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A Hybrid Modelling approach for simulating the diffusion of COVID-19 and how it affects patient levels at healthcare facilities

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Abstract

COVID-19 is an infectious disease that has had a massive impact across the entire world and should not be taken lightly. Many countries have had immense increases in cases which have resulted in the collapse of healthcare facilities; consequently, leading to deaths due to unavailability of capacity for treatment of infected individuals. This report studies the diffusion of the disease along with its respective effect on accumulation levels of patients at healthcare facilities through the use of a real world hybrid model. The model itself makes use of a modified SEIR model that differentiates between regular and severely infected individuals which is used to feed agents (patients) into the second model which simulates patient flows within a hospital. The results obtained from experimentation highlighted the significant impact that changing the number of contacts has on the accumulation numbers at the hospital as well as the amount of deaths. The other results highlighted the lower impact of varying infectivity, and the approximate amount of beds required in order to avoid any casualties due to lack of resources.

Disclaimer

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List of Abbreviations and terms:

- SEIR: Susceptible Exposed Infected Recovered
- SIR: Susceptible Infected Recovered
- DES: Discrete Event Simulation
- SD: System Dynamics
- UMCG: University Medical Center Groningen
- RIVM: Rijksinstituut voor Volksgezondheid en Milieu
- SARS: Severe Acute Respiratory Syndrome
- MAE: Mean Absolute Error
- MSE: Mean Squared Error
- MAPE: Mean Absolute Percentage Error
- Python: high-level general-purpose programming language generally used for mathematical calculations .
- Vensim: System Dynamics modelling software
- Anylogic: Simulation Software for Business and Engineering Applications
- KPI: Key Performance Indicator



1. Introduction

As is well known, COVID-19 is an infectious disease which causes people to experience respiratory illness, among other symptoms; it can also vary its effects on patients who possess previous or recurring medical problems (WHO,2021) (Lai et al., 2020). This means that it is not a disease to be taken lightly, hence the need for governments to find ways to monitor its effects on population and its systems. To emphasize the severity of the situation, worldwide there have been 171,538,402 cases out of which 3,566,634 have resulted in deaths; on the other hand, the Netherlands has had 1,65 million cases and 17.623 deaths, this information is relevant as of the 1st of June 2021 (WHO,2021). The number of cases is seen as quite troublesome when comparing them to the country's population of roughly 17.162 million people (Worldometer.info, 2021). Additionally, concern arises from the amount of cases due to its effect on the amount of people requiring treatment at hospitals, specially during infection peaks. Thus, the Dutch Government wishes to better understand the propagation of COVID-19 in order to have a clearer overview of the hospital capacity management. The end goal is to be able to make informed decisions in accordance with the results and try to avoid the collapse of the healthcare system. The focus of the research will be on the north of the Netherlands; More specifically in the province Groningen, where the UMCG is the main intensive care treatment facility for patients who are suffering from severe cases of COVID.

Given the evident need of exchanging information between the different models the most ideal way to assess the situation would be through the construction and use of a hybrid model. This model would use different modelling techniques in order to capture the appropriate behaviours of the different scenarios being studied. According to Mustafee et al. (2017) Hybrid simulation consists of performing simulations that run under the use of at least two modelling methods, which include either System Dynamics, Discrete Event or Agent Based Simulation. It has been argued that multiple methodologies together have the potential to provide a more complete way of dealing with complex real world phenomena. The research being carried out focuses on the disciplines of System Dynamics and Discrete event modelling working together. Additionally, The combination of these two types of models provides accurate results while running under less assumptions (Chaha et al. 2013). To elaborate more on the individual models themselves it is worth noting that the diffusion of the disease will be modeled through the use of System Dynamics; more specifically, an SEIR model will be adopted in order to produce the most accurate results possible. This model will run



under real time data provided by the Dutch governmental websites. On the other hand, the Discrete event modelling will be applied in order to simulate the flow of patients within the COVID-19 healthcare facilities at the UMCG. Both models together will simulate the propagation of the disease throughout the population, and how the amount of interactions between individuals affects the number of infected, and severely infected individuals. The severely infected individuals are those who then are considered as requiring treatment and thus are fed into the DES model in order to simulate the treatment process they must go through in order to recover, and or possibly perish. Overall, this model will provide insights on the infected population over time and the occupancy of beds within the treatment center.

The following sections of this paper will be divided in the following manner. First, some background information is provided in order to give additional context to the reader for the following sections, also including a brief introduction into the stakeholders of the system. Secondly, the Methodology section is elaborated, by providing a conceptual model and framework as an overview of the system to be modeled; as well as, elaboration on the individual models, their connections, and how they are calibrated in order to produce the desired results. Lastly, experiments with varying scenarios are executed in order to produce a set of results to be able to analyze and act upon.

2. Problem Formulation

This chapter introduces the objective and research questions, therefore giving insight on how the problem is looked at and tackled. Additionally, it introduces the individuals or stakeholders involved within the problem setting.

2.1 Research Objective

The aim of this research project was to create a real world hybrid model within eight weeks that closely simulates the behaviour of the COVID-19 pandemic in the Groningen province in accordance to the data on the RIVM website; and allows the government to take action to avoid patient admissions from surpassing the capacity within the COVID Center at the UMCG. The model should provide insight on the effectiveness of the healthcare facility to treat incoming patients; and also on whether the facility has enough resources to manage the workload.



2.2 Research Question

-How can the real world Covid-Hospital model be built in order to replicate the Covid-19 propagation within the province of Groningen, and consequently provide insight on patient accumulation levels within the Hospital?

2.3 Stakeholders

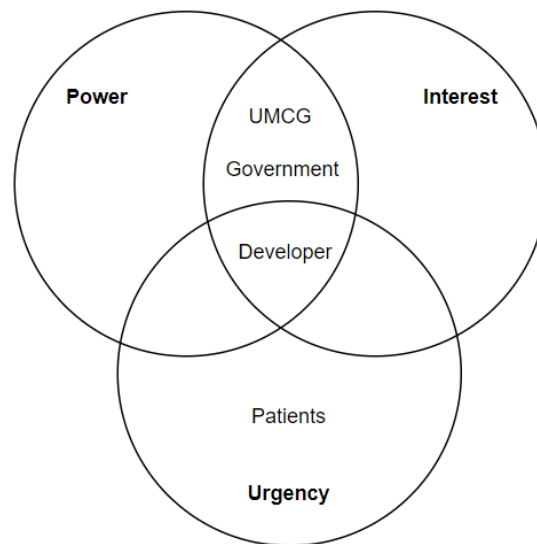


Figure 1: Stakeholder Venn Diagram

Developer

The developer has Power given that he is given the freedom and tools to create the desired model and can execute it based mostly on criteria established by himself. Interest comes from wanting to deliver a robust model to the Government and to the UMCG. Lastly, urgency is due to the fact that the developer still has to meet certain requirements set by the UMCG as well as the Dutch Government in order for the project to be considered successful.

Government

They have power given that they are the ones who are deciding what they require, and what they want to achieve with the model. Their interest on the other hand arises from their necessity to further understand the ongoing pandemic, and to try and avoid having a collapsed healthcare system, and so they can preserve the lives of their citizens.



Hospitals

Hospitals have both Interest and power given that this model can provide them with insight on how many people they can expect to be receiving treatment for COVID-19. This would allow them to better manage the resources they have; Thus, helping the system to avoid total collapse by anticipating envisaged situations and avoid potential casualties. They also have power given that they can provide important information for the modelling process.

Patients

Patients only have urgency given that they are the ones interested in receiving quality treatment in time. If this is possible then they have higher chances of recovering from the virus.

3. Background Literature

This section provides some background knowledge extracted from literature in order to give some basic understanding on the concepts required to tackle the problem through the use of modelling. Moreover, this section also elaborates on the different kinds of modelling disciplines available for use in Hybrid modelling and how they have been used to take on similar projects in the past.

3.1 Transmission and Prevention of the Disease

As it was mentioned before, the virus in question is the one of the ongoing pandemic COVID-19. To become infected with the virus one must come into contact with many particles in order for it to take effect on the individual. This is mostly due to the fact that the human body has many lines of defense against said viruses such as the skin in first instance and secondly the individuals immune system (RIVM, 2021). From this information it is possible to deduce that maintaining oneself in good health and well nourished can go a long way in creating protection against the virus. Additionally, it is worth noting that according to the RIVM (2021), infected individuals produce millions of copies of the virus within their bodies which can mainly be found either in the lungs or in the ‘moist’ parts of the body such as the mouth, throat and or nasal cavity. It can then be deduced that because of the location of the virus sneezing or coughing can produce an expulsion of droplets into the environment which can then infect individuals



who come in contact with them. Due to this certain measures are then taken in order to reduce the risk of spreading the disease amongst the population. The basic rules imposed by the Government of the Netherlands (2021) are as follows: wash your hands thoroughly and regularly, stay 1.5 meters away from others and if someone has symptoms they should stay home and get tested. Additionally, the government has attempted to control the number of contacts between the population, by fluctuating the number of suggested contacts per day throughout the pandemic. As of the most recent update for COVID Measures, the government has increased the number of contacts per day by changing the number of visitors to a household from one to two and also by allowing individuals to meet up in terraces for restaurants (Government of the Netherlands, 2021). From this information, it is possible to deduce that the number of contacts per day would be between three to five at its maximum. It is also worth mentioning that the use of masks is more than recommended and is mandatory while inside confined spaces such as stores, pharmacies and supermarkets.

3.2 Patient Flow within Hospitals

Flows generally refers to the movement of people, equipment and/or information; however, in healthcare it specifically focuses on the movement of people (Health Foundation, 2013, as cited in Leviner, 2019). Logically speaking a good flow is important in order for healthcare facilities to be able to provide the best treatment and care for their respective patients at any given point in time. According to Leviner (2019) an optimal flow allows for minimal waiting times, and often happens when the supply of resources matches the demand; additionally, an optimal flow allows for improved patient safety, overall outcomes and satisfaction. On the other hand, from the information above it is possible to note that if an optimal flow is not created then healthcare facilities will not be able to treat patients due to crowding generated by a lack of organization and use of resources. Moreover, a poor flow can eventually lead to delays in treatment and also crowding or congestion (Leviner, 2019). Due to the way in which COVID spreads between people it is highly important to avoid crowding in these facilities in order to avoid additional and unnecessary new infections. The Flow to be utilized in the DES model elaborated below consists of having patients request treatment, have them wait in a queue until a room (bed) becomes available, followed by the respective treatment, and then exiting the system either recovered or diseased.



3.3 Simulation Methods and Modelling

There are a wide variety of separate modelling techniques utilized for modelling real world disease propagation and pandemics, the most common being the mathematical model behind the common SIR mathematical model (Ng, Turinici and Danchin, 2003). This model however is considered to be quite outdated due to its exclusion of a variety of aspects present in reality. Additionally, this model on its own would only be able to provide insight on the disease's diffusion and would not be able to predict differences between regularly infected or severe patients, rendering it useless for modelling the studied scenario. On the other hand, the hospital capacity management/flow of patients has a possibility to be modelled through softwares that allow its users to work with flow models with Occupancy management and planning packages such as the one used in Millard et al. (2001). This modelling program could then be used in order to compute the occupancy of beds by patients and find the best fit between the exponential equations and the distribution of the length of stay through least squares. This method also seemed to be in line with the second scenario to be modelled; however, has the shortcoming of not having the ability to directly connect to the diffusion model, making it less efficient to work with and thus discarding it as an option as well. Due to the downsides of the aforementioned methods, Hybrid modelling is applied in order to capture the respective behaviors of diffusion of the disease and patient flow. To construct and understand a proper Hybrid model it is important to assess the options available for modelling the different scenarios. The first model to be discussed is the one related to the propagation of the disease. The first model to be considered was the original (System Dynamics) SIR model utilized back in 2003 by researchers in order to model the previous SARS disease. The common SIR model consists of three distinct classes: the susceptible, the infected and the recovered (dead included) (Ng, Turinici and Danchin, 2003). However, as it can be seen by the date of publication and also by the different assumptions used to run simulations with this model, it can be determined that a more complete model should be considered in order to produce the best results. As a result of the SIR model being too simple a more recently updated model such as the SEIR was chosen in order to produce the best possible simulation of the situation (Abou-Ismaïl, 2020). This model differs due to its further elaboration on the aforementioned one by adding an extra stock which specifically measures the amount of exposed individuals. Moreover, the susceptible population also takes into account births and deaths from other causes in the susceptible stock, and additionally, a main



difference is that in the infected stock (category) takes into account the natural death rate as well as the virus induced average fatality rate (Carcione et al., 2020). The equations introduced in Carcione et al. (2020) will be elaborated on within the modelling section of the report. Additional insight on this approach can also be found within the article of Zhou et al (2020) in which a Hybrid modelling strategy is used based on the tessellation structure configure SEIR model, which is used to estimate the scale of the pandemic spread. Agent Based modelling is generally used to approach problems with complex systems in which agents interact with each other and with their environment using simple local rules (Bazghandi, 2012). Agent based modelling could have also proved to be helpful in modelling diffusion of the disease as it has also been previously used for this in other cases, for instance in the modelling of Cholera (Augustijn et al., 2016). The modelling technique however, proves to have some limitations when modelling certain situations. These types of models have the limitation that they need to be at a specific level of description, extensive simulation with them causes performance drops, and most importantly agents are generated and modelled individually. For these reasons and due to the number of individuals involved in the simulation the choice for the SEIR modelling technique will be System Dynamics. After finding a suitable model to simulate the propagation of the disease it was essential to then find the best modelling approach and consequent model to best simulate the flow of patients through a hospital. The remaining modelling method is DES which can be used in order to keep track of the state of a system as time progresses, the state more specifically refers to the conditions or status of the system at a certain point in time (Jacob, 2013). This means this modelling technique can indeed be used in order to model the flow through the healthcare facility. To emphasize this point, according to Best et al (2014) discrete event simulation can be used to estimate how certain changes to complex healthcare systems (e.g. Hospitals, Emergency department) affect its operational performance (e.g. Capacity management).

4. Modelling

This section includes both the Conceptual framework and model to provide a clear overview of the stages required to execute the research project, and of what is to be included in the respective models. After these are introduced, the models are explained individually alongside their respective calibration processes. The section closes off by explaining how the Hybrid model works and how its validity was tested.



4.1 Conceptual Framework

In this section a conceptual framework is provided in order to further understand the different stages one requires for executing research using hybrid simulation. To build the respective framework the method explained in Brailsford et al. (2019) as cited in Huisman (2021) is used as a reference; In this paper the main stages described are the real world problem, the conceptual model, the computer model and the solution and its understanding. Within the current project, the real world problem relates to controlling the number of cases in the province of Groningen in order to reduce the spread of disease as much as possible and consequently decrease the number of hospital admissions (Severe patients). The conceptual model is depicted below in order to visualize the overall idea of what is to be expected from the hybrid model. Moreover, this conceptual model also provides insight on how the models are interconnected and what information is exchanged between them. Then, the model described within the conceptual model will be introduced into the Anylogic software where the models are then linked to each other and can be experimented upon. However, before both models are connected to each other it is important to run them through a calibration process separately in order to assess the quality of their outputs. Then, after they are interconnected, additional calibration and experimentation can proceed. As it was mentioned before, the different scenarios will be analyzed and studied in order to reach a comprehensive understanding of the situation. The figure below shows how each of the different stages is composed (Figure 2).

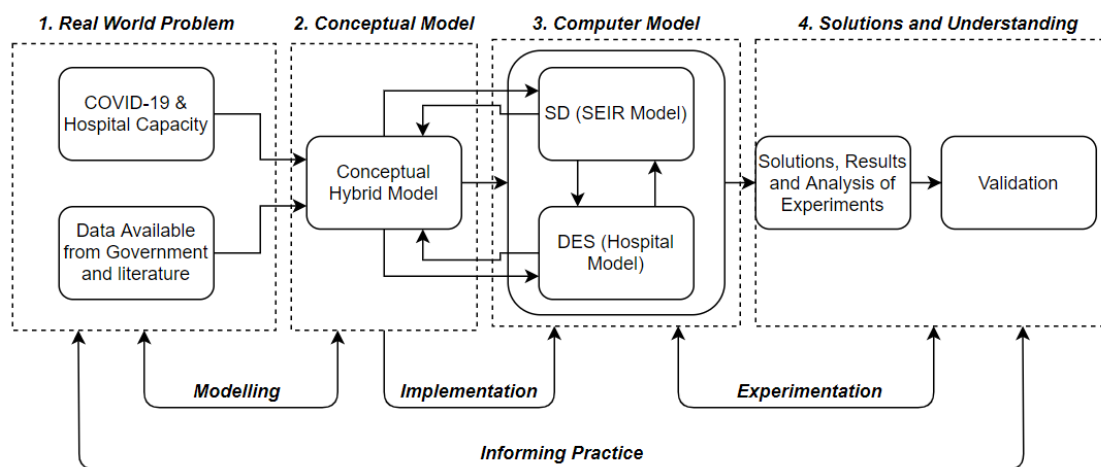


Figure 2: Conceptual Framework based on Brailsford et al (2019) theory



From the figure above (Figure 2) it is possible to observe that the process is iterative and goes back and forth between stages in order to produce the best outcome in each one of them. First of all, modelling is done through the evaluation of the real world problem and can be visualized through a conceptual model, information goes back and forth in order to have a model which includes all of the relevant aspects to the problem. After the model is conceptualized, its implementation can occur within the preferred software; in this software the models are built and calibrated. Then, after the models are built, multiple iterations of testing can be executed in order to partake in the process of experimentation. Afterwards, from the solutions it is possible to conduct informing practice. Validation and verification of the conceptual model, the model, the scenario and the situation also occurs in between the stages respectively.

4.2 Conceptual Model

Below is the conceptual model (Figure 3) in which the hybrid model is briefly described and introduced visually. As it was mentioned earlier, the hybrid-model models the propagation of the disease and how this affects the influx of severely infected patients going into the healthcare facilities (UMCG). The model on the top represents the SEIR model (*System Dynamics*) in a simplified manner, making the inclusion only of the main stocks of the system (Susceptible, Exposed, Infectious, Recovered). From the SEIR model it is possible to see that it differs from the conventional model by separating the infectious and severely infected individuals. This fraction of severely infected individuals is then fed into the hospital model, where said individuals become agents (Patients) in the DES model where they proceed to requesting treatment at the facility. The second model (*Discrete Event*) models the flow of patients through the UMCG, where they arrive when requesting the treatment, followed by a waiting period, then examination, followed by the respective treatment, and lastly the individuals either leave the system as treated (Recovered) or treated (Diseased). The DES model then feeds the recovered individuals back to the SEIR model, adding the number of recovered patients to the recovered population stock. In the figure below (Figure 3) the simple arrows represent connections between the different sections, and the one with the rhombus in the middle represents flows in the stock and flow (SD) model.

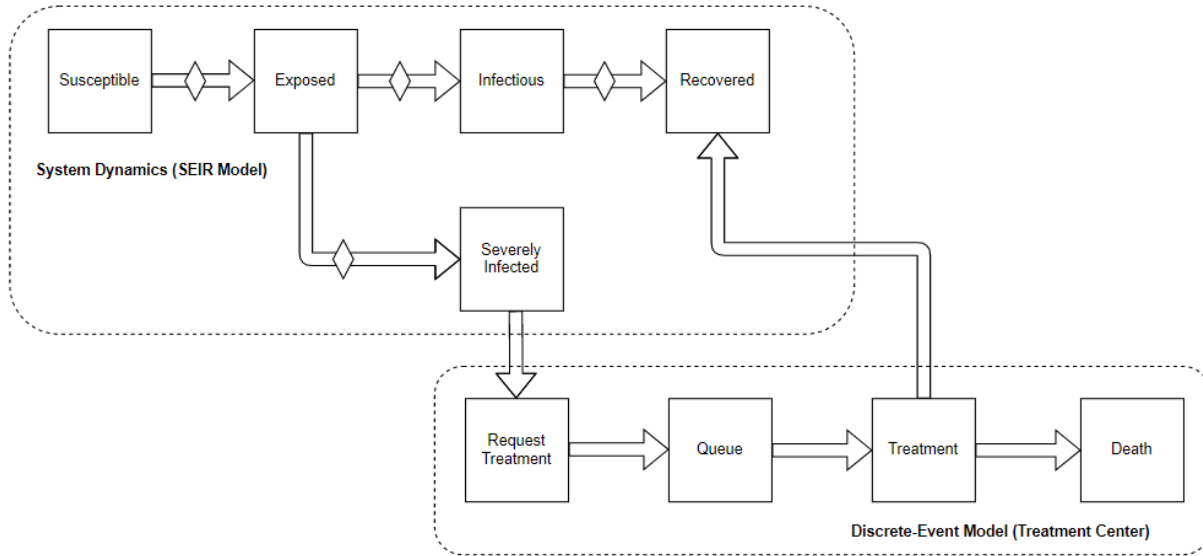


Figure 3: Conceptual Hybrid Model

4.3 SEIR Model (System Dynamics)

This model is used to represent the propagation of the Disease within the province of Groningen. The equations will now be explained in order to provide further understanding on how the model works (Carcione et al., 2020).

$$\begin{aligned}
 S' &= \Lambda - \mu S - \beta S \frac{I}{N} \\
 E' &= \beta S \frac{I}{N} - (\mu + \epsilon) E \\
 I' &= \epsilon E - (\gamma + \mu + \alpha) I \\
 R' &= \gamma I - \mu R
 \end{aligned}$$

In the equations above the parameters are defined as follows in accordance to Carcione et al. (2020):

- Λ : Per Capita birth rate
- μ : Per Capita death rate
- α : Virus Induced average fatality rate (Excluded from model due to its inclusion within the hospital model)
- β : Probability of disease transmission per contact times the number of contacts per unit time
- ϵ : Rate of progression from exposure to infectious



- γ : Recovery rate of infectious individuals

The first equation represents the Susceptible population, it takes into account the incoming natural birth rate and subtracts the outgoing natural death rate and rate of disease transmission per contact. In this specific instance, the natural birth and death rates are ignored from all equations due to the simulation time as well as the lack of province specific information; additionally, these rates would also prove more significant and or helpful when modelling the entire population of the Netherlands instead. For clarity μ and Λ can be omitted from the equations (equal to 0). The second equation subtracts the rate of progression from exposed to infectious from the incoming rate of disease transmission per contact. There is a slight difference in the model built for this scenario due to the fact that it splits the rate of progression into progression from exposed to infectious and progression from infectious to severely infected. The equation would therefore look as follows instead:

$$E' = \beta S \frac{I}{N} - (\epsilon)E - (\epsilon \cdot \omega)E$$

In this equation, ϵ represents the reciprocal of the incubation period, and ω represents the percentage of severe cases in the province of Groningen. Additionally, there is a fifth equation due to the differentiation between infected and severely infected that can be described as follows:

$$SI' = (\epsilon \cdot \omega)E$$

The third equation represents the infected population and takes into account the incoming rate of progression from exposed to infected, and subtracts from it the recovery rate. Lastly, the fourth equation represents the recovered individuals and only takes into account the incoming recovery rate. To give some additional information regarding the flows of the model the first one (SE) relates to going from Susceptible to Exposed, which is computed by multiplying the fraction of the population susceptible times the Beta variable which represents the probability of transmission per contact. The second set of flows leave the Exposed stock and either feed into the Severe (SI) or the Infected (EI) stock; both flows are computed similarly by taking the value of Exposed individuals and dividing it by the incubation period. The only remark to be made in this instance is that the ES flow also takes into account a percentage multiplier to correctly simulate the amount of severely infected individuals. The final flow Infected-Recovered (IR) takes the infected individuals and divides them by the duration



of the disease. After the models are interconnected, the recovered stock will also take into account the incoming recovered patients from the DES model. In the appendix (Appendix 1), a visual representation of the model can be observed .

4.3.1 SD Calibration (Verification & Validation)

Verification

The model in question is the System Dynamics SEIR model with an extra compartment taking into account that a percentage of the exposed individuals have a chance of becoming severely infected. In order to know whether the model was built properly some verification is required in order to determine whether the output of the model matches the theoretical dynamics of the original model it is based upon. For verification purposes the data used is the one used for testing in Carcione et al. (2020). These numbers include a population of 10 Million, Beta is 0.75/day, and the Initial stock values are $S = \text{Total Population} - \text{Exposed} - \text{Infected}$; $E = 20000$, $I = 1$ and $R = 0$. The severely infected population information is not available for this research and thus will be multiplied by 0 for verification purposes and will be included only for the validation. Verification and Validation is done in Vensim for ease, which is a software for SD modelling. The Graphs displayed below represent the results obtained from inputting the aforementioned values into the model and the other is the one obtained by Carcione et al. within their research paper.

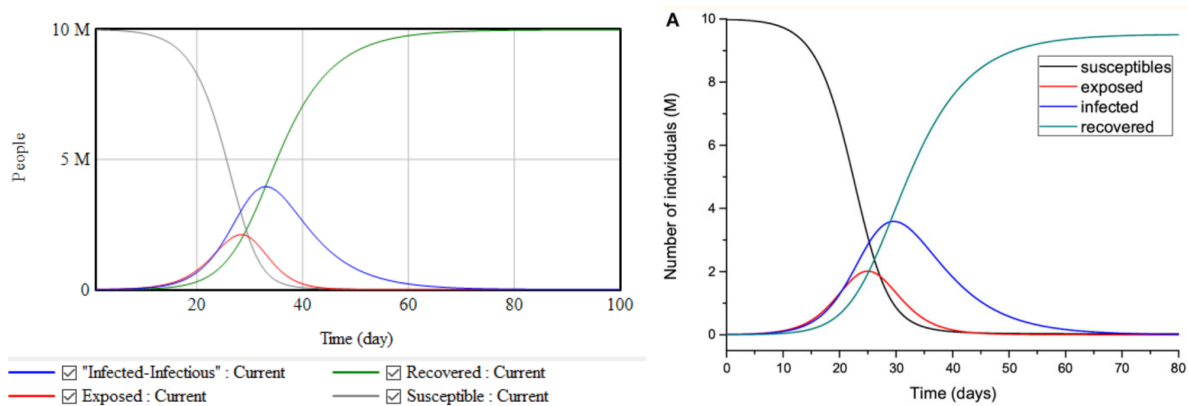


Figure 4: Graphs of SEIR model Behavior, Constructed and one provided in theory

As it can be seen from Figure 4, the model behaves as intended and both graphs display the same maximum number of infected individuals, which is around the four million



mark. It is worth mentioning that if the severely infected population were to be taken into account from the aforementioned case, healthcare facilities would be considerably overwhelmed. For instance, assuming only a small fraction of the population gets infected (1%-5%) severely yields between 40000- 200000 individuals which would most definitely be too much for healthcare facilities to handle anywhere in the world.

Validation

Information from the province of Groningen was obtained from the RIVM (2021) website; the period of time in discussion is the most recent peak which was between the 1st of February until the 21st of February of 2021. The initial number of infected individuals to begin with is equal to 136. The first recorder value for cases per day is 25 and the last recorded number is 64 and will be used as a reference point in order to calibrate and evaluate the models accuracy with respect to real life. It is also worth mentioning that the model follows the current set of rules established by the Dutch government which specify only two contacts per day with other individuals and the infectivity rate is adjusted in order to best fit the available figures. Additionally, and also in accordance with the information provided by the RIVM (2021), the incubation and duration of the disease are taken as the averages 7.5 and 14 days respectively. In accordance with the method elaborated on Ala'raj et al.(2021), the MAE and MSE are computed alongside MAPE for additional insight on the accuracy of the results. The formulas for each of the errors are the following:

$$MAE = \frac{1}{N} \sum_{t=1}^N |y(t) - y'(t)|$$
$$MSE = \frac{1}{N} \sum_{t=1}^N (y(t) - y'(t))^2$$
$$MAPE = \frac{100}{N} \sum_{t=1}^N \frac{|y(t)-y'(t)|}{y'(t)}$$

In the formulas depicted above, y represents the actual data and y' represents the modelled values. It is also worth mentioning that these formulas will be used to assess the infected individuals (i.e. Cumulative cases) and the recovered are excluded given the lack of real life information regarding the value of this stock of the population. From the data obtained from the model, the data from the RIVM (2021) and using the following parameters (Table 1), the different errors were computed as shown below (Table 2):



Table 1: Model Parameters

Parameter	Value	Source
Number of Contacts	2	RIVM (2021), Calibration
Probability of Disease Transmission	0.0808239	Calibration
Initial Exposed	181	Calibration

The method in question to evaluate the model is the least squares method which is more thoroughly explained in the works of Miller (2006) in which it is stated that this method is a procedure to best fit a line to available data using linear algebra and calculus. The general formula for the method is as follows:

$$E(a, b) = \sum_{n=1}^N (y(n) - f(x(n), b))^2$$

In this specific case $y(n)$ relates to the observed values in reality and $(fx(n), b)$ represents the previously introduced y' which relates to the modelled values. The end goal of the method is to find a value of b that minimizes the sum of the squared residuals. In other words the MSE must be computed and minimized in order to obtain the best possible fit.

Table 2: Calculated Error Values

Type of Error	Value
MSE	78.88
MAE	6.9
MAPE	29.45%

The method for optimization was executed within a script constructed in Python, where the minimization of the error function yielded the results available in table 1. The method utilized the actual information available within the RIVM website and the values produced by the SEIR model on Vensim in order to find the best possible fit to the data. The theory and pseudocode behind the methods can be observed in the PySD Cookbook (2015). From the errors above (Table 2), it is possible to deduce that the



model does not resemble reality as closely as can be desired in terms of the number of the infected individuals per day; However, in this instance the amount of deviation between the numbers comes down mostly due to the fact that the RIVM website updates the number of cases per day based on the testing done as results come out rather than on the day the test was done. Due to this certain days deviate much more than others and thus create outliers within the data and increase the error by quite a big margin. Nevertheless, the values prove to be promising considering that through the first iterations of testing the model with an approximation value which yielded an MSE of around 400 and a MAPE closer to 40%. Additionally, the model currently does simulate the number of cumulative cases quite closely within the given time frame; the number of cumulative cases in reality is 684 within 21 days and the model predicts 693 within the same time frame, below is an image (Figure 5) displaying the cumulative cases over time.

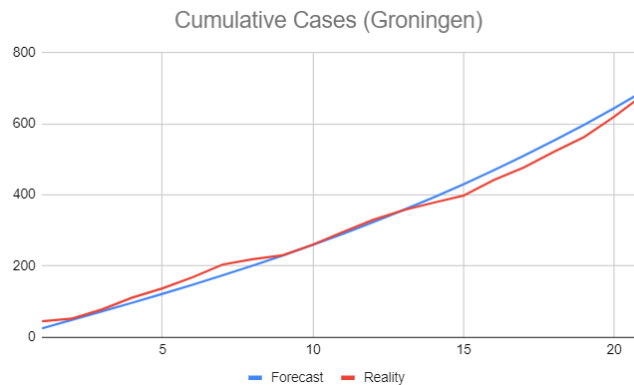


Figure 5: Cumulative Cases in the province of Groningen over time (21 days)

4.4 Hospital Model (Discrete Event)

Discrete event modelling is used in this project in order to simulate the flow of patients within a treatment facility (UMCG). The model to be described in this section is loosely based on the conceptual model created by Best et al. (2014); the model describes the flow of patients through an acute care hospital in Ghana. The model consists of a series of stages through which patients go through in order to be treated and eventually leave with the desired treatment. The flow of the patients through the model is as follows:

1. A source is fed incoming agents (patients) who require treatment for COVID-19.



2. The model then introduces the patients into the facility and redirects them to a queuing process after which they are registered for an introductory examination process.
3. After they have been registered the patients are then moved to a waiting room.
4. As an examination room becomes available, the patients are brought in for an introductory examination in order to assess the conditions of the patient. It is worth noting testing is not required as it is assumed that the patients entering the hospital have gotten tested and their symptoms worsened before arriving.
5. There is a queue present before the upcoming section in order to control the amount of people within the COVID facility at the UMCG which has a hypothetical limit of 28 patients.
6. If the restricted area is then free to receive patients, a room(Bed) is seized from the existing resources and the patient is moved into the treatment facility.
7. The patient then goes through the treatment process which has a triangle delay set up in the following manner (Treatment time*0.9, Treatment time*1.1, Treatment time). This is done as so due to the variable being stochastic and not deterministic. After this process is finished the seized resources are released.
8. The next step the model takes is to differentiate between the patients who exit the treatment as recovered or diseased in which the chances are 0.999 and 0.001 respectively according to local data.
9. Depending on the state the patient leaves the system they will either be accumulated within the recovered exit; or they are accumulated within the Treated Diseased exit (Morgue).

4.4.1 Calibration

Below is a table (Table 3) providing all of the separate values pertaining to the hospital model and their respective sources, followed by an explanation of the values themselves.

Table 3: Values for the Hospital DES model

Parameter/Variable	Value	Source
Number of Beds	28	Assumption
Treatment Time	11.5 days	CDC (2021)
Percentage Recovered	0.99982	RIVM(2021)



Percentage Deceased	$1.8 \cdot 10^{-4}$	RIVM(2021)
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To further elaborate on the models behaviour, values, and assumptions; firstly, there is a the fact that if the restricted area is overflowed with patients, then patients not allowed to enter (in queue) have a certain amount of time before they too perish considering that they do indeed require treatment before respiratory failure occurs. The limit of people within the restricted area is loosely based on the findings of Deschepper et al. (2021) in which it is stated that most of the European countries possess around 11.9 beds per 100 thousand inhabitants. Given the population of the province of Groningen this adds up to 28 beds in total. Secondly, the model's treatment time is based on information from the CDC (2021) who stated that the treatment time for patients introduced into hospital care is between 10-13 days, which explains the choice of delay type as well. Lastly, the model possesses a select output item after treatment, where the patient can either exit as recovered or diseased, the percentages in this selector are based on real data from the RIVM (2021). The amount of diseased in the province of Groningen throughout the pandemic equals to 45 out of 250000 meaning that 0.018% of the population perished as a result of COVID and 99.982% of individuals recover and or have not been infected. This model can be seen in Appendix 2.

4.5 Hybrid Model

This section will further elaborate on the interconnectivity between both the SD and DES model. The models are connected in a way in which they feed each other agents (patients/recovered individuals) in order to closely simulate how the processes of diffusion, treatment and recovery occur over time. The first connection between the models comes from the stock named Severely Infected Individuals which was elaborated on in the section for the System Dynamics SEIR model; this connection is made possible through the use of an event and a parameter, which takes the number of severely infected individuals at a certain point in time and add them up in integer form in order to be able to feed them into the DES model. It is worth mentioning that the event only feeds the infected individuals into the hospital model within a certain interval of time. This can be changed depending on what assumption is made with regards to how quickly patients show up at the treatment facility (UMCG). The other connection consists of feeding the recovered individuals from the DES model back to the SD model's recovered stock in order to maintain the dynamics of the model as accurately as possible. This is done through the use of the action function within the sink named



“RecoveredExit“ where every time a new agent enters it a recovered person is added to the Recovered stock . Additionally, a separate stock will not be created in order to count the number of individuals who are diseased as a result of the treatment not being successful due to them already being accumulated in a sink block in the hospital model, where they can be visualized with ease. The model also counts the amount of diseased individuals due to a lack of capacity for treatment in a separate sink within the model. It is also worth noting that the model runs under the assumption that only individuals who are severely infected can perish, and everyone who is only mildly infected will go through a regular recovery process at home. Another way to make the Hybrid model more accurate would be to add a feedback loop into the susceptible population where the recovered individuals become susceptible to the disease after a certain period of time. This last loop is only included if the model is run for more than half a year given that if this is not the case the loop is irrelevant as the individuals would not have gone through enough time to become susceptible again. The hybrid model can be observed in Appendix 3.

4.5.1 Calibration of the Hybrid Model

The calibration of the Hybrid occurs under the same time frame as the one used for the Calibration of the SEIR model above. The data from the first 21 days of the month of february are used in order to be able to replicate the behavior observed in reality. This reality is quantified within the RIVM website where a wide range of province specific values are available which prove helpful when comparing the ones produced in the model with the ones from reality. The SEIR model produces the same results as were described above; however, now the severe cases stock is not ignored in order to be able to produce agents (patients) for the hospital (DES) model. The DES model is also running on all of the parameter values found within sources that were explained in section 4.4.1. The data intended to be replicated by the model according to the RIVM (2021) is that the number of admitted patients within the 21 day time frame has to be equal to 27, and the number of casualties has to be equal to 0. When trying to replicate said figures the final parameter which relates to the percentage multiplier of people who become severely infected was found to be equal to 0.038 (3.8%). This figure of 3.8% is considerably close to the one reported by the CDC (2021) which is equal to 5%, meaning that this figure can be considered realistic. When using this value in simulation the results obtained do indeed resemble reality as a whole, leading to the conclusion that the model is now calibrated fully and can be used to run the different experiments. The following section will elaborate more on how the model is used in practice.



5. Simulation

This section relates to the experiments to be done in order to produce results from the constructed Hybrid model. It elaborates on the test scenarios to be executed in order to produce relevant results & conclusions.

5.1 Description of the Experimentation Process

As it was elaborated in the objective and the research question the main focus and or purpose of the research project and consequently the model is to find a way to control the amount of patients entering healthcare facilities over time. In order for the number of patients to be at a desirable level it is important to first control the propagation of the disease itself, which is represented in this instance through the use of a SEIR model. The objective function of the model within the testing scenarios will revolve around maintaining the number of exposed individuals as low as possible over a designated period of time. However, scenarios revolving around worst cases will also be used in order to assess the capability of hospitals to treat incoming patients. The objective function can be represented as follows:

$$E = F(x, \beta)$$

Where E represents the Exposed stock, and F(x) represents the function/equation within the stock that causes the values to fluctuate over time; additionally, Beta plays a role within the increasing or decreasing of the stock's value through the influence contacts per day and probability of infection per contact (the varying parameters within the SD model). From this function, it is possible to note that any test scenarios must revolve around the variation of the parameters of the SD model, in order to produce different outcomes from which conclusions can be drawn. Additionally, it is worth noting that through the use of this hybrid model, it will be possible to determine the amount of resources required within the hospital in order to manage more critical situations such as additional waves, and or different strains of the virus. The main key performance indicators utilized to assess the scenarios are the number of deceased individuals as a result of a lack of treatment and the percentage of the usage of beds over time.



5.2 Description of Simulation Scenarios

The different scenarios to be described in this section will be executed utilizing the parameter variations function within Anylogic in order to be able to produce multiple replications of each of the described scenarios. The experimentation process consists of four different scenarios, each of them relating to different combinations of changes within the two selected parameters; each base scenario runs 80 replications in total, 10 for each iteration. Moreover, for the second set of scenarios 72 iterations are run with 10 replications each (720 replications in total).

The first scenario relates to the easing of the COVID-19 measures established by the government, which were previously introduced in the background information section. More specifically, this scenario relates to increasing the number of contacts per day between people due to the decreasing amounts of patients entering hospitals as well as the decrease of general cases per day. The aim of this specific scenario is to predict the impact of easing said measures and to observe if hospitals have the capacity to handle a sudden increase in patients as a result. The second scenario relates to the appearance of a possible mutation of the virus in which the probability of infection per contact increases due to the higher infectivity of the new strand. The variation of parameters will be between the base value of 0.0808239 and 0.1508239, the decision of this range is loosely based on the information provided by the CDC (2021). The source describes the new strands as being able to spread quicker and more efficiently; however, due to a lack of additional numerical evidence the infectivity will be assumed to increase by 0.7 from its calibrated value. Scenario Number three is a worst case which assumes a higher number of contacts per day than the base case while also having an increased probability of infection (0.1) due to easing regulations on protective wear (e.g. Masks in establishments). The second set of results 1.1, 1.2, and 1.3 are executed in order to evaluate for each of the scenarios how many beds would be required in order to be able to handle the peaks without suffering casualties. However, it is worth mentioning that if the number of beds required becomes unrealistic, then a limit has to be set on what parameters (i.e. measures) can be increased (i.e. eased). It is worth mentioning that the two key performance indicators (i.e. KPI) for these experiments are the number of diseased individuals due to unavailability of treatment and the Utilization of the emergency rooms (Beds). The values for the parameters used in the base cases are displayed below in Table 4.



Table 4: Values for the base cases of the different scenarios run in order to evaluate the situation

Parameters	Scenario 1	Scenario 2	Scenario 3
Population	250000	250000	250000
Probability of Infection	0.0808239	0.0808239-0.1508239	0.1
Number of Contacts	2-9	2	2-9
Emergency Rooms (Beds)	28	28	28

Table 5: Values for the Emergency rooms (Beds) for the additional parameter variations of the three base scenarios

Parameters	Scenario 1.1	Scenario 2.1	Scenario 3.1
Emergency Rooms (Beds)	30-110	30-110	30-110

It is worth noting that all of the other parameters excluded from the table above remain the same as they were described in the previous sections of the report, and thus have no need to be shown a second time.

6. Results

These sections will include the discussion of the results produced by the model through the different scenarios and will provide insight on how certain parameter fluctuations caused certain behaviors.

6.1 Interpretation of Results & Conclusions

As it was mentioned before, this section provides the results for all of the separate scenarios and their respective comparisons to each other and the base case described within the calibration process of the model. The first set of results (S1) shows a very



large exponential growth in deaths as the number of contacts increases from 2-9 in the parameter variation (Appendix 4). To highlight the impact of varying this parameter, every time an additional contact per day was added the mean value of deaths increased by an average value of 45. Additionally, from the results of this experiment it can be seen that the usage of beds increases by 16% just by varying the base value from two to three; Afterwards, from the confidence intervals displayed in the results (Appendix 5) it can be observed that there is not only an overlap between the intervals, but also the exponential growth curve levels off and the results have less significant variations. For scenario two (S2) the increase of the value of infectivity through parameter variation did not have as significant of an impact as varying the amount of contacts per day. To emphasize the lesser impact of this parameter, the average increase of deaths between each iteration is roughly 3 in comparison to the 45 caused by the simulations in S1. From the results displayed in Appendix 6 it is possible to observe that the first few variations of the parameter produce close to no-fluctuation in the number of deaths, only managing to produce one on its fifth increase of the parameter value. From Appendix 7 it is possible to observe that increasing infectivity only fluctuates usage of beds by an average of 3% and as a result all confidence intervals have an overlap due to the proximity in their respective mean values. It is also worth mentioning that the results for average deaths vary greatly between both of the last iterations of S1 and S2. For S1 the final mean value is equal to 364 deaths while S2 is only 20, from this difference it is possible to conclude that the aforementioned Beta variable is influenced more aggressively by the number of contacts per day. Scenario number three (S3) displays the consequences of easing too many measures too quickly quite well, in this specific instance, it is assumed that the infectivity increases as a result of not enforcing distancing and use of a mask and also individuals are no longer discouraged with meeting with many others. The first observation to be made is that the increase of contacts per day affects the average number of deaths quite significantly after a certain point. In the figure provided below it can be seen that the average increases quite aggressively after the contacts reach the figure of five per day (Appendix 8) going from 58 to 115 to 201 and so on. The average increase in the mean values between each iteration is equal to 89 which is almost double of the average found on S1. On the other hand, the usage of beds as a KPI in this instance is helpful in highlighting the extensive gap between the base case and the respective iterations where the initial gap is around 15% in comparison to the average of around 3% between all of the other average values (from 3-9 contacts per day). The results for the average usage of beds can be consulted in Appendix 9 where it can be seen that the average values after three contacts per day possess increasing overlaps in their respective confidence intervals. A logical conclusion



from S3 is that the easing of measures should be done as gradually as possible in order to limit the resurgence of cases, thus avoiding hospitals from overflowing, and avoiding unnecessary casualties. An observation worth mentioning is that within the first set of results, anytime the average-usage-of-beds is below 45%, no deaths occur as a result of a lack of capacity. Below is table 6 which summarizes the respective KPIs for each scenario with the respective variations used.

Table 6: Results of Averages ok KPIs for Scenarios 1,2 & 3

S1			S2			S3		
Contacts	Average of Deaths	Average of UsageOfBeds	Infectivity	Average of Deaths	Average of UsageOfBeds	Contacts	Average of Deaths	Average of Usage of Beds (%)
2	0	35%	0.0808239	0	35%	2	0	42%
3	5	51%	0.0908239	0	39%	3	21	57%
4	27.5	59%	0.1008239	0	43%	4	58	64%
5	59.3	64%	0.1108239	1	47%	5	115	67%
6	105.7	67%	0.1208239	5	50%	6	201	70%
7	168.1	69%	0.1308239	10	53%	7	323	72%
8	252.8	71%	0.1408239	15	56%	8	491	74%
9	364.4	73%	0.1508239	21	57%	9	709	75%

The second set of results relates to reusing the three base cases, along with variations in the amount of hospital beds in order to produce conclusions regarding the necessary amount of them required so no casualties are suffered. The number of beds within the hospital can range between 30 and 110. The first case (S1.1) is the one where contacts per day fluctuate alongside the number of beds which produced the following results (Table 7).



Table 7: Number of beds required to have 0 casualties (S1.1)

Contacts	Number of Beds Required
2	30
3	35-40
4	60
5	90
6	>110
7	>110
8	>110
9	>110

From the results above it can be seen that sudden increases in the number of contacts per day can lead to the amount of required resources becoming unreasonable, exceeding the higher bound limit established. The second case (s2.1) relates to the fluctuation of the infectivity along with the number of beds. Below are the results for the second set of iterations (Table 8).

Table 8: Number of beds required to have 0 casualties (S2.1)

Infectivity	Number of Beds Required
0.0808239	30
0.0908239	30
0.1008239	30
0.1108239	35-40
0.1208239	35-40
0.1308239	35-40
0.1408239	40-50
0.1508239	40-50

From the results displayed above, it can be deduced that in the event of an increase in infectivity without many contacts per day, the hospital could handle the worst case scenario of 15% infectivity with around 40-50 beds. The third and final scenario (S3.1)



fluctuates the number of contacts per day with a higher (constant) infectivity rate while also fluctuating the number of beds in order to assess how many may be required to fulfill patients' needs in the case of this more catastrophic scenario. Below is a table summarizing the results (Table 9).

Table 9: Number of beds required to have 0 casualties (S3.1)

Contacts	Number of Beds Required
2	30
3	40-50
4	80-90
5	>110
6	>110
7	>110
8	>110
9	>110

From the results above, it is possible to deduce that in the event of increased infectivity either because of a lack of measures and or a new strand, increasing the number of contacts are detrimental to the ability of a hospital to treat patients. As can be seen above, if the number of contacts exceeds five, then the hospital already needs a large amount of beds in order to be able to treat all incoming patients. From Tables 7 & 9 it is possible to see that the additional infectivity not only increases the number of beds required with fewer contacts but also increases the number of beds required faster for the lower bound values of contacts (3-5 per day).

6.2 Recommendations

This section is designed to provide recommendations on how both the government and the hospitals can work together in order to avoid reaching concerning accumulation levels of patients. Logically, if the accumulation levels are maintained as low as possible along with the presence of an appropriate amount of resources, then casualties can be avoided entirely. From the results section it was possible to reach the conclusion that sudden increases in the number of contacts affect the number of both infected and severe patients quite significantly in comparison to the infectivity rate. From this



conclusion the first recommendation to be made is that as long as the government manages to maintain contacts as low as possible then hospitals will most definitely be able to handle all of the incoming patients. For instance, this could be observed in the base case where individuals were only allowed to meet with a maximum of two people per day according to government regulations. However, in the event that the number of infected individuals decreases then perhaps more contacts can be allowed without producing catastrophic results. Due to the aforementioned impact of this parameter it is worth mentioning that this should be done gradually to avoid the resurgence of additional disease peaks. In accordance with the current measures mentioned in Government.nl (2021) the number of contacts per day has now increased from two to four per day which could in turn affect hospital admissions and accumulation levels. If so, the government will more than likely reduce the number yet again; nevertheless, in the specific case of the province of Groningen, a suggestion based off of the results is that the UMCG should have at least 60 beds ready in order to be able to handle potential patients. It is also worth mentioning that any increases over the five contacts could still be considered risky at the moment; however, if this is an idea for the governments reopening plan then they should assure themselves that cases are low enough to limit propagation or should request the hospital to have more than 110 beds available to prepare for any worst case scenarios. The likelihood of the UMCG having 110 beds only dedicated to COVID is unlikely and thus in this instance control over the propagation seems like the more viable plan. The final recommendation revolves around the impact of increased infectivity along with increasing contacts, and it relates to avoiding any increases in infectivity due to the easing of measures. To elaborate further from Table 9 it could be seen that the number of required beds increases quite quickly in comparison to how it occurs in the case presented in Table 7; Thus, the government should avoid easing the measures related to social distancing and or use of masks inside closed spaces in order to avoid any additional risks when slowly increasing the number of allowed contacts.

6.3 Future Work

The model worked on throughout the development of this project showed promising results with respect to modelling both of the desired situations (Diffusion and Hospital) required to study and analyze the accumulation levels of patients at healthcare facilities. Nevertheless, the results could be made even more accurate through additional close collaboration with both the Dutch Government and the UMCG or any other healthcare facility around the country. This collaboration could provide not only additional data



which could be useful for expanding the existing SEIR model, but also would allow a potential expansion of the hospital model in which routing within the facility plays a role, as well as the schedule of the staff among other aspects. Additionally, the model would then be running under real life data for the chosen hospital allowing for more accurate results due to the exchange of assumed/predicted data based on literature for the real data within the facility. On the other hand, the expansion of the SEIR model through collaboration would revolve around the addition of aspects which are not available to the general public. An example for a valuable addition to the model would be the region/city specific number of vaccinated individuals, which at the moment is only available as a general figure for the entirety of the population.

7. Bibliography

- Abou-Ismaïl, A., 2020. Compartmental Models of the COVID-19 Pandemic for Physicians and Physician-Scientists. *SN Comprehensive Clinical Medicine*, 2(7), pp.852-858.
- Ala'raj, M., Majdalawieh, M. and Nizamuddin, N., 2021. *Modeling and forecasting of COVID-19 using a hybrid dynamic model based on SEIRD with ARIMA corrections*. *Infectious Disease Modelling*, 6, pp.98-111.
- Augustijn, E., Doldersum, T., Useya, J. and Augustijn, D., 2016. Agent-based modelling of cholera diffusion. *Stochastic Environmental Research and Risk Assessment volume*, [online] (30). Available at: <<https://doi-org.proxy-ub.rug.nl/10.1007/s00477-015-1199-x>> [Accessed 28 February 2021].
- Bazghandi, A., 2012. *Techniques, Advantages and Problems of Agent Based Modeling for Traffic Simulation*. [online] Core.ac.uk. Available at: <<https://core.ac.uk/reader/25749192>> [Accessed 29 April 2021].
- Best, A., Dixon, C., Kelton, W., Lindsell, C. and Ward, M., 2014. Using discrete event computer simulation to improve patient flow in a Ghanaian acute care hospital. *The American Journal of Emergency Medicine*, 32(8), pp.917-922.
- Brailsford, S. C., T. Eldabi, M. Kunc, N. Mustafee, and A. F. Osorio. 2019. "Hybrid simulation modelling in operational research: A state-of-the-art review". *European Journal of Operational Research* 278(3):721-737.
- Carcione, J., Santos, J., Bagaini, C. and Ba, J., 2020. A Simulation of a COVID-19 Epidemic Based on a Deterministic SEIR Model. *Frontiers in Public Health*, 8.
- CDC. 2021. About Variants of the Virus that Causes COVID-19. [online] Available at: <<https://www.cdc.gov/coronavirus/2019-ncov/variants/variant.html>> [Accessed 4 June 2021].
- CDC. 2021. *Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19)*. [online] Available at:



- <<https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html>> [Accessed 15 May 2021].
- Chahal, K., T. Eldabi, and T. Young. 2013. “A conceptual framework for hybrid system dynamics and discrete event simulation for healthcare”. *Journal of Enterprise Information Management*.
- Coronavirus Dashboard. 2021. *Hospital admissions*. [online] Available at: <<https://coronadashboard.government.nl/landelijk/ziekenhuis-opnames>> [Accessed 20 March 2021].
- Deschepper, M., Eeckloo, K., Malfait, S., Benoit, D., Callens, S. and Vansteelandt, S., 2021. Prediction of hospital bed capacity during the COVID– 19 pandemic. *BMC Health Services Research*, 21(1).
- Government of the Netherlands. 2021. *Dutch measures against coronavirus: basic rules for everyone*. [online] Available at: <<https://www.government.nl/topics/coronavirus-covid-19/tackling-new-coronavirus-in-the-netherlands/basic-rules-for-everyone>> [Accessed 28 April 2021].
- Government of the Netherlands. 2021. *Step 1: shops and outdoor seating at restaurants and cafés will partially reopen; evening curfew lifted*. [online] Available at: <<https://www.government.nl/latest/news/2021/04/20/step-1-shops-and-outdoor-seating-at-restaurants-and-cafes-will-partially-reopen-evening-curfew-lifted>> [Accessed 28 April 2021].
- Government.nl. 2021. *Step 3: nearly everything to reopen, subject to certain conditions*. [online] Available at: <<https://www.government.nl/latest/news/2021/05/28/step-3-nearly-everything-to-reopen-subject-to-certain-conditions>> [Accessed 4 June 2021].
- Huisman, I., 2021. *Applying a calibrated Hybrid Model to investigate and reduce transmission of SARS-COV-2 in a nursing home department within a province in the netherlands*. Masters. University of Groningen, Department of Industrial Engineering and Management.
- Jacob, M., 2013. Discrete Event Simulation. *Journal of Science Education*, 18(1).
- Lai, C., Shih, T., Ko, W., Tang, H. and Hsueh, P., 2020. *Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): The epidemic and the challenges*. *International Journal of Antimicrobial Agents*, 55(3), p.105924.
- Leviner, S., 2019. *Patient Flow Within Hospitals: A Conceptual Model*. [online] SAGE Journals. Available at: <<https://doi.org/10.1177/0894318419881981>> [Accessed 28 April 2021].
- Millard, P., Christodoulou, G., Jagger, C., Harrison, G. and McClean, S., 2001. *Modelling hospital and social care bed occupancy and use by elderly people in an English health district*. *Health Care Management Science*, 4(1), pp.57-62.
- Miller, S., 2006. *The Method of Least Squares*. [online] Web.williams.edu. Available at: <https://web.williams.edu/Mathematics/sjmillier/public_html/BrownClasses/54/handouts/MethodLeastSquares.pdf> [Accessed 20 May 2021].



Mustafee, N., S. Brailsford, A. Djanatliev, T. Eldabi, M. Kunc, and A. Tolk. 2017. "Purpose and benefits of hybrid simulation: contributing to the convergence of its definition". In the 2017 Winter Simulation Conference (WSC), 1631–1645. IEEE.

Ng, T., Turinici, G. and Danchin, A., 2003. A double epidemic model for the SARS propagation. *BMC Infectious Diseases*, 3(1).

PySD-Cookbook. 2015. *Fitting a model's parameters with run-at-a-time optimization*. [online] Available at: <https://pysd-cookbook.readthedocs.io/en/latest/analyses/fitting/Fitting_with_Optimization.html> [Accessed 2 June 2021].

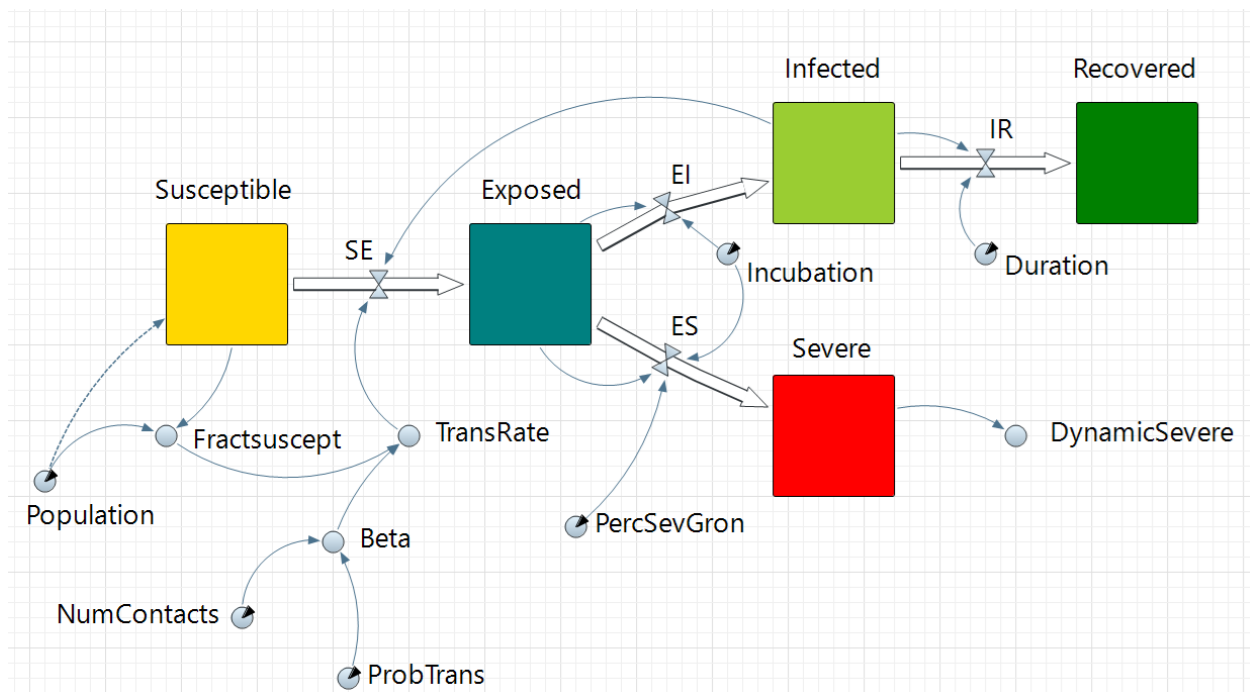
RIVM. 2021. *The spread of COVID-19*. [online] Available at: <<https://www.rivm.nl/en/novel-coronavirus-covid-19/spread>> [Accessed 28 April 2021].

WHO, 2021. *Coronavirus*. [online] Who.int. Available at: <https://www.who.int/health-topics/coronavirus#tab=tab_1> [Accessed 14 March 2021].

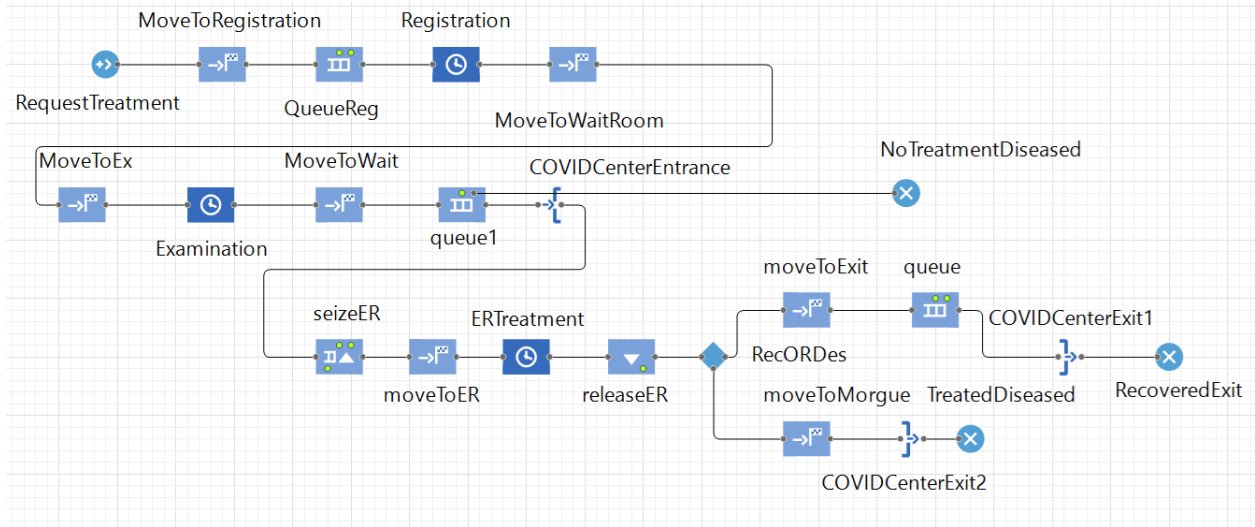
WHO, 2021. *WHO Coronavirus (COVID-19) Dashboard*. [online] Covid19.who.int. Available at: <<https://covid19.who.int/>> [Accessed 14 March 2021].

Worldometers.info. 2021. *Netherlands Population (2021) - Worldometer*. [online] Available at: <<https://www.worldometers.info/world-population/netherlands-population/>> [Accessed 20 March 2021].

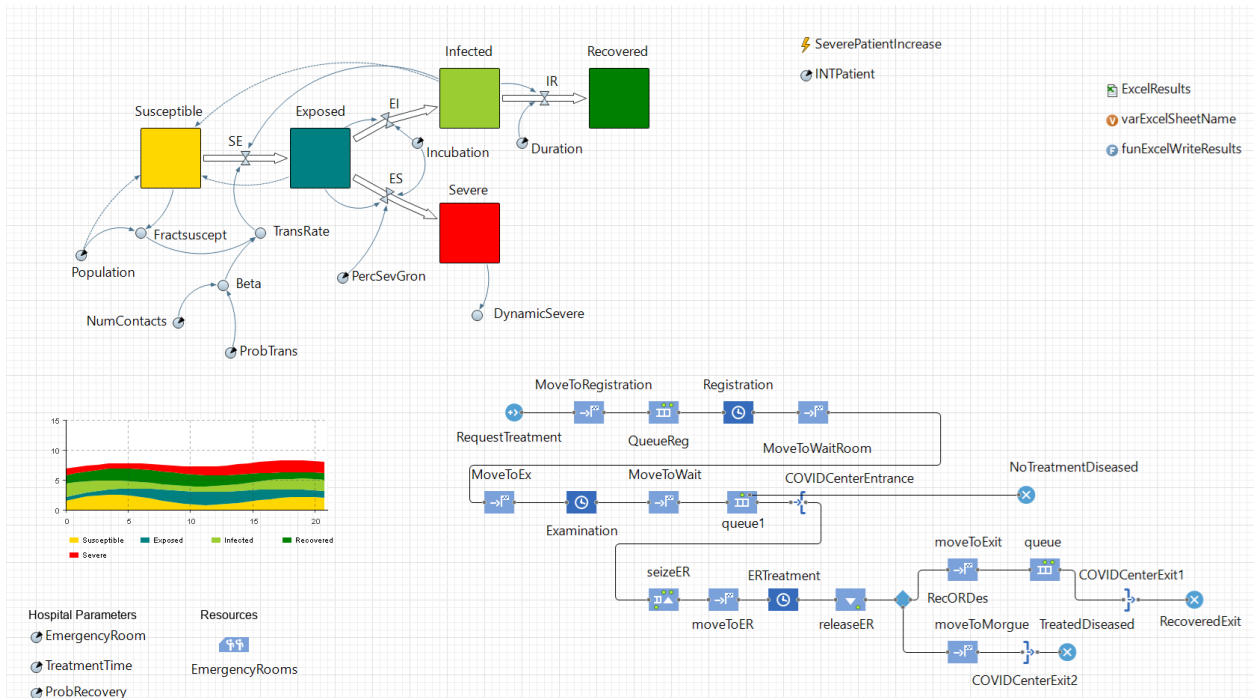
8. Appendix



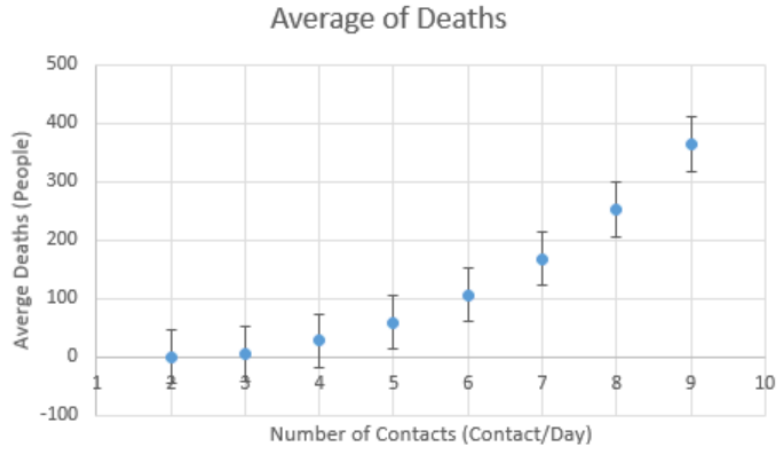
Appendix 1: SEIR model built in Anylogic



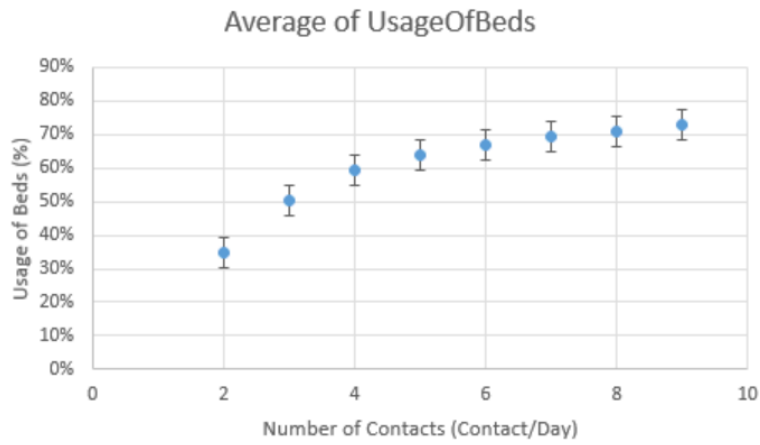
Appendix 2: Discrete event hospital model



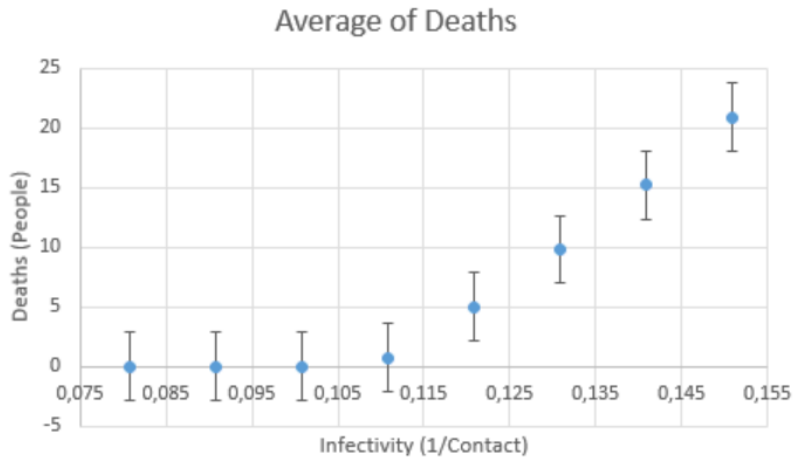
Appendix 3: Hybrid Model in Anylogic



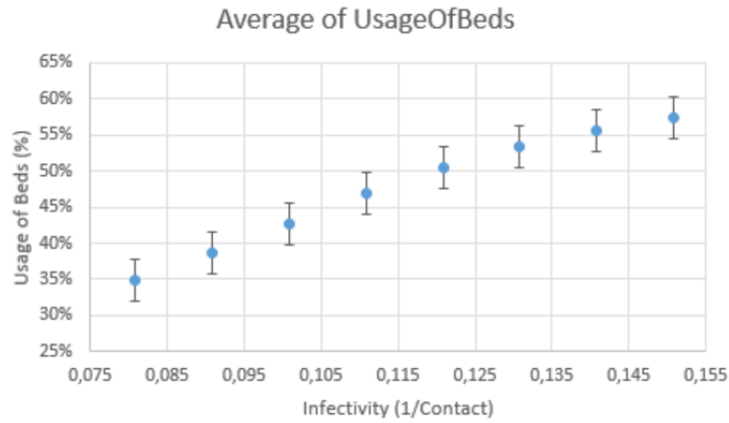
Appendix 4: Average Deaths (S1)



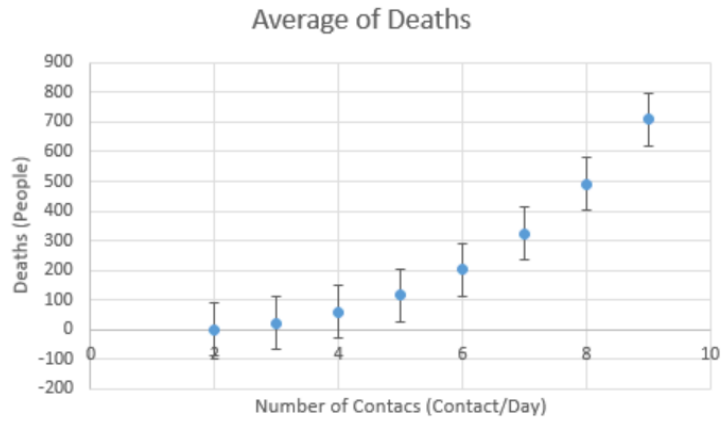
Appendix 5: Average usage of beds (S1)



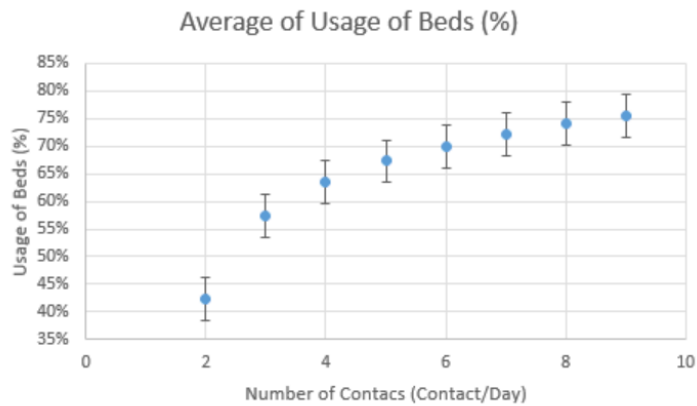
Appendix 6: Average Deaths (S2)



Appendix 7: Average usage of beds (S2)



Appendix 8: Average Deaths (S3)



Appendix 9: Average usage of beds (S3)