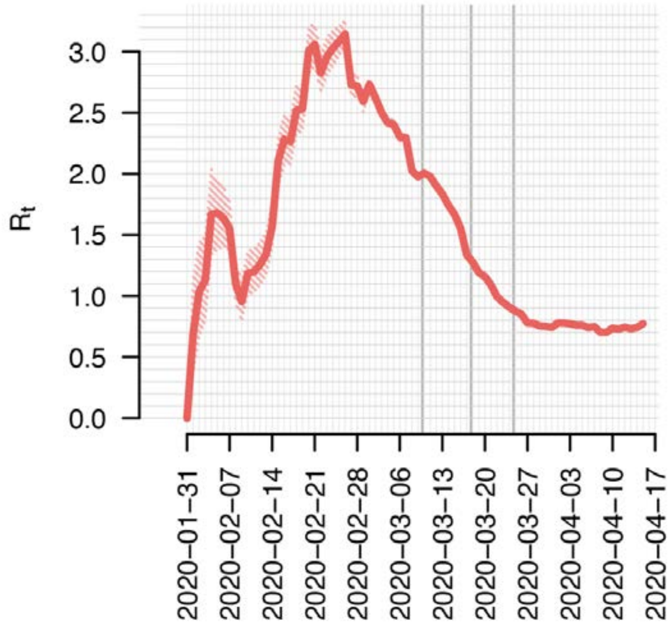
Date	Location	Interventions
February 23	Lombardy Veneto	Creation of red zones in 11 municipalities of Lombardy and around the municipality of Vo' Euganeo in Veneto; ban of mass gatherings; school closure
March 2	Emilia-Romagna	Ban of mass gatherings; school closure
March 5	All Italian regions	School closure
March 8	Lombardy 5 provinces in Emilia-Romagna 5 provinces in Piedmont 3 provinces in Veneto 1 province in Marche	Closure of all non-essential productive activities; stay-home mandate except for well-documented special cases (health or work-related)
March 11	All regions of Italy	Closure of all nonessential productive activities; stay-home mandate except for well-documented special cases (health or work-related)

Appendix Table 2. Regions characterized by periods of exponential growth before the national lockdown issued in Italy on March 11, 2020

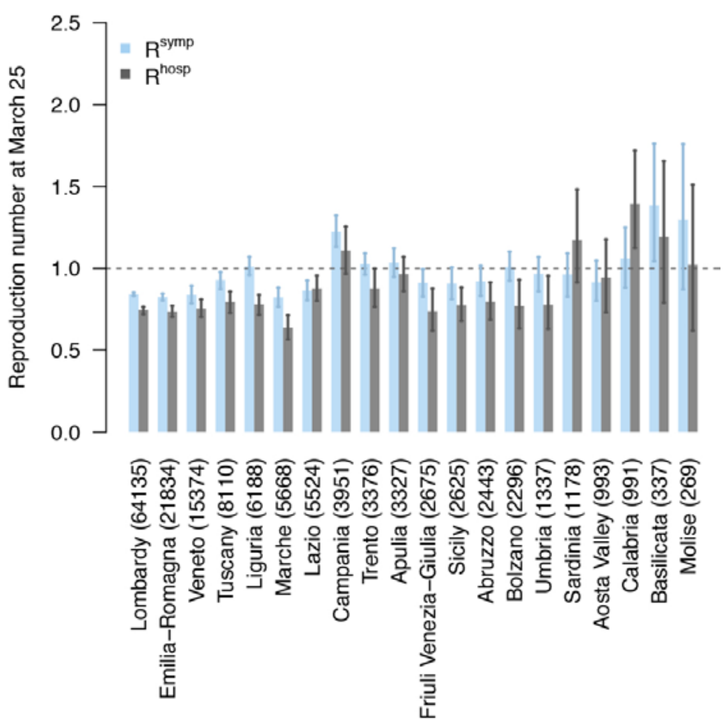
Region	From	To
Campania	February 27	March 5
Emilia-Romagna	February 20	February 27
Lazio	February 27	March 5
Liguria	February 27	March 5
Lombardy	February 13	February 20
Marche	February 20	February 27
Toscana	February 27	March 5
Veneto	February 15	February 22



Appendix Figure 1. Number of lab tests (left) and lab-confirmed incident cases (center) per 100,000 population, and proportion of positive tests (right) in all regions and 2 autonomous provinces of Italy, as reported by the Italian Civil Protection Department (*2*). Note that lab-confirmed cases refer to infections occurring several days and up to few weeks before the reporting date, due to delays related to development of symptoms, seeking for medical care, execution of tests, and reporting to national authorities.



Appendix Figure 2. Estimates of the reproduction number over time, using the time series of COVID-19 cases in Italy by date of symptom onset.



Appendix Figure 3. Estimates of the reproduction number at March 25, using the time series of COVID-19 cases by date of symptom onset (R^{symp}) and the time series of hospitalized cases by date of hospital admission (R^{hosp}).