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1 Introduction

In early 2020, after a December 2019 outbreak in Wuhan-China, the World Health Organization identified SARS-CoV-2 as a new type of coronavirus. The outbreak quickly spread around the world raising global awareness.

COVID-19 is a disease caused by SARS-CoV-2 that can trigger what medical experts call a respiratory tract infection. It can affect the upper respiratory tract (sinuses, nose, and throat) or lower respiratory tract (windpipe and lungs). It spreads the same way other coronaviruses do, mainly through person-to-person contact. Infections range from mild to deadly. SARS-CoV-2 is one of seven types of coronavirus, including the ones that cause severe diseases like Middle East respiratory syndrome (MERS) and sudden acute respiratory syndrome (SARS). The other coronaviruses cause most of the colds that affect us during the year but aren't a serious threat for otherwise healthy people. It is also normal for a virus to change, or mutate, as it infects people and this virus has done so. There are several variants which have been named for the regions they were first discovered but they have now spread to other areas and countries, some proving to be more contageous as well as more deadly.

The goal of this project is examine the impact of COVID-19 spread by using a custom epidemiological model. The model itself is an extended SEIR model comprising of six compartments corresponding to discrete human groups: susceptible, exposed, infectious, vaccined and recovered. The model parameters are initially calibrated according to the study performed by Mwalili et al.[2] and then the estimated set of model state and parameters is used to assess the model prediction skill by investigating the initial COVID-19 spread in Greece.

2 Methods

Simulation and modeling is becoming a standard approach to understand complex biochemical processes. Therefore, there is a big need for software tools that allow access to diverse simulation and modeling methods as well as support for the usage of these method.

COPASI is an open-source software application for creating and solving mathematical models of biological processes such as metabolic networks, cell-signaling pathways, regulatory networks, infectious diseases, and many others. In this case, this software was utilized as an epidemic simulator since the the biochemical reactions networks resemble the viruses behaviour.

As an extra step, the same model without the vaccination part, was implemented in python for this project as well.

2.1 Model

The basic SEIR model is expanded to six compartments to simulate the epidemic of COVID-19. Six state variables are considered within a population, that is, S(t), E(t), I(t), R(t), D(t), and V(t), denoting the number of susceptible, exposed (infected, but not yet infectious), infectious (symptomatic and asymptomatic), recovered, dead, and vaccinated cases, respectively. Thus, the human population is denoted by $N(t) = S(t)+E(t)+I(t)+R(t)+D(t)+V(t)$.

The transmission flow of the Coronavirus disease is described by the proposed model in Figure 1.

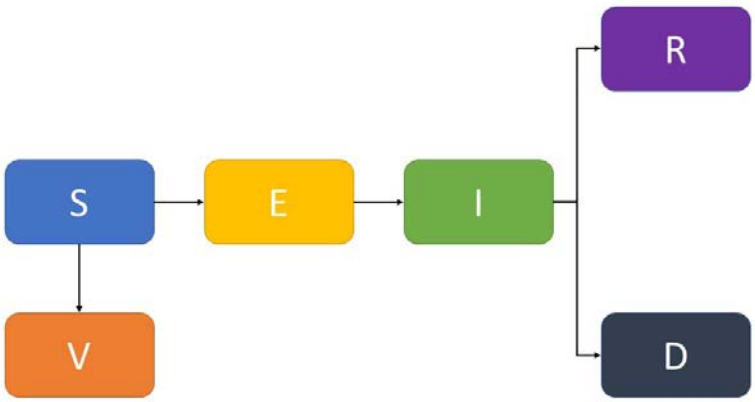

Figure 1: The *SEIRD-V* epidimiological model as derived by extending the basiv SEIR model.

2.2 Differential equations

The model culminates to a six-dimensional system of ordinary differential equations as follows.

$$
\begin{aligned}
\frac{\mathrm{d}([\mathrm{E}] \cdot V_{\mathrm{Main}})}{\mathrm{d}t} &= -V_{\mathrm{Main}} \cdot \left(\mathrm{sigma}_{(\mathrm{Infected})} \cdot [\mathrm{E}]\right) \\
&\quad + V_{\mathrm{Main}} \cdot (\mathrm{beta} \cdot [\mathrm{I}] \cdot [\mathrm{S}]) \\
\frac{\mathrm{d}([\mathrm{S}] \cdot V_{\mathrm{Main}})}{\mathrm{d}t} &= -V_{\mathrm{Main}} \cdot (\mathrm{beta} \cdot [\mathrm{I}] \cdot [\mathrm{S}]) \\
&\quad - V_{\mathrm{Main}} \cdot (\mathrm{alpha} \cdot [\mathrm{S}]) \\
\frac{\mathrm{d}([\mathrm{I}] \cdot V_{\mathrm{Main}})}{\mathrm{d}t} &= +V_{\mathrm{Main}} \cdot \left(\mathrm{sigma}_{(\mathrm{Infected})} \cdot [\mathrm{E}]\right) \\
&\quad - V_{\mathrm{Main}} \cdot ((1 - \mathrm{p\_d}) \cdot \mathrm{gamma} \cdot [\mathrm{I}]) \\
&\quad - V_{\mathrm{Main}} \cdot (\mathrm{p\_d} \cdot \mathrm{gamma} \cdot [\mathrm{I}]) \\
\frac{\mathrm{d}([\mathrm{R}] \cdot V_{\mathrm{Main}})}{\mathrm{d}t} &= +V_{\mathrm{Main}} \cdot ((1 - \mathrm{p\_d}) \cdot \mathrm{gamma} \cdot [\mathrm{I}]) \\
\frac{\mathrm{d}([\mathrm{D}] \cdot V_{\mathrm{Main}})}{\mathrm{d}t} &= +V_{\mathrm{Main}} \cdot (\mathrm{p\_d} \cdot \mathrm{gamma} \cdot [\mathrm{I}]) \\
\frac{\mathrm{d}([\mathrm{V}] \cdot V_{\mathrm{Main}})}{\mathrm{d}t} &= +V_{\mathrm{Main}} \cdot (\mathrm{alpha} \cdot [\mathrm{S}])
\end{aligned}
$$

2.3 Model Parameters

The parameters used in the COVID-19 transmission model diffrentials equations are given in the following table.

Model parameter name	Meaning	Case/Reference
alpha	Vaccination rate	0.04 per day [1]
beta	Contact rate	ASSUMED
gamma	Mean recovery rate	0.06 per day [2]
sigma	Incubation rate	0.09 [2]
p_d	Covid Fatality rate	0.0018 [2]

2.4 Assumptions

Needless to say, a few assumptions were made, in order to accomodate the COPASI model and provide basic but solid predictions. First of all, the human population is considered constant involving no natural deaths and births. Travelling from region to region is also not included in the general schema.

Regarding the transmission, human are the only vessels of the virus so no other pathogenic factors exist in the specific context. Moreover, there are no reinfections for humans that have already recovered or been vaccinated. Consequently, the latter gain full immunity once they have been vaccinated. Also, it is worth stressing that the rate of successful immunization by vaccination is not considered.

Some effects like seasonal effects, natural deaths or births have not been considered in this model, since their effect is not as crucial as the aforementioned. However, compartments or parameters like quarantine and reinfections may enhance the overall model performance and should be taken into consideration in future work.

3 Results - Discussion

The initial values used were S(0)=93000,E(0)=1000,I=100,R(0)=0,V(0)=0, D(0)=0. Figure 2 depicts the change in the populations as time increases from 0 to 90 days. During the first 5-10 days, the susceptible number drops noteably and as a consequence the exposed number is incremented accordingly. The fact that this fluctuations happens so abruptly is an early sign that this model may not be generalized successfully.

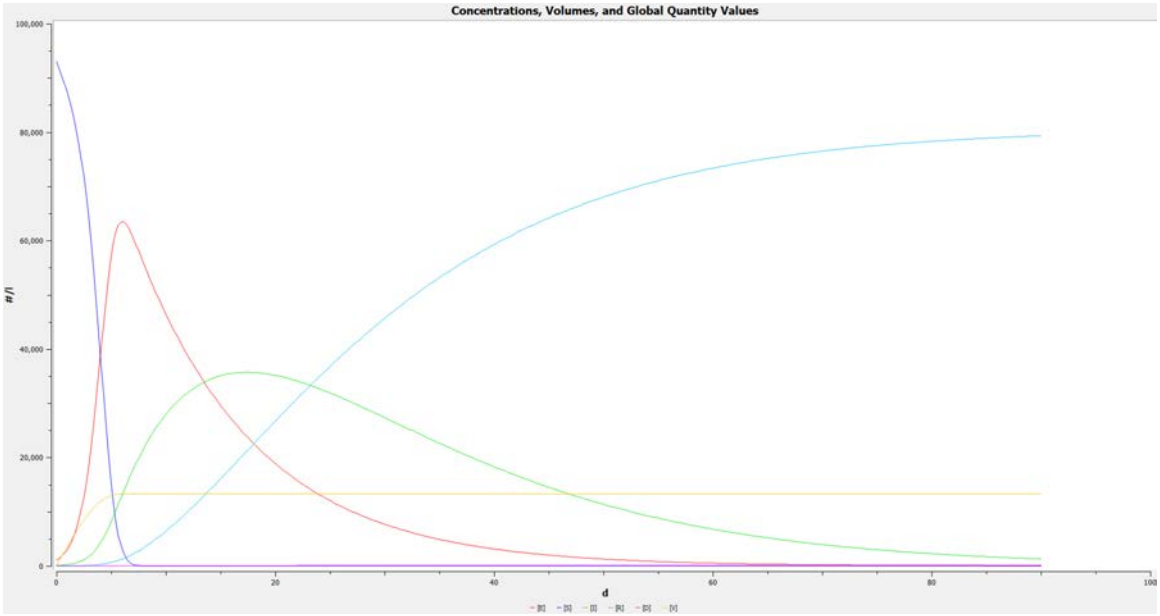

Figure 2: Results of *SEIRD-V* model for 90 days

3.1 Parameter Sensitivity

COPASI also allows the calculation of sensitivities of the model with respect to various parameters. Generally a sensitivity is a measure for how much a specific "observable" (this means any number that can be obtained by numerical analysis of the model) changes when a given parameter is changed.

In other words, the expected values of various parameters involved can be used to evaluate the robustness, i.e., 'sensitivity' of the results from these changes and identify the values beyond which the results change significantly. Sensitivity analysis identifies priority needs for improving knowledge. Indeed, this analysis reduces the uncertainties of the parameters of the assessment and then, decisions about the phenomenon under study can be taken.

Alpha
Alpha is the rate at which vaccinations are performed. Viewing figure 3, one can see that more vaccinations mean that a greater percentage of susceptible people gain immunity which results in flattening the curve.

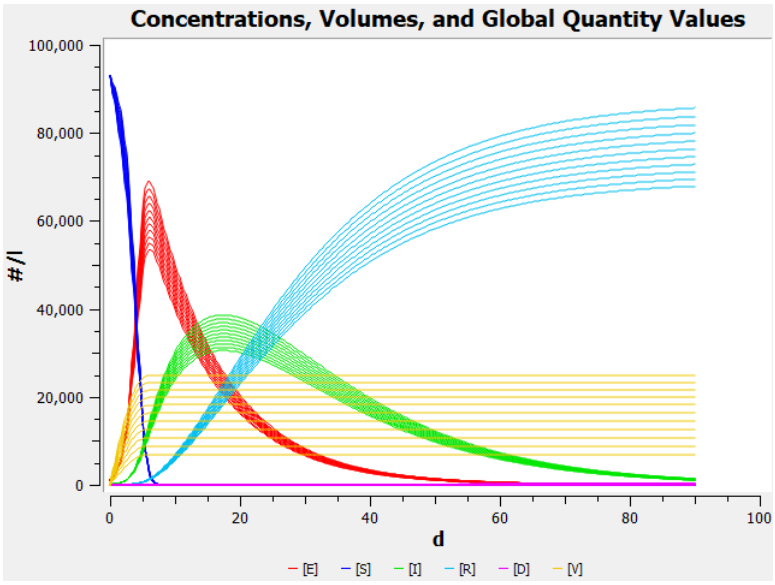

Figure 3: Sensitivity analysis based on **alpha** parameter

Beta

Beta is the virus contact rate. As it seems from the figure below, it affects mainly the initial spread of the virus while the other compartments also show some minor fluctuations.

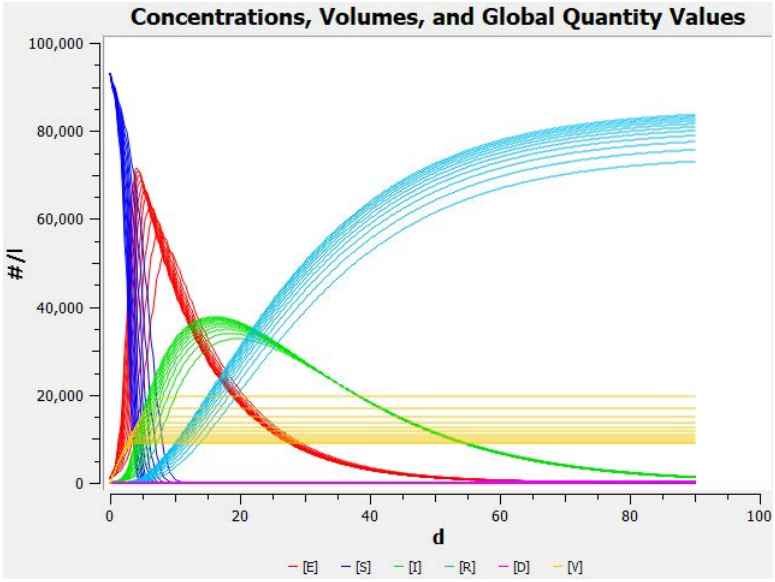

Figure 4: Sensitivity analysis based on **beta** parameter

Gamma

Gamma is the rate at which the infected people recover from the virus. The influenced compartments are obviously the *infected* and the *recovered*.

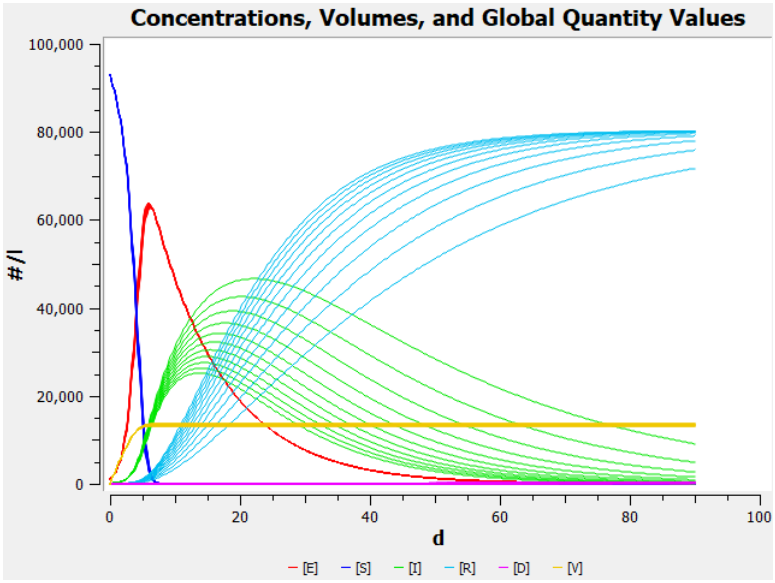

Figure 5: Sensitivity analysis based on **gamma** parameter

P_d

As suspected, the death rate from coronavirus, did not actually interfere with the sensitivity of the other parameters-compartments, since the population is constant and the reduction of it is inevitable in this model.

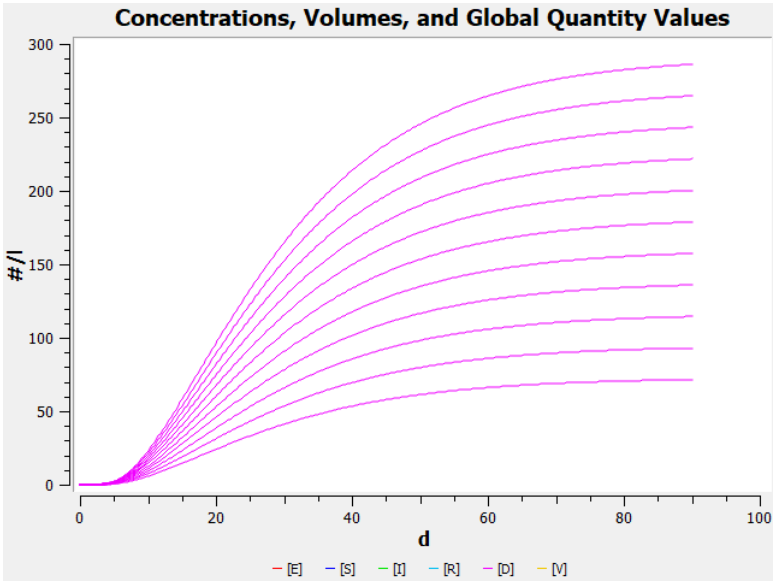

Figure 6: Sensitivity analysis based on **p_d** parameter

Sigma

Sigma is the parameter which denotes the incubation period, meaning the time in which the virus symptoms start to appear. Once, again this parametes affect the others considerably and especially, the *exposed* and *recovery* compartments.

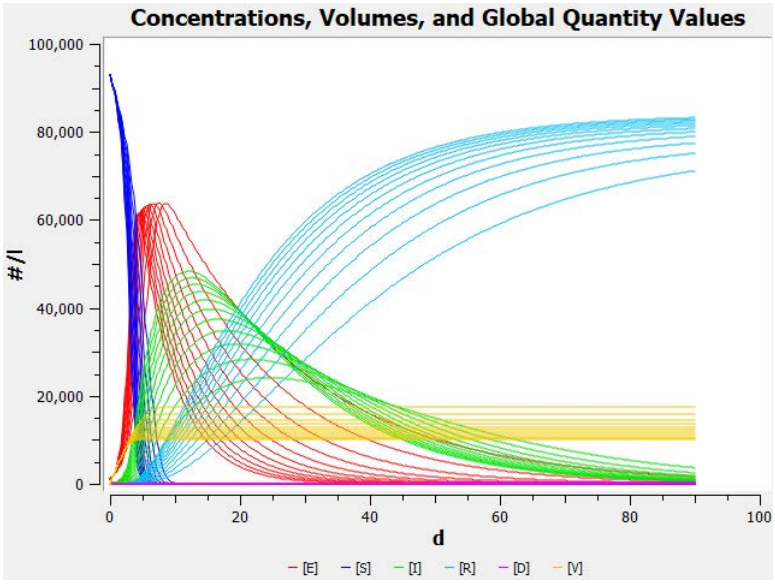

Figure 7: Sensitivity analysis based on **sigma** parameter

3.2 Prediction

The SIERD-V model was set to predict 90 days of the coronavirus spread in Greece since the first confirmed case was on 26 February 2020 when a 38-year-old woman from Thessaloniki who had recently visited orthern Italy, was confirmed to be infected. Figure 8 exhibits the confirmed cases during this first wave of the pandemic in Greece [1].

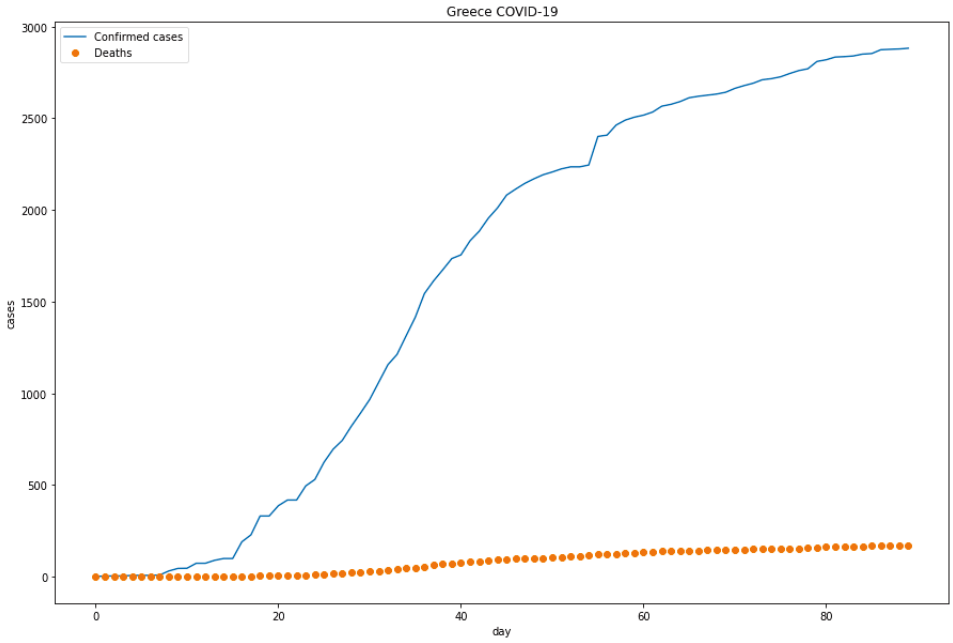

Figure 8: Confirmed cases and deaths during the first COVID-19 wave in Greece [1]

The SIERD-V results under the same circumstances provides some interesting insights as figure 9 suggests.

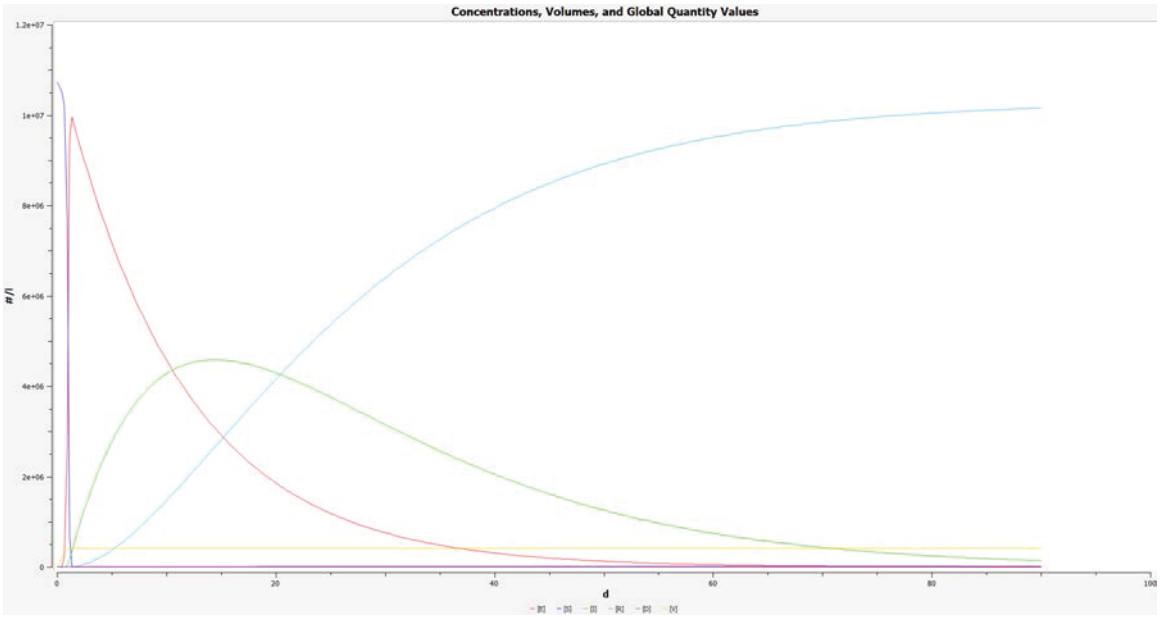

Figure 9: SIERD-V predictions for the first COVID-19 wave in Greece

Evidently, the proposed model failed to deliver a smooth initialization of the virus spread. Perhaps, this deviation from reality is due to the significantly different tested population number. Specifically, the initial population was 93.000, while the one set for Greece validation was 10.724.599, which is 10x times greater. Notice that the goal was to create a model that can be generalized to a broader set of regions, but this is not exactly the case in epidemiological models.

4 Conclusion

Previous studies have shown that more complex models may not necessarily be more reliable in making predictions due to the larger number of model parameters to be estimated [3]. Based on this, the proposed model SIERD-V in this project, may not be perfectly tuned and missing some basic factors-measures against COVID-19 like lockdowns-quarantine, but it is a great baseline to start with nonetheless.

In the predictability experiments, the model provided some encouraging results for long-term predictions, with a relatively small ensemble size, but for short-term it is quite inaccurate. Results, also, show that intensifying the vaccination campaign significantly decreases the number of confirmed cases and deaths.

All things considered, the uneven impact of COVID-19 in different types of regions and the territories mostly affected demonstrates the necessity of strategies for reacting to a possible forthcoming of infections that could be locally and regionally tailored, according to the needs of each region, with possible implementation of local containment and mitigation policies. The proposed model can serve as a baseline tool for health authorities to plan, prepare, and take such appropriate measures and decisions to control the pandemic.

References

[1] E. O.-O. Max Roser, Hannah Ritchie and J. Hasell. Coronavirus pandemic (covid-19). *Our World in Data*, 2020. https://ourworldindata.org/coronavirus.

[2] S. Mwalili, M. Kimathi, V. Ojiambo, D. Gathungu, and R. Mbogo. SEIR model for COVID-19 dynamics incorporating the environment and social distancing. *BMC Research Notes*, 13(1), July 2020.

[3] W. C. Roda, M. B. Varughese, D. Han, and M. Y. Li. Why is it difficult to accurately predict the COVID-19 epidemic? *Infectious Disease Modelling*, 5:271–281, 2020.