

disCOVIDer19

A path-guide inside the COVID-19 pandemia

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"The laws of history are as absolute as the laws of physics, and if the probabilities of error are greater, it is only because history does not deal with as many humans as physics does atoms, so that individual variations count for more" (I. Asimov, Foundation and Empire)

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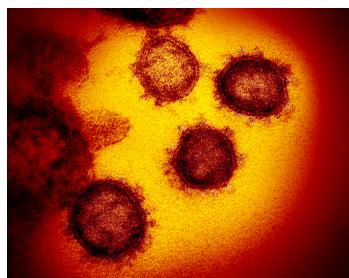
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ABSTRACT

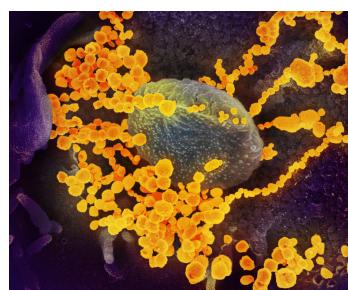
1 INTRODUCTION

1.1 Background

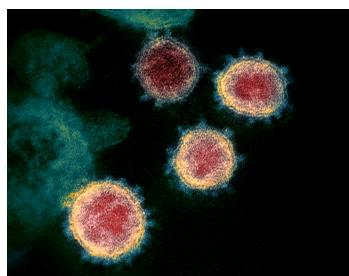
In December 2019 different cases of pneumonia were reported in Wuhan (China) [7]. Their origin was later ascribed to a new virus classified as *Severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2) whose TEM and SEM pictures are reported in the Fig. 1. The origin of this virus is still subject of scientific debate between the scientific community, however one of the most common opinion is that this virus comes from bats, in particular the genus *Rhinolophus* [8]. The most compelling feature of this virus is its ability to spread via coughing and sneezing [9], and also by touching infected surfaces [10]. Differently with respect to the SARS-CoV the virus seems to have a lower mortality rate [11, 12].



(a) Transmission electron microscope (TEM) image of SARS-CoV-2—also known as 2019-nCoV, emerging from the surface of cells cultured



(b) Scanning electron microscope of the SARS-CoV-2 emerging from the surface of cells cultured



(c) TEM image of SARS-CoV-2. Note the spikes that give the name coronavirus to the virus



(d) SEM image of the virus

Figure 1: Different pictures of the virus as reported by the NIAID's Rocky Mountain Laboratories (RML) in Hamilton, Montana [1]

In January the Chinese government imposed the quarantine for the city of Wuhan (almost 11M people); the quarantine was later expanded to the full province of Hubei (60M people) and then to the neighbour provinces Huanggang, Ezhou and Xianning. The virus

then spread in Canada, Germany, Thailand and Japan and then in other different countries including Italy [13]. In Italy the first cases, two Chinese tourist from Hubei, were reported in Rome [14]; then other cases were reported in Codogno (Lodi, Lombardy). Later the virus spread almost in all regions of Italy with a higher density in Lombardy, Veneto, Emilia-Romagna, Piemonte and Marche. Starting from 22nd of February, the Italian government started to impose the quarantine (red-zone) for eleven different municipalities, in particular Codogno, Casalpusterlengo, Lodi (included the neighbour municipalities) and Vo'. From this date onward, different restrictive measures were imposed starting from regions with the highest number of cases: public entrainment were almost suspended as well as schools and universities. Workers (in public and private sectors) were allowed, when possibile, to work at home (smart-working). Such measures culminated with a decree approved by the Italian government that divided Italy in three areas: the red zones, in which the municipalities with highest number of cases in which all the population was subjected to quarantine; the yellow zones (Lombardia, Veneto, Emilia Romagna) where schools, universities and public events, sports as well cinemas were suspended; the rest of Italy, in which no restrictive measures were adopted [15]; however 3 days later all schools and universities were suspended [16]. The restrictive measures were also extended up to all Italy with a further decree [17].

1.2 Historical Background

In the last centuries several cases of pandemic diseases were recorded: from our point of view, their dynamic is useful to understand and perhaps to model that further peaks may succeed the first one even with a highest death rate.

THE DEADLIEST PANDEMICS IN HUMAN HISTORY: THE SPANISH FLU

The first one, which happens to be the biggest human pandemic (in terms of spread just as much as deaths [18]), is the Spanish Flu: this name is quite misleading since it was not originated in Spain, though the Spanish press was the first one to talk about it. Indeed, at that time (1917-1918) almost every other country was involved in the Great War and consequently the censorship was applied to the press. The origin of this disease is still under research: some scholars focused on the United States [19, 20], on France [21] and on Asia [22]. The disease was ascribed to the virus A/H1N1, a subtype of influenza A Virus. The spread of the disease was strongly amplified by the fact that many people lived in very bad hygienic conditions. As one can see from Fig.2 there were basically three waves: the initial spread, the second wave and the third wave. The second wave, that was the most

lethal one, coincides with the end of the war and with the coming back of the troops: the close contact inside the trains, and the diffusion of the troops inside their home villages/cities increased abruptly the contagion rate and then the death rate. Furthermore, this effect was amplified by the fact that a more deadly mutation of the virus became widespread [23]. As pointed out by different scholars, such effect was enhanced by the fact that sick people, which infection potential was higher, were transferred by train to the hospitals. Immediately, the virus spread with a higher rate [24]. As it is possible to note from Fig. 3 this second wave was largely more deadly for young people with respect the first wave. Finally, looking at plot 2, a third wave also manifested itself in the beginning of 1919: here, the mortality was higher with respect to the first one, but lower to the second one. In the end, this pandemic infected 500 million people and killed something between 17 and 50 million [25]. It is worth noting that, just to compare, the casualties in the Great War were from 8.8 to 10.7 million among soldiers and 11 million among civilian [26]

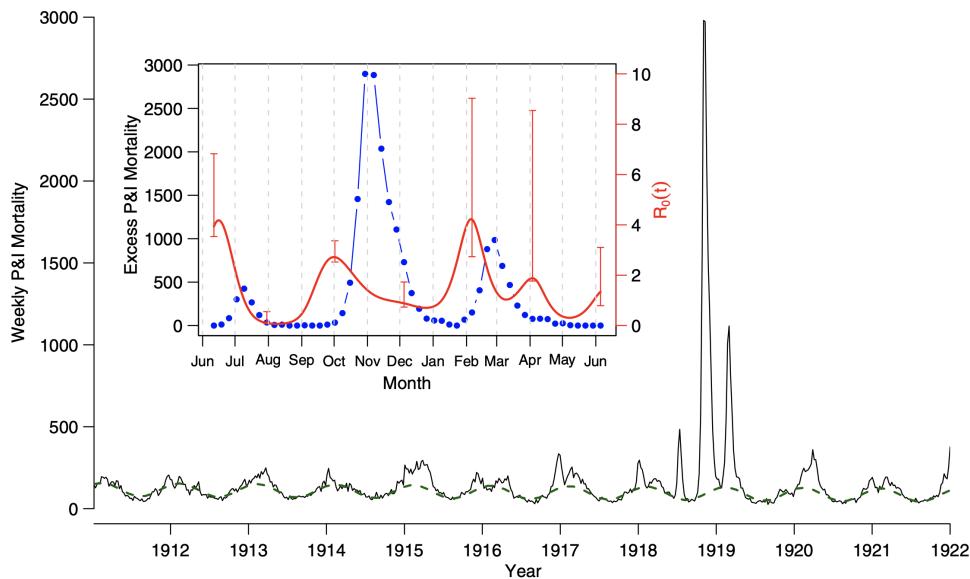


Figure 2: Pneumonia and Influenza mortality from 1910-1922 in London: note the three peaks due to the spanish flu. The variation of the diffusion rate R_0 is reported in the box. Image source: Ref. [2]

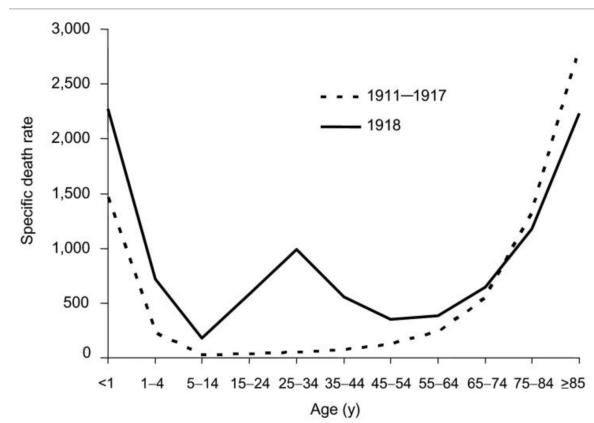


Figure 3: Mortality range distribution for the two waves of Spanish flu: note that the second one was more severe for the young people. Image source: Ref. [3]

THE ASIAN INFLUENZA (H2N2) In 1957 different cases another virus of influenza (A/H₂N₂) spread in China starting from Guizhou [27] . In this case, at difference with respect to the Spanish flu, the scholars were able to isolate the virus (the virus of the former was only isolated in 1933). It was proposed that the virus may be originated from mixing of avian and human influenza (see Fig. 4). The virus diffused in Hong Kong in April then in Singapore, Taiwan and Japan and then globally [28] . While for the US a crucial role for the spread was supposed to be played by naval bases [29, 28], for Europe the same role was played by the land route through Asia [30, 28]. Scholar also pointed out the role of a church conference in Iowa [31] where almost 1600 people from all countries met. Furthermore the opening of school in fall increased abruptly the spread of the virus (40-60 % clinical attack rate) [32, 28]. Also in this case it was reported a second wave (or perhaps others one, see Fig. 5) more lethal than the first one [33] . In this case, contrarily to the Spanish Flu a vaccine was developed although [32], it was argued that its diffusion was not effective to diminish the effect of the pandemics [34]. It was nothing that according to scholars [35] no effective measures of quarantine or other non-pharmacological one were undertaken by the authorities [35] due to the mild symptoms [28]. The total toll for this pandemic was from 1 to 1.4 million deaths according to the WHO [36]: from our point of view this pandemic is a counterfactual teaching lesson about what happens when a pandemic is underestimated (and so no restrictive measure is taken) due to its relative mild symptoms

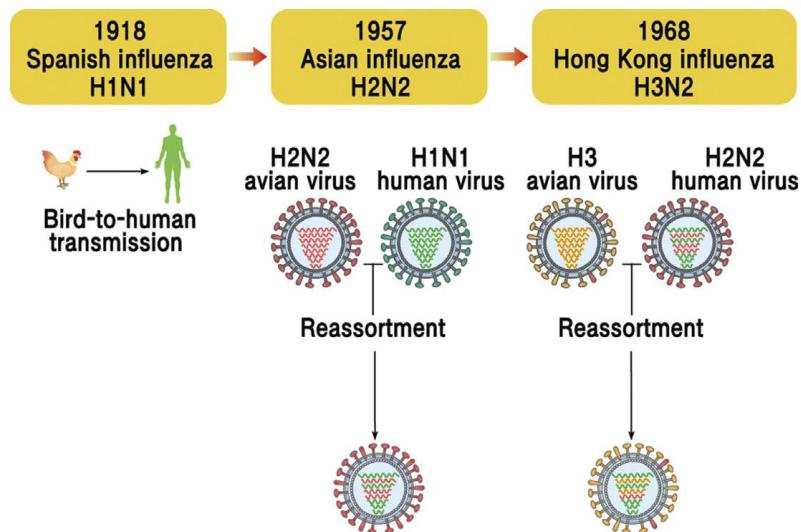


Figure 4: Wang-ShickRyu diagram for the explanation of the Spanish, Asian flu and Honk-Kong flu . Image source: Ref. [4]

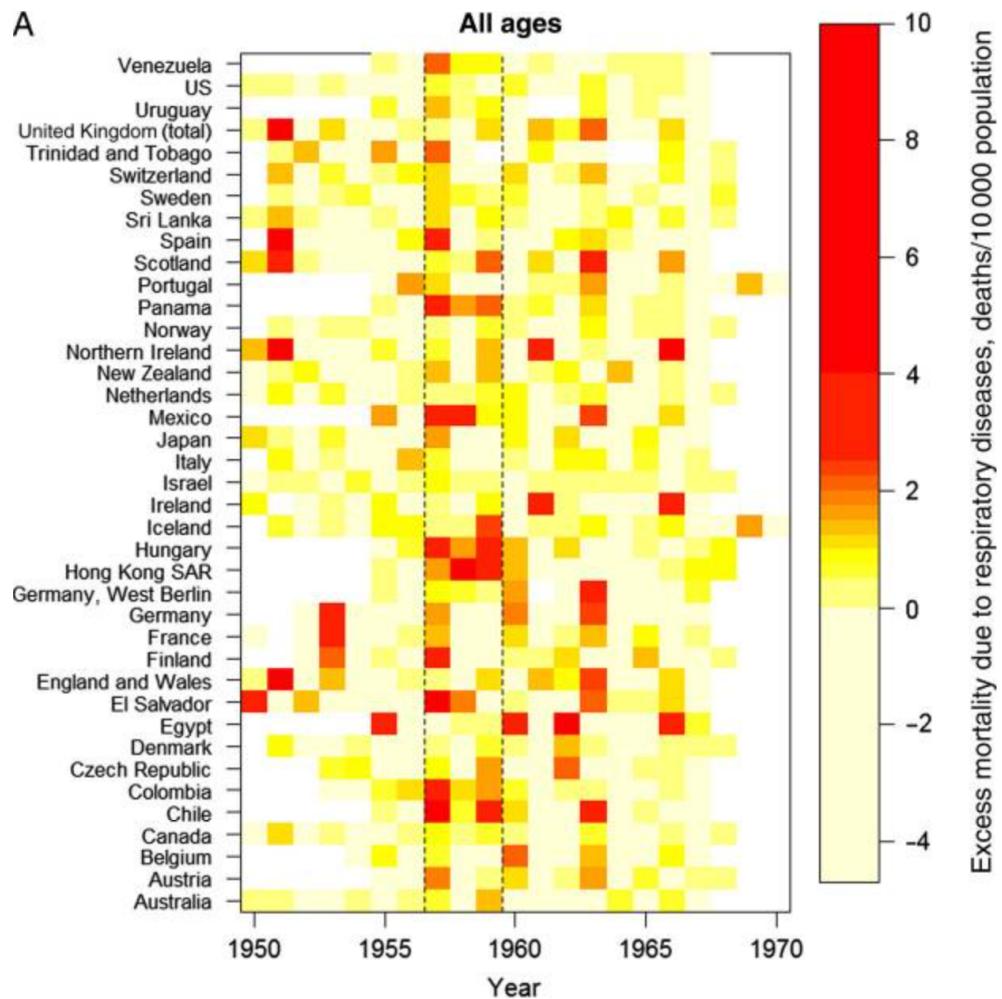


Figure 5: Excess mortality due to respiratory disease from 1950 to 1970 as reported by Viboud et al. The dashed lines marks the timing of the Hong Kong flue. Image source: Ref. [5]

MOTIVATION In order to have a thorough insight of the spread of the COVID-19 disease and its effects on italian population, we propose a ShinyApp, called disCOVIDer19, that gathers, presents and analyzes the numbers of new and cumulative infections, hospitalized and intensive care patients, deaths and recoveries, over the whole country and over its individual regions and provinces. A detailed guide to the functioning of the App is available in sections 3 and 4. As regards the analysis panel, we fitted the cumulative cases with a logistic curve, in order to get a bird-of-eye view on the general and specific trends as well as on the effectiveness of the restrictive measures imposed by the Italian government. The theoretical foundations of this fit and how to manage and use it will be discussed in the section 2 and 4.3. Beside the logistic curve, we also considered a statistical approach, largely diffused among economists, that considers the number of total cases in each day as a time series: on this basis we were able to make use of a particular tool, which will be briefly introduced in the section 2, that allowed us to make a further forecast about future cases. This latter becomes useful in case of large deviations from logistic distribution. Finally, we must remark that our approach is informational: we do limit ourselves to list and comment our findings without claiming rather delicate conclusions, especially about predictions, which many people hinge on nowadays and many lives too, unfortunately.

2 THEORETICAL BACKGROUND

Several models were proposed in the literature for modelling the spread of a disease [37]: here, we are going to consider a relative simple model taken from the growth dynamics of populations.

2.1 Population growth dynamics

The dynamics of population was founded by Thomas Malthus in 1817 [38] with his well known equation:

$$x_{n+1} = x_n(1 + r) \quad (1)$$

where x_n stands for the population at time and r the growth rate. Renaming x to P and applying recursive substitution, we get:

$$P_{n+1} = P_0(1 + r)^{n+1} \quad (2)$$

in which P_0 represents the initial population. This discrete model can be reshaped in to a continuous one in the following way:

$$\dot{P}(t) = rP(t) \quad (3)$$

That's a first order ODE with separable variable. Integrating yields:

$$P(t) = P_0 e^{rt} \quad (4)$$

Malthus, of course, did not believe that the population could grow ad infinitum with an exponential trend and, since he estimated that the resources growth follows a linear path, he argued that, at the intersection of the two curves, a consistent part of the population will not have access to the resources. Thus he expected that the exponential growth realizes only in the first part of the growth. Basing on these arguments, in 1838 Belgian mathematician Pierre-François Verhulst developed a model [39] whose new feature and key point was the maximum size of the population allowed by resources, that is the natural upper limit of coexisting individuals in a particular environment, usually called the *carrying capacity*, here indicated as K (P and r have the same meaning of the previous model):

$$\dot{P} = rP \left(1 - \frac{P}{K}\right) \quad (5)$$

that has the following analytic solution:

$$P = \frac{K P_0 e^{rt}}{K + P_0 (e^{rt} - 1)} \quad (6)$$

In Fig.6 this solution is compared to the Malthusian one: as one can see, the logistic growth shows a saturation effect towards the asymptote of carrying capacity. This completes Malthus's intuition, as it represents population growth before and after the intersection between the linear resources curve and the natural exponential growth. It is worth noting that in a neighbourhood of the origin the two curves are identical; later, the logistic curve bends down, still increasing, till it reaches the saturation region, in which it becomes almost flat.

2.2 Application to the epidemiology

The dynamics of the two models described before can be used to shape the spread of an infection [40, 41] in this case the population P is replaced with the total number of infected people, P_0 with the number of initially infected people, r with the spreading rate and the carrying capacity K with the maximum number of people that can be infected. The latter is the key point for the modelling: in principle, this parameter would be equal to the population number; in practice, due to restrictive measures and, possibly, vaccines, a large share of the total population won't enter the computation, thus lowering the carrying capacity. So, we can argue that the effectiveness of the restrictive measures can be inferred from the behaviour of the cumulative curve (except, of course, if the number of infected people is close to

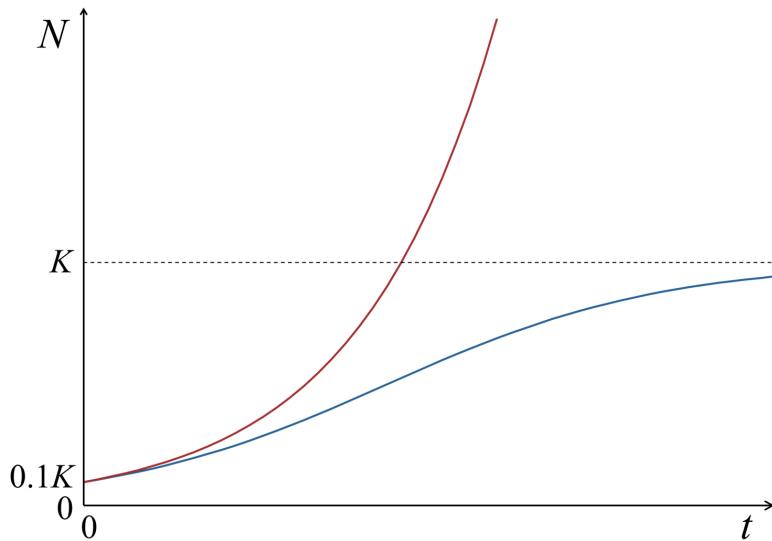


Figure 6: The Malthusian growth (red line) compared to the logistic growth (blue line). The carrying capacity is marked with a black dashed line. Image taken from [6]

the population size). It is worth noting that, for each non-quarantined infected, the carrying capacity is increased up according to the individuals that can be infected by these subjects. If this contribution is not negligible a new logistic growth may be found, with of course an exponential starting behaviour. Thus the prediction with the logistic curve should be taken as an evaluation of the impact of restrictive measures and as the *best scenario* that may occur. For this reason it is advisable to see the logistic curve as a local (in time) estimator. In fact, one can model a differential set of equation were the carrying capacity is time dependent. This possibility may be considered by the authors in a future version of this App. Furthermore, we remind that other similar models such as Gopertz, Richards or Bertalanffy can be used to shape the COVID-19 outbreak[41]: the authors may consider to include them in a future version of this App.

2.3 Time series approach

2.4 An ab-initio approach: the SEIR model

3 DATA ORIGIN

4 PANELS

4.1 Home

The home panel provides an overview of the COVID19 spread in Italy. The data shown are synchronised with the civil protection database. Whenever the App is started, a check for the updates is performed and their occurrence is indicated in the *most recent updates* section. The home panel consists of two main sections: the choropleth map and the summary statistics. The choropleth map (Fig. 7) is an interactive heat map with breakouts by region and by province tracking the number of Covid-19 cases.

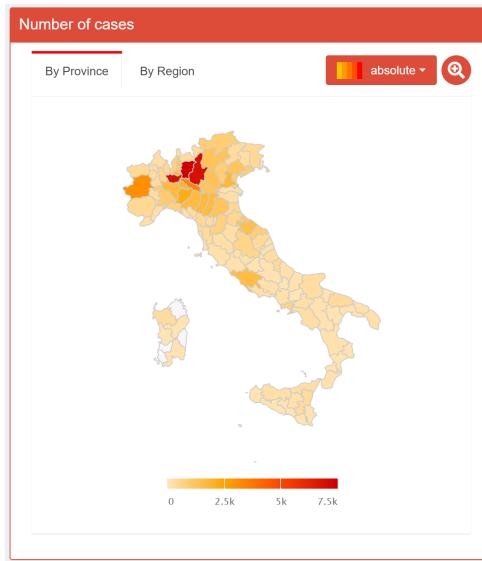


Figure 7: Choropleth map by province showing absolute number of Covid-19 cases

Beyond the raw absolute number of total cases by province/region we propose two other indicators which introduce some form of normalisation to improve the comparability of the different geographical areas. These indicators are percentage and density (Fig. 8).

The percentage indicator is calculated dividing the total number of COVID19 cases by the population of the respective region/province (the latter retrieved from Istat [42, 43]).

$$\text{percentage cases} = \frac{\text{total cases}}{\text{local population}} \times 100 \quad (7)$$

This indicator ensures that the number of cases in more populated areas are not over-indexed compared to less populated ones. Similarly, it ensures less populated areas are not under-indexed. The density indicator accounts for the territorial extension (in km^2) of re-

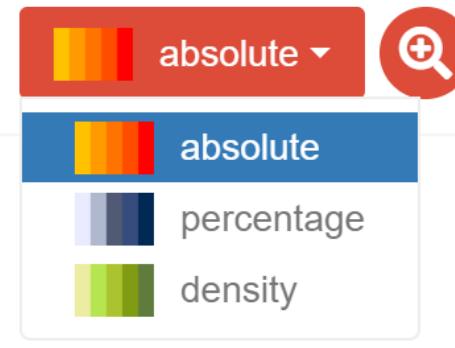


Figure 8: Input selector where the user can choose the three different break-outs absolute, percentage, and density

gions/provinces expressed in parts per thousand (%) and is calculated as follows:

$$\text{density cases} = \frac{\text{total cases}}{\text{territorial extension}} \times 1000 \quad (8)$$

This indicator combines the population density with infection spread, offering a control over space. Indeed, it is directly proportional to population density and to percentage cases:

$$\begin{aligned} \text{density cases} &= \frac{\text{total cases}}{\text{local population}} \cdot \frac{\text{local population}}{\text{territorial extension}} \times 1000 \\ &= \text{percentage cases} \cdot \text{density population} \times 1000 \end{aligned} \quad (9)$$

It is enhanced by densely populated territories, which, by the way, may in turn enhance spread infection too. Finally, the summary statistics section (Fig. 9) provides some barometer level statistics regarding the current total number of COVID19 cases in Italy with three further breakouts: intensive care, hospitalised, and home isolation.



Figure 9: Boxes with synchronised barometer level statistic about the Coronavirus

4.2 Data Inspection

The *Data Inspection* panel provides a data visualisation of the general information and a deeper overview about the hospital occupancy,

growth monitoring and test tracking for the COVID19 in Italy. It is divided in main two section: introduction and deeper inspection. In first chart (Fig. 11a) of the introduction are presented the general information about the total cases, total recovered, total hospitalised and intensive care occupancy. It is possible to select the entire Italian country or a particular region or province. Moreover, it is possible to visualise and filter the raw data for country, region and province in the panel Raw Data (Fig. 10b). In the deeper inspection panel there are four charts: the first two charts are in two different panels of a box and visualise information about intensive care occupancy in the Italian hospital in different regions, while the others represent the growth monitoring of total cases and test tracking. It is worth noting that the occupation may be higher than their total number, due to the fact that the places in intensive therapy that we considered may be upgraded (see the section 3). In the first chart 10a is represented the percentage hospital occupancy in the selected day divided by capacity with respect to the initial intensive care capacity at the start of the pandemic.

$$\text{percentage occupancy} = \frac{\text{occupancy}}{\text{capacity}} \times 100 \quad (10)$$

The second chart (Fig. 11c) visualises a bar chart of the hospital occupancy and capacity of intensive care in different region of Italy at the selected day. The third chart (Fig. 11b) represents the percentage growth and growth change of total cases day by day. The fifth chart (Fig. 10c) visualises the daily cases with respect to the daily tests.

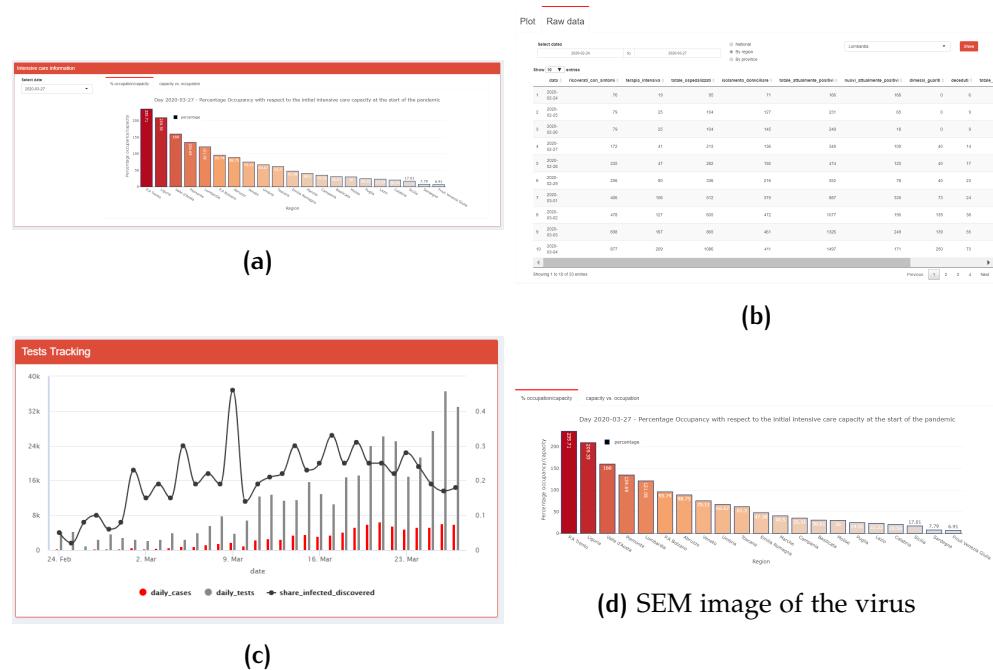


Figure 10: •

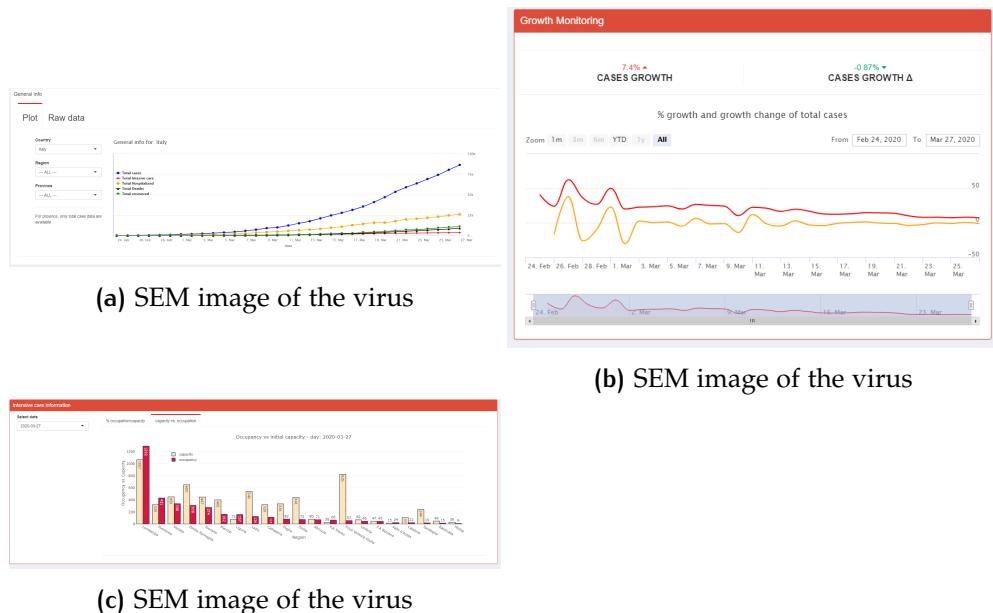


Figure 11

4.3 Data Analysis

Panel *Analysis* explores different mathematical models for shaping the infection's time series, namely the ones introduced in Section 2. As previously argued, each of these model's predictive power hinges on uncertain actual scenarios, such as the effectiveness of restrictive measures, the presence of several independent and spread outbreaks, and so on.

Package [44] has been used for growth curve fitting. This package provides function *SummarizeGrowth*, which inputs the time series of sample data and outputs the model represented by the growth metrics. Such parameters include those of the logistic equation that best fit the data, namely K , P_0 and r , as in Eq.6. The reasons why this package was chosen are chiefly two. At the one hand, it performs non-linear curve fitting with the Levenberg-Marquardt algorithm [45], which happens to be one of the most robust nls algorithms. For this step, function [46] is used. On the other hand, the package is endowed with methods for background correction.

At the top of analysis panel the user is allowed to pick one dataset among national, by region and by province. Hence, any following analysis will use the selected dataset as input (the user can browse the raw dataset in panel inspection, see paragraph 4.2).

The first section is devoted to the logistic model. An input box (Fig.12a) lists several dynamic inputs:

1. A date range that the calculator will use for curve fitting. The option to choose initial and final dates different from those at,

respectively, the beginning and the end of the dataset, is useful in two ways:

- It allows to cut initial dates which possibly correspond to zero or constant infections data, as a consequence of a delay in the outbreak in that territory. Actually, an automatic process will do so after the choice of territory, adjusting the initial date to the first day whose new infections exceed a given threshold (currently set to 1).
 - It allows to compute the available prediction n days ahead, by cutting the last n dates, and compare it to the real data.
2. A check-box *standardise positive cases by total swabs*. If selected, the share of infected among the tested, instead of the infected themselves, will be used for computations and rendering. This may be useful to capture the selection bias, but only in the scenario in which tests are randomly assigned to the population, or at least are assigned with a logic common to all dates and territories. This option is not currently available for provinces.
 3. Plot type selection boxes. The available plot types are cumulative cases and new cases. (The user can always show and hide plot's components by clicking on their label in the legend).
 4. Residuals plot type. Four options for graphically rendering the residuals: Residuals vs. fitted values; Standardized residuals vs. fitted values; Autocorrelation; Square root of absolute residuals vs. fitted values.

The output is displayed within three boxes:

1. Inside the [12b](#) box the sample points, the fitted logistic curve and a confidence band at 95 % level for the logistic curve are overlayed. The user can view the sample and fitted values by hovering over or touching (for touch-screen devices) them [12b](#). In addition, if *new cases* is selected, a plot of sample cases differences (which correspond to new cases, in fact) is shown over the logistic estimated distribution [12c](#). The latter is simply obtained by deriving the right hand side of formula (4.3.1):

$$N'(t) = \frac{\left(\frac{K-N_0}{N_0}\right) K r e^{-rt}}{[1 + \left(\frac{K-N_0}{N_0}\right) e^{-rt}]^2} \quad (11)$$

The user is suggested to take full advantage of plotly features. Besides showing points labels when passing over it and enabling plot selection by clicking on label items, plotly charts are endowed with a sequence of tools shown at the top-right of the box [13a](#).

2. Summary output box [13c](#) contains principal information about the selected model and a list of goodness-of-fit tests on the residuals.
3. Residuals box contains the plots of residuals, rendered in the user-chosen fashion. (see Fig.[13b](#)).

Input

Choose fitting interval

24 Feb

Standardise positive cases by total swabs

Plot type

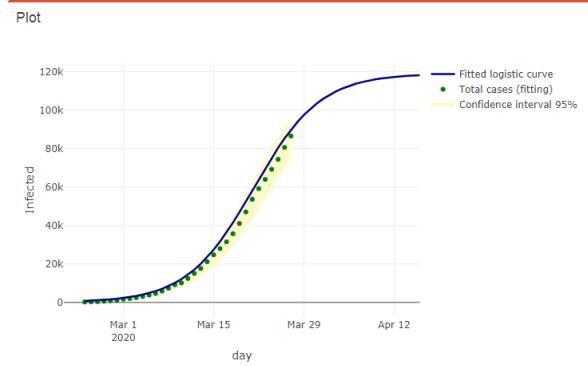
Cumulative cases
 New cases

Residuals

Residuals plot type

Residuals

(a) Set of useful tools for navigating into plots, by plotly.

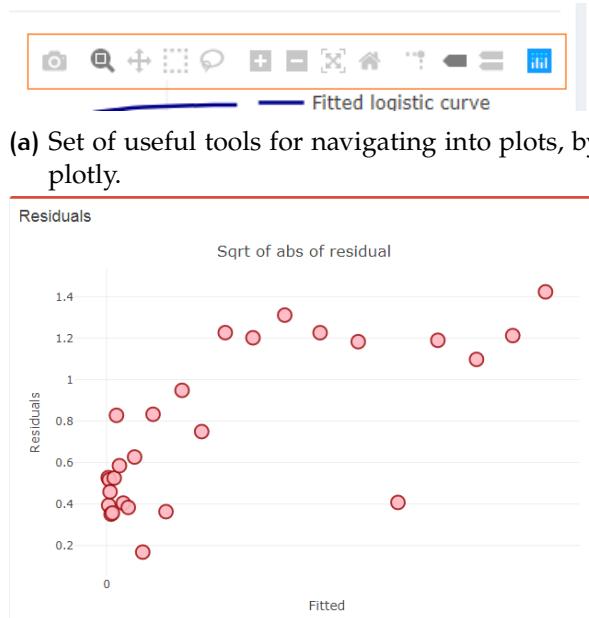


(b) Summary output box of logistic section.

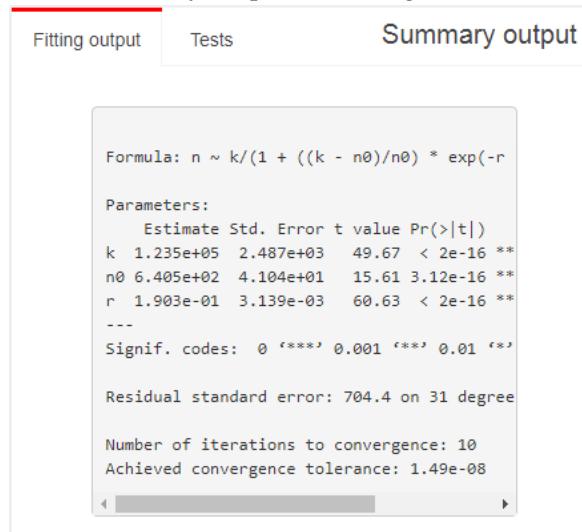


(c) One plot of nls residuals: square root of absolute residuals vs. fitted values.

Figure 12



(b) Summary output box of logistic section.



(c) One plot of nls residuals: square root of absolute residuals vs. fitted values.

Figure 13

5 CONCLUSIONS

6 PACKAGES USED

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