Modeling COVID-19: Challenges and results

By Maíra Aguiar

Weird times we are living in. While lots of technological, medical and scientific advances are generated in a short period of time, we are now fighting a pandemic, trying to stop the spread of a new virus that has not only killed thousands of people but has also crippled our economies as lockdowns were implemented.

In December 2019, a severe respiratory syndrome (COVID-19) caused by a new coronavirus (SARS-CoV-2), was identified in China and spread rapidly around the globe. COVID-19 was declared a pandemic by the World Health Organization (WHO) in March, 2020. As of this writing, about 25 million cases were confirmed with more than 830 thousand deaths - a global case fatality ratio (CFR) of approximately 3.5%.

COVID-19 symptoms can range from mild (or no symptoms) to severe illness, with signs and symptoms appearing between 2 to 14 days after exposure. With many asymptomatic individuals, everyone is at risk of getting COVID-19. SARS-CoV-2 infection results in disease severity and death according to a hierarchy of risks, with age and pre-existing health conditions enhancing disease severity [1]. If the young and "healthy" individuals are not severely affected, SARS-CoV-2 has put at a greater risk our beloved parents and grandparents. An effective vaccine would be the best way to prevent COVID-19 infections and while its development is ongoing, epidemiologists and public health workers are the frontline of this battle, fighting with well known public health surveillance strategies of testing, contact tracing and isolation of infected individuals.

While the global case fatality ratio (CFR), a measure that is often used to evaluate the severity of the epidemics, starts to decrease over time, there are too many unknowns about COVID-19 dynamics. Why do we observe so different CFR in different countries around the globe? Are there differences in population susceptibility to SARS-CoV-2 infection and how much would that affect the course of infection in the population? What is the influence of seasonality on COVID-19 transmission? Would it be enough to contain the epidemics, such as other Influenza Like Illnesses (ILIs), even when traveling restrictions start to be lifted and imported cases from the southern hemisphere would be likely to be detected? What is the proportion and the role of the mild and asymptomatic infected individuals? Are they transmitting more or less than the symptomatic severe infected? And to which extent the acquired immunity and its duration against SARS-CoV-2 will play a role in the so called herd immunity without vaccination? Too many open questions that scientists are trying to answer by laboratory experiments, field work and theoretical studies.

As the COVID-19 pandemic is unfolding, research on mathematical modeling became imperative and very influential, not only in understanding the epidemiology of COVID-19 but also in helping the national health systems to cope with the high demands of hospitalizations, for example, providing projections and predictions based on the available data. Used as a public health guiding tool to evaluate the impact of intervention measures, governments have already taken important decisions based on modeling results. The COVID-19 pandemic has resulted in an avalanche of epidemiological modeling papers [2, 3, 4, 5, 6, 7, 8], most of them using simple models such as the SIR (Susceptible-Infected- Recovered) or SEIR (Susceptible-Exposed-Infected- Recovered) in mechanistic or probabilistic frameworks to understand and predict the spread of the disease in a population. With valuable results, modeling the dynamics of COVID-19 is very challenging, as we still know very little about the disease. More complex models would be able to give more accurate projections about specific vari-

ables such as number of hospitalizations, intensive care units admissions (ICUs) and deaths, for example, over the course of the epidemics. However, to build useful models, good quality empirical data and its understanding, as well as a close collaboration among mathematical modelers, field and laboratory researchers as well as public health stakeholders are essential.

Here I present my experience, as part of the Basque Country Modeling Task Force (BMTF), in monitoring the development of the COVID-19 epidemic to assist the Basque Health Managers and the Basque Government during the lockdown lifting measures.

In March 2020, a multidisciplinary task force was created to assist the Basque Health managers and the Basque Government during the COVID-19 responses. BMTF is a modeling team, working on different approaches, including stochastic processes, statistical methods and artificial intelligence. The primary BMTF objectives were to describe the epidemic in terms of disease spreading and control in the Basque Country and to give projections on the national health system necessity during the increased population demand on hospital admissions. With a valid modeling framework, we now monitor disease transmission when the country lockdown was gradually lifted towards the so called "new normality".

We use stochastic SHARUCD-type models (susceptible (S), severe cases prone to hospitalization (H), mild, sub-clinical or asymptomatic (A), recovered (R), patients admitted to the intensive care units (U) and the recorded cumulative positive cases (C) which includes all new positive cases for each class of H, A, U, R, and deceased (D)) - an extension of the well known simple SIR model. Epidemiological data used to validate and parametrize the models are provided by the Basque Health Department and the Basque Health Service (Osakidetza), continually collected with specific inclusion.

In our first modeling attempt, disease severity was decided upon infection with a proportion η of infected individuals going to develop severe symptoms prone to hospitalization or $(1-\eta)$ to develop mild or no symptoms [9]. Mild

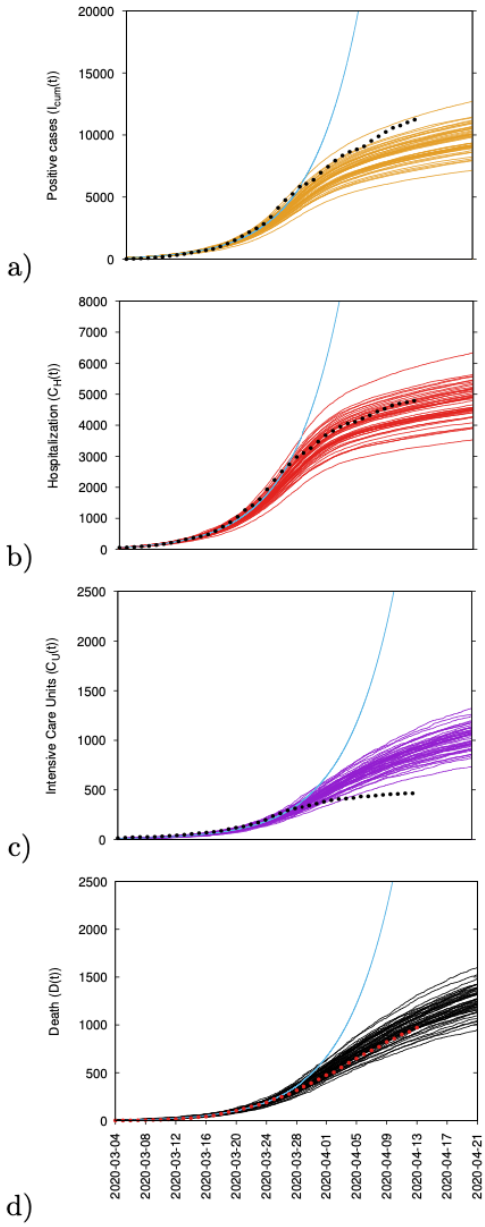

Figure 1: Ensemble of 200 stochastic realizations of the initial SHARUCD-model. Empirical data are plotted as black/red dots. In a) cumulative positive cases I_{cum}(t), in b) cumulative hospitalized cases C_H(t), in c) cumulative ICU admissions C_U(t) and in d) cumulative deceases cases D(t). The mean field solution without control is shown as a blue line.

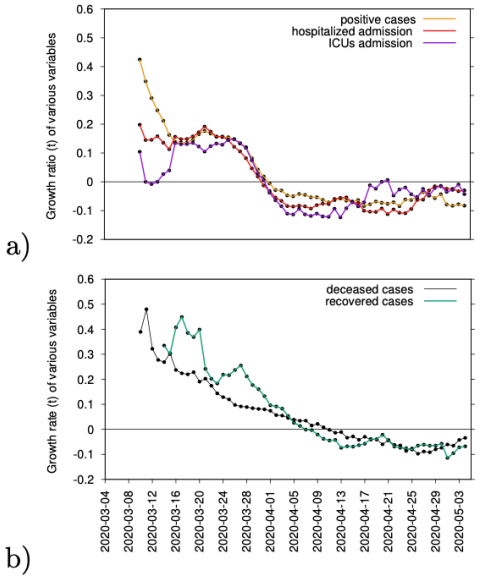

Figure 2: Growth rates estimations for various variables. In a) PCR positive cases (yellow), hospitalizations (red) and ICU admission cases (purple) and in b) growth rate for recovered (green) and deceased cases (black) notified in the Basque Country.

and asymptomatic individuals were assumed to transmit the disease more efficiently ($\phi\beta$, with $\phi > 1$) than the severe cases which would be first cases identified, at least at the beginning of the pandemic when testing capacity was low. In this approach, hospitalized cases could recover, die or go to ICU, i.e., ICU was considered a progression in severity of hospitalized cases. Parameter insecurities were calculated numerically with likelihood functions conditioned on the others and the data from all 5 model variables and fixed as the model was able to describe the disease incidence during the exponential phase of the outbreak. Partial lockdown implemented on March 16, 2020 was shown to decrease disease transmission in the Basque Country, with effects observed on March 27, 2020, well before the full lockdown on March 31, 2020.

The effect of the disease control measures was introduced using a standard sigmoid function which was able to describe well the gradual slowing down of the epidemic, see Fig. 1.

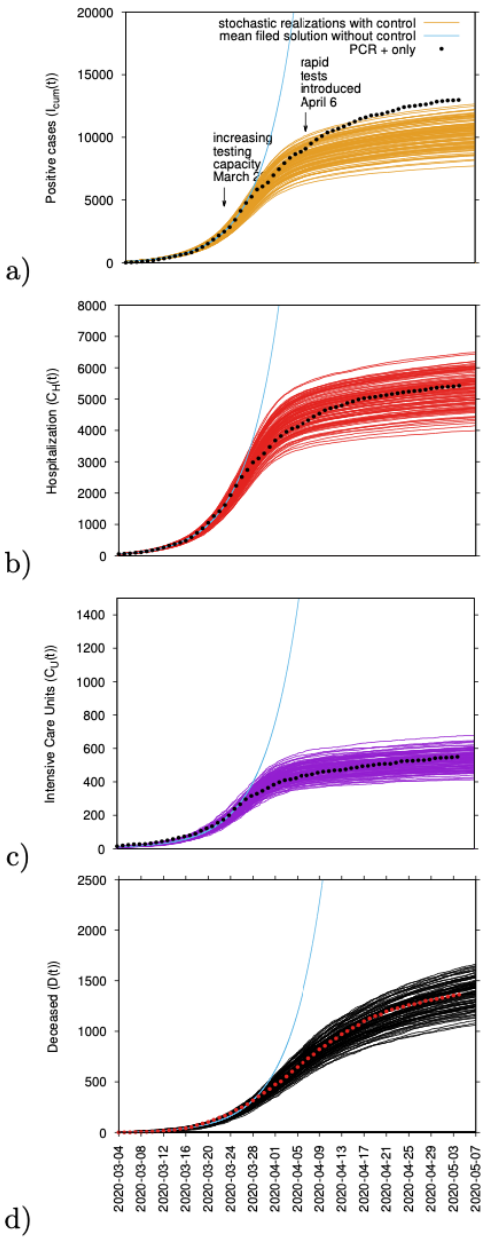

Figure 3: Ensemble of 200 stochastic realizations of the ICU refined SHARUCD-model. Empirical data are plotted as black/red dots. In a) cumulative positive cases I_{cum}(t), in b) cumulative hospitalized cases C_H(t), in c) cumulative ICU admissions C_U(t) and in d) cumulative deceases cases D(t). The mean field solution without control is shown as a blue line.

Analysis of the momentary reproduction ratio and momentary growth rates [10] have shown two groups of growth behaviour in response to the lockdown measures. Synchronization of the ICU admission cases with the cumulative tested positive cases and hospitalizations was observed, following the sigmoidal function behaviour, and the deceased and recovered cases showing a delay in response to the control measures of 8 to 10 days, see Fig. 2.

These findings have led to the first refinement of our model, with the transition into ICU admissions changed to a ratio, with infection causing from asymptomatic up to very severe cases. In good agreement, the refined model can now describe well the hospitalizations, the ICU admissions and the deceased cases (see Fig. 3), well matched within the median of the 200 stochastic realizations from the model [11]. Although the cumulative incidences for tested positive cases could only be described qualitatively, following the higher realizations range due to the increasing testing capacities in the Basque Country since March 22, 2020, we now work on further model refinements evaluating the role of seasonal effect, the "new normality" after lockdown lifting and the impact of imported cases and increase testing capacity (see Fig. 4).

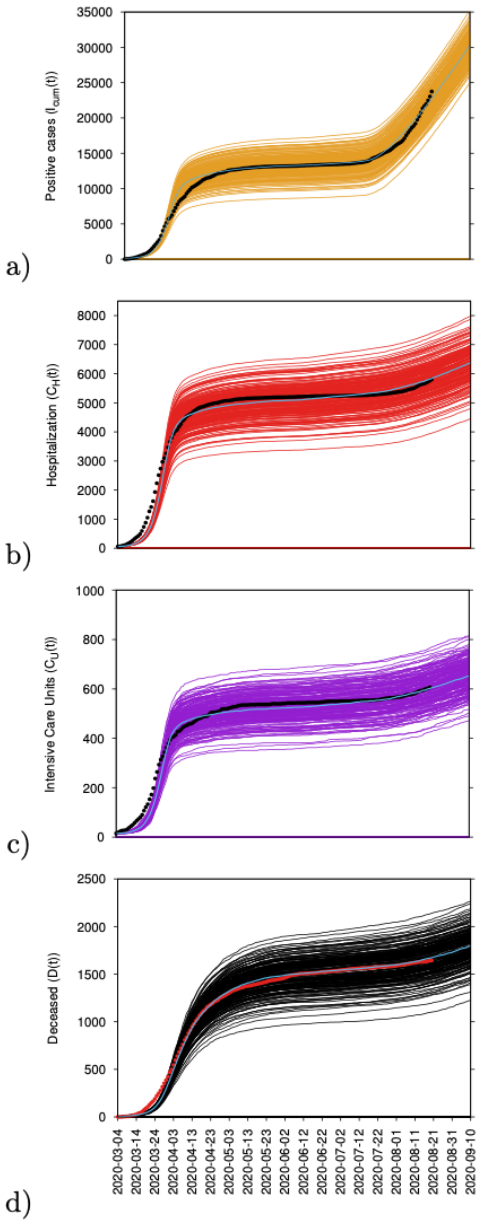

Figure 4: Ensemble of 200 stochastic realizations of the import and seasonality refined SHARUCD-model. Empirical data are plotted as black/red dots. In a) cumulative positive cases I_{cum}(t), in b) cumulative hospitalized cases C_H(t), in c) cumulative ICU admissions C_U(t) and in d) cumulative deceases cases D(t). The mean of the stochastic simulations is shown as a blue line. This is working in progress with a detailed analysis to be publicly available soon [11].

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ESMTB Thematic panels

The field of mathematical biology continues to grow, and ESMTB has therefore decided to foster interactions in subgroups, where society members can meet and interact within more focused areas. Membership to the societys thematic panels is open to all members. New thematic panels may be formed by petition to the ESMTB Board at any time.

Guidelines for the establishment and operation of ESMTB thematic panels

The ESMTB welcomes the fostering of specialised interest groups among its members, groups to be henceforth designated as *thematic panels* (name subject to discussion) to inspire, advance and promote activities within the scope of ESMTB. Thematic panels are organised within a certain theme and are hosted by a chair. The following guidelines shall apply to their establishment and operation.

1. Groups of at least 20 members may apply for the establishment of a thematic panel with the ESMTB board. Applications should be sent to the ESMTB secretary and be signed by the founding chair of the panel. A short description of the scope and scientific interests must be provided.
2. Affiliation to such panels is free of charge and open to all interested members, who may join in at any time. Membership in the panel ends with the end of membership in ESMTB.
3. The panel members will manage the operation of the panel on a democratic basis; in particular, they nominate (or elect) the chair in regular intervals. The chair is the representative of the panel and serves as the contact person for the ESMTB board. When the chair changes, the secretary of ESMTB should be informed as soon as possible.
4. ESMTB may financially sponsor (if budget is available) the activities of the panels, upon request by the panel's representative.
5. ESMTB expects each panel to produce periodic summary documentation reporting on the activities of the panel and indicating likely directions of development in the research area covered by the panel.
6. The ESMTB secretary is charged with facilitating panel operations and briefly reporting to the board on current developments.
7. ESMTB will host on the society's webpage, in the Newsletter, the Communications, and social media news related to the activities of the thematic panels, as provided by the panel representatives.
8. Thematic groups and their members consent the ESMTB to store and process their names and contact data.