Predicting the evolution and control of the COVID-19 pandemic in Portugal [version 1; peer review: awaiting peer review]

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Abstract
Coronavirus disease 2019 (COVID-19) is a worldwide pandemic that has been affecting Portugal since 2 March 2020. The Portuguese government has been making efforts to contradict the exponential growth through social isolation measures. We have developed a mathematical model to predict the impact of such measures in the number of infected cases and peak of infection. We estimate the peak to be around 2 million infected cases by the beginning of May if no additional measures are taken. The model shows that current measures effectively isolated 25-30% of the population, contributing to some reduction on the infection peak. Importantly, our simulations show that the infection burden can be further reduced with higher isolation degree, providing information for a second intervention.

Keywords
COVID-19, Pandemic Control, Predictive modeling, Simulation, Social Isolation, Mathematical model
Introduction
Coronavirus disease 2019 (COVID-19) is already considered a world pandemic which is starting to have dramatic effects in Europe, where, as of 27 of March, 265,421 cases have been reported\(^1\). COVID-19 infection in Portugal has been growing exponentially with an average rate of 34±13% new cases per day from 2 March and is far from reaching the peak by the end of March. As of March 27, 4268 infection cases and 76 deaths have been reported\(^2\). The highest infection burden is found in Porto (317 cases, 7.4%) and in Lisbon (284 cases, 6.7%) but the disease is present throughout the entire country. As in other countries, infection occurs mostly in individuals' with ≥40 years of age (71.9% males; 69.3% females). Death occurs mostly in males (64.5%) all with ≥50 years of age.

Predictive models estimate that the peak of COVID-19 infection globally will be between mid-April and May, with an estimated total of 48 million people infected\(^3\). As with most other countries, the Portuguese national health care system cannot deal with the increasing demand of care due to limited ventilators and care units\(^4\). Therefore, the Portuguese government together with the National Health Directorate (DGS) declared a state of emergency and adopted interventional populational measures (IM) on 18 March 2020 in an attempt to drop the peak of infections even if at the cost of prolonging the infection time. These measures are based on the isolation of people at home, social distancing and adopting protective antiseptic policies. Most forecasting models are based on the number of cases reported and do not take into account the effects of these government-imposed measures and behavioral change. Thus, how these measures impact the evolution of the COVID-19 infection and can prevent the expansion of the epidemic is unknown. Recently published mathematical modelling studies of COVID-19 transmission have already provided useful insights that can be used to guide public health measures and resource allocation to better control this pandemic\(^5\). However, most parameters of statistical models have been estimated with high degree of uncertainty, resulting in predictions with wide intervals of confidence\(^6\). Compartmental models such as susceptible, infected and resistant (SIR) models are deterministic approaches that have been successful in describing the dynamics of virus infection in populations, including COVID-19\(^7\). Here, we provide a simple SI model that describe the dynamics of transition of COVID-19 in Portugal during the first 21 days and predicts the impact of isolation measures towards the expected peak of infection.

Methods
Basic transmission dynamics of COVID-19 was modelled using a simple mathematical model based on a system of two ordinary differential equations (ODE) developed specifically for this purpose (Equation 1 and Equation 2). The equations reflect the number of people infected (I) and susceptible (S) to infection per unit of time (dI/dt and dS/dt). In this model, we accounted for the reported average time of duration of infection (τ) of 14 days\(^8\). The model was calibrated by adjusting the rate constant (k) to approximate the total infection value reported by the DGS at 17 March. No further fitting was performed in this model. The effect of isolating different fractions of the population was modelled through the variation of parameter α in Equation 1 and Equation 2. We assumed that protective measures were 99% effective, accounted through model parameter β. The ODEs were encoded and solved using PLAS software version 1.2.0.120, where a series of simulations were carried scanning various values of the α parameter\(^8\). Simulations were carried with the initial two cases reported by the DGS and considering only the population of the grand Lisbon and Porto areas (total of 6.5 x 10\(^8\)) since they represent most of the susceptible population (see Figure 2). Further analysis, computations and plots were conducted using Python 3 in the Jupiter Notebook ipython 7.8.0 programing environment under Anaconda distribution version 4.7.12. Data regarding the daily evolution of number of total infected in Portugal by COVID-19 was collected from the DGS web site (https://covid19.min-saude.pt/ponto-de-situaçao-atual-em-portugal/) from 2 to 27 March 2020 (see Source data, Table S1\(^9\)). The model is available as Extended data\(^9\).

\[ \frac{dI}{dt} = k(1 - \alpha)SI + \alpha kBSI - \frac{1}{\tau} I \]  
(\text{Equation 1})

\[ \frac{dS}{dt} = -k(1 - \alpha)SI - \alpha kBSI \]  
(\text{Equation 2})

Results and discussion
Simulation of the first 18 days with our model was able to describe the exponential increase of the number of confirmed cases reported by the DGS between 2 and 18 March 2020 (Figure 1). The predicted peak time for this scenario was 49 days which would be by the 21 of April. This is within the estimated range predicted by statistical modelling of US, Italy and Korea scenarios\(^8\). Further, the predicted numbers of cases for the end of March if no measures were taken would be around 42,000. This is also in agreement with the number released by the DGS to the social media based on the infection reported by the DGS at 17 March. No further fitting was performed in this model. The effect of isolating different fractions of the population was modelled through the variation of parameter α in Equation 1 and Equation 2. We assumed that protective measures were 99% effective, accounted through model parameter β. The ODEs were encoded and solved using PLAS software version 1.2.0.120, where a series of simulations were carried scanning various values of the α parameter\(^8\). Simulations were carried with the initial two cases reported by the DGS and considering only the population of the grand Lisbon and Porto areas (total of 6.5 x 10\(^8\)) since they represent most of the susceptible population (see Figure 2). Further analysis, computations and plots were conducted using Python 3 in the Jupiter Notebook ipython 7.8.0 programing environment under Anaconda distribution version 4.7.12. Data regarding the daily evolution of number of total infected in Portugal by COVID-19 was collected from the DGS web site (https://covid19.min-saude.pt/ponto-de-situaçao-atual-em-portugal/) from 2 to 27 March 2020 (see Source data, Table S1\(^9\)). The model is available as Extended data\(^9\).

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Figure 1. COVID-19 spreading on Portuguese population up to 19 of March. Left, the distribution of confirmed cases on 19 March are depicted in the map. Right, evolution of the cases between 2 and 19 of March. Lines indicate simulation using the mathematical model and blue dots correspond to the confirmed cases reported by DGS.

70–75%) that suggest further isolation percentages may be more effective and still within a plausible of pandemic time. Based on the fraction of hospitalized and mortality reported by the DGS on 27 March 2020, together with our model predictions, we computed several infection indicators for these intervals (Table 1).

Our model analysis indicates that current government-mandated measures may shift the expected peak of infections towards the beginning of May and can cause a substantial reduction in the infection numbers (Figure 2, Table 1). Thus, the predicted peak in the number of cases without any isolation measures would be around 2 million, whereas the intervention measures have decreased it to around one half of the cases (Table 1). In addition, the estimated reduction of hospitalized patients and death cases on peak would be predicted around 39,000 and 12,000 people, respectively. Our simulations also indicate that the peak of infection can be further reduced by ~3.5-fold with a delay to November if 70% of the population were isolated at home and follows the government recommendations. For higher percentages of isolation (>75%), our model predicts a substantial reduction in the number of infections and delay of peaks, stopping the COVID-19 epidemic. These solutions would result in much less total mortality and hospitalization requirements on peak in comparison to the current trend (Table 1, Figure 2). Meanwhile, this comes with the burden of prolonging the time of pandemic to almost a year, which can be economically unbearable. In alternative, further isolation to 50–60% of the population may be also a solution that substantially reduce most pandemic indicators and shifts the ending of the pandemic to September, with the peak between June and July. The results obtained during simulations are available as Extended data, Table S2.

Although our model precisely described the exponential curve and explains the shift in the temporal evolution of DGS data, it has limitations that may compromise the exact values of predictions. The fact that we only assume two compartments (susceptible and infected) considering the main populated cities (Lisbon and Porto) as one is huge approximation that neglects regional dynamics. Thus, the model is just an approximation that reflects an average trend and may fail to explain regional observations. In this model we also neglected many important parameters of infection transmission such as age groups, types of social interactions, contact dependent probability, and viral load dependent probability. The inclusion of these parameters would definitely make the model more realistic. However, this data is not available for the Portuguese case and these models require accurate processing of data curation for suitable validation. We have bypassed these limitations by aggregating all of these parameters into one constant, which was fitted to the available data. Overall, the predictions shown here should be taken as semi-quantitative estimates within an upper and lower case-scenarios.
Figure 2. Simulation of the dynamics of COVID-19 spreading on Portuguese population with different percentages of social isolation. Above, predicted total infected population in the month of March. The starting of the isolation measure is depicted by IM and the arrow indicates the time of change. Below, Predicted peak of infection.

Table 1. Predicted ranges (upper and lower values) for several COVID-19 infection indicators.

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Current control (25–30% isolation)</th>
<th>Mild control (50–60% isolation)</th>
<th>Optimal control (70–75% isolation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Infected</td>
<td>4,648,087 – 4,791,783</td>
<td>3,295,201 – 3,910,457</td>
<td>1,354,146 – 2,202,358</td>
</tr>
<tr>
<td>Total death</td>
<td>41,594 – 44,421</td>
<td>18,141 – 27,406</td>
<td>2,723 – 7,623</td>
</tr>
<tr>
<td>Infected (on peak)</td>
<td>2,335,835 – 2,494,627</td>
<td>1,018,771 – 1,539,093</td>
<td>152,938 – 428,124</td>
</tr>
<tr>
<td>Hospitalized (on peak)</td>
<td>193,740 – 206,911</td>
<td>84,499 – 127,656</td>
<td>12,685 – 35,509</td>
</tr>
</tbody>
</table>
Conclusions
In this work we demonstrate the potential of modelling COVID-19 dynamics of infection as a useful support tool for predicting the impact of corrective measures. Government-mandated measures to isolate the Portuguese population at home effectively prevented COVID-19 from reaching dramatic numbers in Portugal but still can be substantially improved to reduce the infection peak. Our estimates may help guiding additional measures to control the COVID-19 epidemic in Portugal.

Data availability
Source data

This project contains the following source data used in the present study:
- Table S1 (CSV). (The number of confirmed cases in Portugal officially reported by the DGS.)

Extended data

This project contains the following extended data:
- model_code (TXT). (Code used for the model.)
- Table S2 (CSV). (Results obtained during simulation.)
- Python-code (MD). (Python code used with this model.)

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

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