ARI COVID-19 EPIDEMIOLOGICAL MODELLING FOR AFRICAN COUNTRIES

The African COVID-19 Modelling Research Group,
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Contents

Background

The study of the occurrence of a disease is called epidemiology (Hethcote, 1989). A disease is called a pandemic when there is a rapid increase of cases of the disease in a relatively short time and a disease is endemic if it is within the population for a relatively long time. Diseases can be caused by various agents such as bacteria and viruses and can be transmitted by various mode of transmission, such as human to human contact, reservoir to vector to human such as in malaria. Every disease has a specific agent and mode of transmission (Hethcote, 1989). COVID-19 is the disease caused by the SARS-CoV-2 (Severe acute respiratory syndrome coronavirus 2). The 'CO' stands for corona, 'VI' for virus, and 'D' for disease. Formerly, this disease was referred to as '2019 novel coronavirus' or '2019-nCoV.' (Guo et al., 2020; WHO, 2020a). Coronaviruses are a large family of viruses which may cause respiratory infections ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) (Shereen et al., 2020). The SARS-CoV-2 virus is a zoonotic virus, which is found in bats, a common reservoir for Coronaviruses. However, there is a suspected inconclusive intermediate host between the transmission of the SARS-CoV-2 from bats to humans (Shereen et al., 2020; WHO, 2020b). In December 2019 and January 2020, there was an unusually large number of cases with respiratory illnesses in the province of Wuhan City, Hubei Province, China. The SARS-CoV-2 was identified and isolated on the 7th of January in China (Zheng, 2020).

On January 30, 2020, the WHO declared the COVID-19 outbreak a global health emergency and on March 11, 2020, a global pandemic (WHO, 2020c). In Africa, most reported cases were sighted within March 2020 mostly due to importation (WHO, 2020d). In response to the COVID-19 pandemic, most of Africa initiated national lockdowns in March in line with recommendations from WHO guidelines (Africa CDC, 2020). SARS-CoV-2 is transmitted via droplets and fomites during close unprotected contact between an infector and infectee. The airborne spread of the virus has not been reported for SARS-CoV-2 and it is not believed to be a major driver of transmission based on the available evidence (WHO, 2020b). There are 3 basic types of predictive stochastic compartmental transmission models for infectious diseases. These are the SI, SIS and SIR model (Hethcote, 1989). These compartmentalise a population into classes as a function of time. There are four major classes in these models. These are the Susceptible class-(S) (these are individuals in a population who can incur the disease, however, have not been infected yet), Exposed class (E) (these are individuals in a population who are infected however are still not yet infectious), Infective class (I) (these are individuals who are infected and are infectious that is transmitting the disease to others) and Removed/Recovered (R) (these are individuals who have recovered from the disease with immunity, isolated or died). In the SI model infected individuals do not recover whilst in the SIS model individuals recover with no immunity and in the SIR model individuals recover with immunity (Hethcote, 1989).

COVID-19 has been modelled with the SEIR model (Binti Hamzah et al., 2020; Frost et al., 2020; Mukandavire et al., 2020; SACMC, 2020; Wees et al., 2020). This takes the assumption that individuals infected recover with immunity. However, this assumption is still inconclusive as there are no conclusive clinical studies to this effect (Alberta Health Services, 2020). However, a recent study published in Nature Medicines suggests potential immunity of recovered cases (Long et al., 2020). There are still key questions regarding the strength of the immune response produced regarding a secondary infection of COVID-19. There is no current evidence of pre-existing immunity of COVID-19 in humans. Therefore everyone who has not assimilated the virus is assumed to be susceptible (WHO,

2020b). The COVID-19 virus attacks respiratory cells resulting in an over-response by the immune system (Cytokine storm syndromes). The result is the generation of fluids and inflammation, damage to respiratory cells especially in severe and critical cases (Astuti & Ysrafil, 2020). Severe and critical COVID-19 cases need assisted/mechanical breathing. COVID-19 causes various symptoms such as coughing/sore throat, fever, myalgia or fatigue, respiratory symptoms, pneumonia. In severe and critical cases, it can cause dyspnoea, respiratory failure, septic shock, and multiple organ failure (Gaythorpe et al., 2020; Huang et al., 2020).

Most reported symptomatic cases (about 80-99 %) have been mild whilst 1-5 % have been severe (Verity et al., in press; WHO, 2020b). There are indications that asymptomatic cases of COVID-19 account for a large proportion of the total cases, about 40-80 % (Day, 2020; Inui et al., 2020; Sutton et al., 2020). The average incubation period of COVID-19 has been estimated to be between 4-6 days (Tindale et al., in press; Li et al., 2020; WHO, 2020b; Zaki et al., 2020) while the average serial interval for COVID-19 is between 3 to 4 days (Du et al., 2020; Nishiura, Linton & Akhmetzhanov, 2020). There is evidence of pre-symptomatic transmission of COVID-19 (WHO, 2020e) with a pre-symptomatic infection period between 1-4 days (Byrne et al., 2020; Wei et al., 2020; WHO, 2020b). The average infection period is estimated to be between 2 to 5 days (Binti Hamzah et al., 2020). For asymptomatic cases, the infectious period is estimated to be between 6.5 to 9.5 days (Byrne et al., 2020). The estimated mean duration from symptom onset to hospital discharge was 18.1 days and 4 days longer to death than hospital discharge (Byrne et al., 2020). COVID-19 seems to develop to the severity in patients who are over the ages of 60 years old and those with underlying conditions such as hypertension, diabetes, cardiovascular diseases, chronic respiratory disease, and cancer (WHO, 2020b). The COVID-19 disease in children is relatively rare with a small proportion of individual under 19 developing severe or critical symptoms (WHO, 2020b).

About the ARI COVID-19 SEIR Model

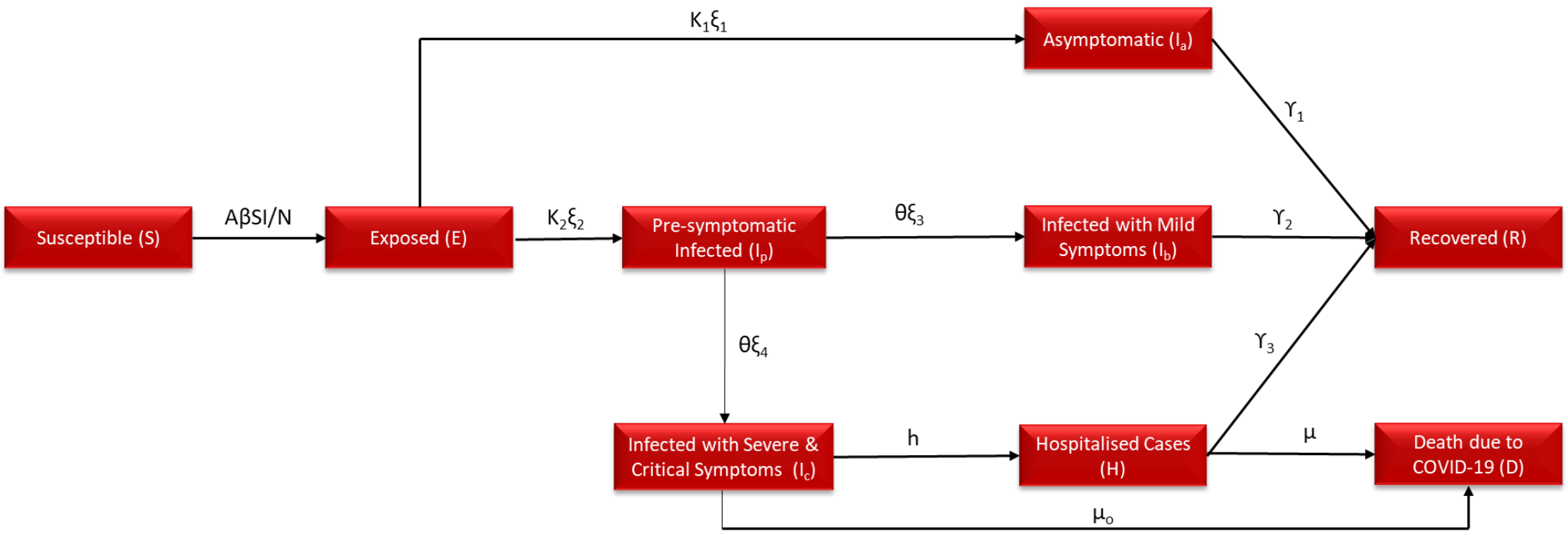
ARI modelled COVID-19 using the SEIR model. The SEIR model was chosen due to the potential of immunity development by individuals who recover from COVID-19. Epidemiological models provide the ability to predict the macroscopic behaviour of diseases using microscopic descriptions. With COVID-19 being a relatively new disease, accurate data is limited thus most models are likely to be inaccurate. However, modelling COVID-19 can provide some insights to the pandemic that can try help address certain issues. For ARI, our SEIR Model had the following objectives:

- Determine potential cases of COVID-19 in Africa.
- Determine African government responses and their impact in the COVID-19 pandemic in Africa.
- Determine the Healthcare System preparedness to the COVID-19 pandemic in Africa.
- Determine the potential seroprevalence of COVID-19 in the African population.

The ARI COVID-19 SEIR Model was constructed in a Macro-Enabled Ms Excel File for user-friendliness (visual interaction with parameters) and Database Query Support. This is line with recommendations from the Africa CDC, 2020 to make models more user friendly for African governments. The cells in the model are interlinked allowing for instantaneous results as a parameter is changed. Each Country Activity is modelled as a scenario based on statistical regression analysis of reported COVID-19 Deaths (Base Case) and adjusted parameters (Extended Cases). The model is inbuilt with the following Datasets: African Reported COVID-19 Cases, COVID-19 Test Data, Google Community Mobility Reports, Healthcare System & Access, Population Demographics and Geographics, Temperature, Diabetes, Hypertension, TB & HIV Prevalence and Employment. The Model has a Visual Basic Application (VBA) code for Sensitivity and Variable Analysis. The Model also has an Inbuilt Age and Co-

morbidity Risk Calculator for HIV, Diabetes, Hypertension and TB based on the **ARI's COVID-19 Age & Disease Risk Factors** (ARI, 2020). The file is linked to the ARI Server for Dataset Updates. The base case Model used South African Reported COVID-19 Case and Death Data to develop an understanding of the impact of the National Alert Level lockdowns as well as the risk of age and disease in COVID-19. This base case was then extended to other African countries using adjustment factors in the Effective Daily Contact Number, Symptomaticness, Death and Hospitalisation.

Model Structure



Model Compartments	Definition	Major Assumptions in Model
Susceptible (S)	Individuals within the population of the model who can incur the disease however have not been infected yet.	Before 1st reported case, all country population naïve/susceptible.
Exposed (E)	Individuals within the population of the model who are infected however are still not yet infectious and are in an incubation period.	Relatively short period to pre-symptomatic.
Asymptomatic (I_a)	Individuals within the population of the model who are infected and are infectious that is transmitting the disease to others however are not showing any symptoms throughout their infectiousness.	High proportion of total infections.
Pre-symptomatic Infectious Cases (I_p)	Individuals within the population of the model who are infected and are infectious that is transmitting the disease to others however have not developed symptoms as of yet.	A relatively long period in the incubation period.
Infected with Mild Symptoms (I_b)	Individuals within the population of the model who are infected and are infectious with mild symptoms.	A high proportion of symptomatic cases and do not require hospitalisation.
Infected with Severe and Critical Symptoms (I_c)	Individuals within the population of the model who are infected and are infectious with severe and critical symptoms who have not yet been hospitalised.	Require Hospitalisation.
Infected with Symptoms (I_{bc})	Individuals within the population of the model who are infected and are infectious with mild, severe, and critical symptoms.	
Total Infected (I)	Individuals within the population of the model who are infected and infectious.	
Hospitalised COVID-19 Cases (H)	Individuals within the population of the model who are infected, infectious with severe and critical symptoms and have been hospitalised.	
Death due to COVID-19 (D)	Individuals who have died due to COVID-19 or indirect consequences of the COVID-19 epidemic.	Excess Deaths account for all COVID-19 direct and indirect deaths.
Recovered (R)	Individuals within the population of the model who have recovered from the disease with immunity or partial immunity.	People who recover from COVID-19 develop long-term immunity and re-infection is relatively low.

Model Differential Equations and Parameters

From the conservation of mass:

$$N = S + E + Ia + Ip + Ib + Ic + H + R + D \quad \textbf{Equation 1},$$

where N is the total population

$$Iabc = Ia + Ip + Ib + Ic + H \quad \textbf{Equation 2},$$

where I_{abc} is the total infections

$$\frac{\partial S}{\partial t} = -A\beta S\frac{Iabc}{N} \quad \textbf{Equation 3,}$$

where β is the Effective daily contact rate, this is the average number of adequate contacts per infective per day. The product of S and I in Equation 3 is referred to as the mass incident term. A is the Population density factor a variable developed by ARI. Figure 1 shows the ARI COVID-19 SEIR Population Density Factor Assumption. The Population Density Factor calculation is given by Equation 4.

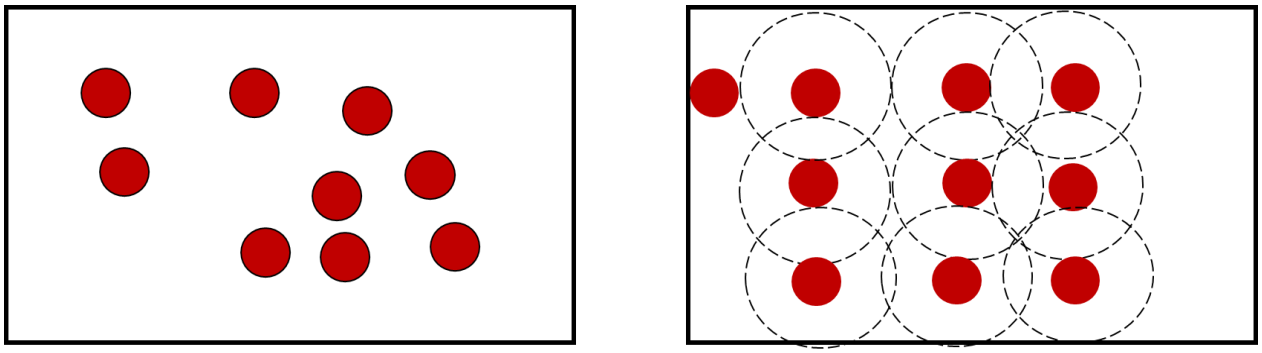


Figure 1 ARI COVID-19 SEIR Population Density Factor Assumption

$$A = -\frac{\frac{\sqrt{\frac{Country\ Area}{\pi}}}{N}}{Effective\ Social\ distance} + 1 \quad \textbf{Equation 4}$$

Where the Effective Social distance is the minimum distance between infector and infectee which prevents infection between the two. For COVID-19 a distance of 1 m has been suggested (Chu et al., 2020). However, it has come to be disputed upon reviews. As the average distance between individual tends towards the effective social distance, the Population Density Factor (A) tends towards 0. The Population Density Factor assumes a uniform distribution of population within a confined area.

$$\frac{\delta E}{\delta t} = A\beta S\frac{Iabc}{N} - k_1\xi_1 E - k_2\xi_2 E \quad \textbf{Equation 5}$$

Where K_1 and K_2 are the rates in which an exposed individual move to the infected class. K_1 is inversely proportional to the average incubation period of COVID-19 Asymptomatic Cases ($T_{inc,\ 1}$) and K_2 is inversely proportional to the average non-infectious incubation period of COVID-19 Symptomatic Cases ($T_{inc,\ 2}$) in the population. ξ_1, ξ_2, $\xi_{3,}$ ξ_4 are the proportions of the exposed and pre-symptomatic who will be Asymptomatic (ξ_1), Symptomatic (ξ_2), Develop Mild Symptoms (ξ_3) and Severe and Critical Symptoms (ξ_4), respectively.

$\xi_1 + \xi_2$=1 **Equation 6**

$\xi_3 + \xi_4$=1 **Equation 7**

$$\frac{\delta Ip}{\delta t} = k_2\xi_2 E - \theta\xi_3 I_p - \theta\xi_4 I_p$$ **Equation 8**

Equation 8 reduces to Equation 9 by substituting Equation 7.

$$\frac{\delta Ip}{\delta t} = k_2\xi_2 E - \theta I_p$$ **Equation 9**

$$\frac{\delta Ia}{\delta t} = k_1\xi_1 E - \Upsilon_1 Ia$$ **Equation 10**

$$\frac{\delta Ib}{\delta t} = \theta\xi_3 I_p - \Upsilon_2 Ib$$ **Equation 11**

$$\frac{\delta Ic}{\delta t} = \theta\xi_4 I_p - hIc - \mu_o Ic$$ **Equation 12**

$$\frac{\delta H}{\delta t} = hIc - \Upsilon_3 H - \mu H$$ **Equation 13**

$$\frac{\delta D}{\delta t} = \mu H + \mu_o Ic$$ **Equation 14**

$$\frac{\delta R}{\delta t} = \Upsilon_1 Ia + \Upsilon_2 Ib + \Upsilon_3 H$$ **Equation 15**

Where, Υ_1, Υ_2 and Υ_3 are the daily recovery rates of individuals with Asymptomatic, Mild Symptoms and Severe and Critical Symptoms in hospitals, respectively. θ is the rate at which pre-symptomatic individuals develop symptoms. h is the rate at which individuals who have developed severe and critical cases are hospitalised. μ_o is the daily death rate due to direct and indirect effects of COVID-19 in individuals with severe and critical symptoms who have not been hospitalised. μ is the daily death rate due to COVID-19 in hospitalised individuals.

$$\frac{\delta Iabc}{\delta t} = \frac{\delta Ia}{\delta t} + \frac{\delta Ip}{\delta t} + \frac{\delta Ib}{\delta t} + \frac{\delta Ic}{\delta t} + \frac{\delta H}{\delta t}$$ **Equation 16**

$$\frac{\delta Iabc}{\delta t} = k_1\xi_1 E - \Upsilon_1 Ia + k_2\xi_2 E - \theta I_p + \theta\xi_3 I_p - \Upsilon_2 Ib + \theta\xi_4 I_p - hIc - \mu_o Ic + hIc - \Upsilon_3 H - \mu H$$ **Equation 17**

$$\frac{\delta R}{\delta t} = \Upsilon_1 Ia + \Upsilon_2 Ib + \Upsilon_3 Ic$$ **Equation 18**

$$\frac{\delta R}{\delta t} = \Upsilon_1(Ia + Ib + Ic) = \Upsilon_1(Iabc)$$ **Equation 19**

Disease Free Equilibrium (DFE)

For the feasible region in the 16th octant of the mathematic model, there exists an equilibrium in which there is no disease. This condition is satisfied by the stability of the rate of change of the population. Thus:

$$\frac{\delta N}{\delta t} = \frac{\delta S}{\delta t} + \frac{\delta E}{\delta t} + \frac{\delta Ia}{\delta t} + \frac{\delta Ip}{\delta t} + \frac{\delta Ib}{\delta t} + \frac{\delta Ic}{\delta t} + \frac{\delta H}{\delta t} + \frac{\delta R}{\delta t} + \frac{\delta D}{\delta t}$$ **Equation 20**

$$\frac{\delta N}{\delta t} = -A\beta S\frac{Iabc}{N} + A\beta S\frac{Iabc}{N} - k_1\xi_1 E - k_2\xi_2 E + k_1\xi_1 E - \Upsilon_1 Ia + k_2\xi_2 E - \theta I_p + \theta\xi_3 I_p - \Upsilon_2 Ib + \theta\xi_4 I_p - hIc - \mu_o Ic + hIc - \Upsilon_3 H - \mu H + \mu H + \mu_o Ic + \Upsilon_1 Ia + \Upsilon_2 Ib + \Upsilon_3 H$$ **Equation 21**

$$\frac{\delta N}{\delta t} = 0$$ **Equation 22**

$$\frac{\delta N}{\delta t} \geq 0 \geq S + E + Iabc + R + D \qquad \textbf{Equation 23}$$

At DFE, E=0, I=0, R=0, D=0 Therefore substitute into Equation 23:

$$\frac{\delta N}{\delta t} \geq 0 \geq S \qquad \textbf{Equation 24}$$

Endemic Equilibrium (EE)

At each point in time, there exists an equilibrium in which there is a maximum/minimum for each class. Thus, taking Equation 3 and Equation 9-15.

$$\frac{\partial S}{\partial t} = -A\beta S \frac{Iabc}{N} = 0 \qquad \textbf{Equation 25}$$

$$\frac{\delta E}{\delta t} = A\beta S \frac{Iabc}{N} - k_1\xi_1 E - k_2\xi_2 E = 0 \qquad \textbf{Equation 26}$$

$$\frac{\delta Ip}{\delta t} = k_2\xi_2 E - \theta I_p = 0 \qquad \textbf{Equation 27}$$

$$\frac{\delta Ia}{\delta t} = k_1\xi_1 E - \Upsilon_1 Ia = 0 \qquad \textbf{Equation 28}$$

$$\frac{\delta Ib}{\delta t} = \theta\xi_3 I_p - \Upsilon_2 Ib = 0 \qquad \textbf{Equation 29}$$

$$\frac{\delta Ic}{\delta t} = \theta\xi_4 I_p - hIc - \mu_o Ic = 0 \qquad \textbf{Equation 30}$$

$$\frac{\delta H}{\delta t} = hIc - \Upsilon_3 H - \mu H = 0 \qquad \textbf{Equation 31}$$

$$\frac{\delta D}{\delta t} = \mu H + \mu_o Ic = 0 \qquad \textbf{Equation 32}$$

$$\frac{\delta R}{\delta t} = \Upsilon_1 Ia + \Upsilon_2 Ib + \Upsilon_3 H = 0 \qquad \textbf{Equation 33}$$

From Equation 2 substitute Equation 27-31

$$Iabc = Ia + Ip + Ib + Ic + H = \frac{Ek_2\xi_2}{\theta} + \frac{Ek_1\xi_1}{\Upsilon_1} + \frac{\theta\xi_3 I_p}{\Upsilon_1} + \frac{\theta\xi_4 I_p}{(h+\mu_o)} + \frac{hIc}{(\Upsilon_3+\mu)} \qquad \textbf{Equation 34}$$

From Equation 34 substitute Equation 27 and Equation 30

$$Iabc = \frac{Ek_2\xi_2}{\theta} + \frac{Ek_1\xi_1}{\Upsilon_1} + \frac{E\xi_2\xi_3 k_2}{\Upsilon_2} + \frac{E\xi_2\xi_4 k_2}{(h+\mu_o)} + \frac{hE\xi_2\xi_4 k_2}{(h+\mu_o)(\Upsilon_3+\mu)} \qquad \textbf{Equation 35}$$

From Equation 26:

$$S = \frac{NE\,(k_1\xi_1+k_2\xi_2)}{A\beta Iabc} \qquad \textbf{Equation 36}$$

From Equation 36 Substitute Equation 35

$$S = \frac{N(k_1\xi_1+k_2\xi_2)\,\theta\Upsilon_1\Upsilon_2(h+\mu_o)(\Upsilon_3+\mu)}{A\beta(k_2\xi_2\Upsilon_1\Upsilon_2\,(h+\mu_o)(\Upsilon_3+\mu)+k_1\xi_1\theta\Upsilon_2\,(h+\mu_o)(\Upsilon_3+\mu)+k_2\xi_2\xi_3\theta\Upsilon_1\,(h+\mu_o)(\Upsilon_3+\mu)+\,k_2\xi_2\xi_4\theta\Upsilon_1\,\Upsilon_2\,(\Upsilon_3+\mu)+hk_2\xi_2\xi_4\theta\Upsilon_1\,\Upsilon_2}$$

Equation 37

The relative critical point for model is when DFE=EE

$$S = \frac{N(k_1\xi_1+k_2\xi_2)\,\theta\Upsilon_1\Upsilon_2(h+\mu_o)(\Upsilon_3+\mu)}{A\beta(k_2\xi_2\Upsilon_1\Upsilon_2\,(h+\mu_o)(\Upsilon_3+\mu)+k_1\xi_1\theta\Upsilon_2\,(h+\mu_o)(\Upsilon_3+\mu)+k_2\xi_2\xi_3\theta\Upsilon_1\,(h+\mu_o)(\Upsilon_3+\mu)+\,k_2\xi_2\xi_4\theta\Upsilon_1\,\Upsilon_2\,(\Upsilon_3+\mu)+hk_2\xi_2\xi_4\theta\Upsilon_1\,\Upsilon_2} \leq N$$

Equation 38

$$\frac{N(k_1\xi_1+k_2\xi_2)\,\theta\Upsilon_1\Upsilon_2(h+\mu_o)(\Upsilon_3+\mu)}{A\beta(k_2\xi_2\Upsilon_1\Upsilon_2\,(h+\mu_o)(\Upsilon_3+\mu)+k_1\xi_1\theta\Upsilon_2\,(h+\mu_o)(\Upsilon_3+\mu)+k_2\xi_2\xi_3\theta\Upsilon_1\,(h+\mu_o)(\Upsilon_3+\mu)+\,k_2\xi_2\xi_4\theta\Upsilon_1\,\Upsilon_2\,(\Upsilon_3+\mu)+hk_2\xi_2\xi_4\theta\Upsilon_1\,\Upsilon_2} \leq 1$$

Equation 39

$$1 \leq \mathrm{Ro} = \frac{A\beta(k_2\xi_2\Upsilon_1\Upsilon_2\,(h+\mu_o)(\Upsilon_3+\mu)+k_1\xi_1\theta\Upsilon_2\,(h+\mu_o)(\Upsilon_3+\mu)+k_2\xi_2\xi_3\theta\Upsilon_1\,(h+\mu_o)(\Upsilon_3+\mu)+\,k_2\xi_2\xi_4\theta\Upsilon_1\,\Upsilon_2\,(\Upsilon_3+\mu)+hk_2\xi_2\xi_4\theta\Upsilon_1\,\Upsilon_2\,)}{(k_1\xi_1+k_2\xi_2)\,\theta\Upsilon_1\Upsilon_2(h+\mu_o)(\Upsilon_3+\mu)}$$

Equation 40

Equation 40 is what is defined as R_o for the ARI COVID-19 Model. R_o is the basic reproductive number. The basic reproductive number is the number of secondary infections that one infected person would produce in a fully susceptible population through the entire duration of the infectious period. Ro provides a threshold condition for the stability of the disease-free equilibrium point (Hethcote, 1989). If Ro is greater than 1 then there is an endemic equilibrium thus there will be an epidemic. If Ro is less than 1 then the disease will die out and remain at a relatively low level to the population size. Looking at Equation 40 Ro can be summarised as a ratio of the daily contact number over the daily recovery rate. It can also be defined by Equation 41:

$$Ro = (Number\ of\ contacts\ per\ time) \times (Probability\ of\ transmission\ per\ contact) \times (Duration\ of\ Infection)$$

Equation 41

The basic reproductive number assumes a completely susceptible population however the variable changes as infections increase. However, it remains an important parameter in epidemiological models. The Ro for MERs was estimated to be 8, Ebola (1.5-2.5) (Chang, 2017), Smallpox (6.9) (Eichner & Dietz, 2003), Measles (12-18) (Guerra et al., 2017). For COVID-19 the Ro is estimated to be between 2-6 (Liu et al., 2020). The effective reproductive number, Re, is the number of secondary infections that one infected person would produce through the entire duration of the infectious period. It is given by Equation 42:

$$Re = Ro \times S$$

Equation 42

Herd immunity is an important concept in epidemiology. Consider if α is the fraction immune due to vaccination. Then Heard Immunity is given by **Equation 43:**

$$Herd\ Immunity(\alpha) = (1 - \frac{1}{Ro})$$

Equation 43

Where Ro is the basic reproductive number. Herd immunity is when the population has enough people immune such that the disease will not spread if it was suddenly introduced randomly in the population.

Modelling the Base Case (South Africa)

South Africa was chosen as a base case for modelling COVID-19 in Africa because it is a good representative of the African Population considering Age Profile and Disease burden. South Africa has the highest Total COVID-19 testing in Africa (Worldometer, 2020) and seems to have relatively better reported COVID-19 Case (surveillance and regular publishing) and vitals (Excess Deaths) data than other African countries. South Africa implemented National Alert Level Lockdowns as a COVID-19 Preventative Measure allowing for a potential study into the effect of this measure amongst other measures on the COVID-19 Basic Reproductive Number. Table 1 shows the model parameters used in the ARI COVID-19 Modelling Base Case (South Africa) and Figure 2 shows the epidemiological model infection to recovery/death timeline.

Table 1: COVID-19 Modelling Parameters used in ARI Base case (South Africa)

Model Parameters	Description	Value Used	Source
β (day^{-1})	Effective Daily Contact Rate	0.14-0.50	Model defined using Statical Regression Analysis
ξ_1-1-ξ_2	The proportion of total infections that are asymptomatic cases	0.75	40-80 % (Day, 2020; Inui et al., 2020; Sutton et al., 2020).
ξ_3-1-ξ_4	The proportion of symptomatic cases that are mild	0.98	80-99 % (Verity et al., in press; WHO, 2020b; Worldometer, 2020)
$T_{inc,1}$ (Day)-K_1 (Day-1)	Time from infection to onset of presymptomatic infectiousness for asymptomatic cases	1	1-4 days (Byrne et al, 2020; Wei et al, 2020)
$T_{inc,2}$ (Day)-K_2 (Day-1)	Time from infection to onset of presymptomatic infectiousness for symptomatic cases	1	1-4 days (Byrne et al, 2020; Wei et al, 2020; Binti Hamzah et al., 2020)
T_p (Day)-θ (Day-1)	Time from presymptomatic infectiousness to onset of symptoms for mild, severe and critical cases	3	1-4 days (Wei et al, 2020; Byrne et al, 2020).
$T_{inf,1}$ (Day)-γ_1 (Day-1)	Time from expected onset of symptoms to recovery for asymptomatic cases (Assumed Infectious)	11	6.5-9.5 days (Byrne et al, 2020).
$T_{inf,2}$ (Day)-γ_2 (Day-1)	Time from onset of symptoms to recovery for mild cases (Assumed Infectious)	2	2-5 days (Binti Hamzah et al., 2020)
T_{disch} (Day)-γ_3 (Day-1)	Time from hospitalisation to discharge for severe and critical cases (Assumed Infectious)	12	(Discharge rate from Reported Hospitalised Cases)
T_h (Day)-h (Day-1)	Time from onset of symptoms to hospitalisation for severe and critical cases (Assumed Infectious)	5	(NICD,2020)
μ_1 (Day^{-1})	Case Fatality Rate (CFR) in hospitalised cases with severe and critical symptoms (Assumed Infectious)	0.0195	(Death rate from Reported Hospitalised Cases)(NICD,2020)

μ_o (Day^{-1})	Case Fatality Rate (CFR) in unreported cases with severe and critical symptoms (Assumed Infectious)	0.0315	(Death rate from Unreported COVID-19 Deaths)(NICD,2020; SAMRC, 2020)
N (People)	Country Population (Assumed Naïve/Susceptible before first reported case)	59308690	(UN, 2020)
A	Population Density Factor	0.995	ARI Parameter
R_o	Basic Reproductive Number	1.37-4.73	Model define
α (%)	Herd Immunity	27-79	Model define

Calculating the Hospital Discharge Rate

The hospitalization rate (h) (rate at which COVID-19 severe and critical cases are admitted to hospitals) was calculated based on clinical information from admitted patients with laboratory-confirmed COVID-19 in selected hospitals in South Africa under the National Institute for Communicable Diseases (NICD) DATCOV surveillance system. This sentinel hospital surveillance system was designed to monitor and describe trends of COVID-19 hospitalizations and the epidemiology of hospitalized patients in South Africa (Jassat et al., 2020). The number of hospitals reporting in the NICD DATCOV surveillance system increased in the reporting period. Initially, 204 Facilities were reporting, and this increased to 434 Facilities by 4 September 2020. Therefore, caution must be taken when taking averages between reporting case dates. The average Daily Hospital Discharge Rate (Υ_3) for COVID-19 patients was calculated using the Number of Discharged Alive and Admitted patients Data in the NICD DATCOV surveillance system from 24 May-17 August 2020. Equation 43 was used to calculate the Daily Discharge:

$$Daily\ Discharge\ (n)_{i+1} = Discharged\ Alive(n)_{i+1} - Discharged\ Alive(n)_i \qquad \textbf{Equation 43}$$

Where n is the number of patients and i is the reported case date.

The average Daily Hospital Discharge Rate (Υ_3) was then calculated using Equation 44

$$\Upsilon_3 = \frac{\overline{Daily\ Discharge\ (n)_{i+1}}}{Admitted_{i+1}} \qquad \textbf{Equation 44}$$

Calculating the Death Rate in Hospitalised Cases

The average Daily Death Rate or Daily Case Fatality Rate (CFR) for COVID-19 patients (μ_1) was calculated using the Number of Daily Deaths and Admitted patients Data in the NICD DATCOV surveillance system from 24 May-17 August 2020. ARI followed the WHO guideline in estimating the CFR (WHO, 2020e). Equation 45 was used to calculate the Daily Deaths:

$$Daily\ Deaths\ (n)_{i+1} = Died\ (n)_{i+1} - Died\ (n)_i \qquad \textbf{Equation 45}$$

Where n is the number of patients and i is the reported case date.

The Daily Case Fatality Rate (CFR) for COVID-19 patients (μ1) was then calculated using Equation 46

$$\mu 1 = \frac{\overline{Daily\ Deaths\ (n)_{i+1}}}{Admitted_{i+1}} \qquad \textbf{Equation 46}$$

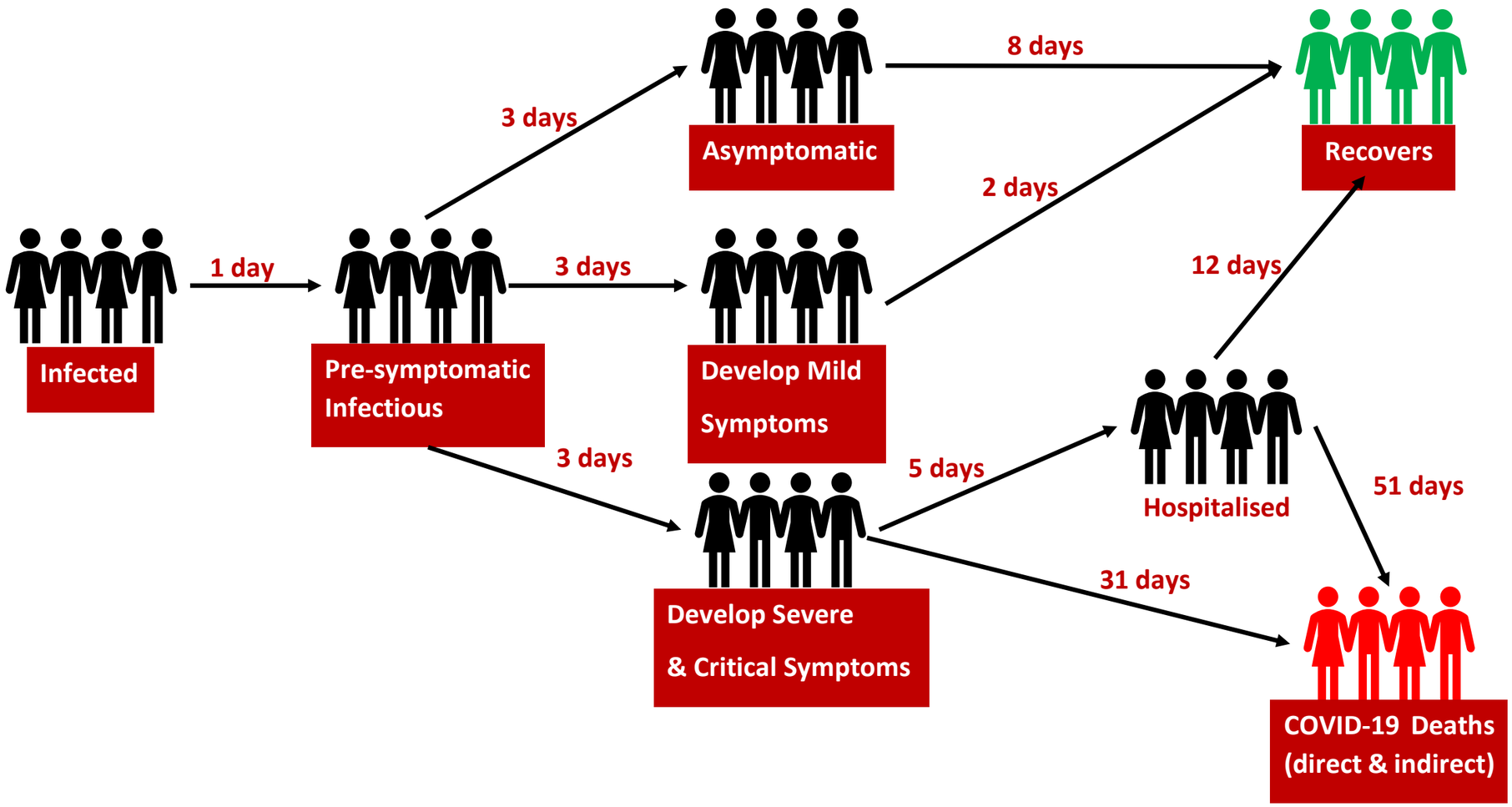


Figure 2: ARI Epidemiological Model Infection to Recovery/Death Timeline

Calculating the Death Rate of Unreported Severe and Critical Cases

Excess mortality is a count of deaths from all causes relative to what would normally have been expected. Excess mortality/deaths allow for accounting for miscounted or underreported COVID-19 Deaths and indirect Deaths related to the COVID-19 pandemic. National statistical agencies publish weekly deaths and averages of past 'normal' deaths (Aron et al., 2020). In South Africa, the South African Medical Research Council (SAMRC) published the Excess deaths from 1 January to 4 August 2020 using information obtained the National Population Register (Bradshaw et al., 2020a). ARI calculated the Unreported Excess Deaths (Natural) to COVID-19 Death Ratio for the period, 25 March to 29 July 2020 with data from Bradshaw et al. (2020) using Equation 47:

$$Unreported\ Excess\ Deaths\ (Natural)\ to\ COVID-19\ Death\ Ratio = \frac{Excess\ Deaths\ (Natural) i - Weekly\ Reported\ COVID-19\ Deaths_{\ i}}{Weekly\ Reported\ COVID-19\ Deaths_{\ i}} \quad \textbf{Equation 47}$$

Where i is the Weekly Reported Date. The daily death rate due to direct and indirect effects of COVID-19 in individuals with severe and critical symptoms who have not been hospitalised (μ_o) was then calculated using Equation 48:

$$\mu_o = \overline{Unreported\ Excess\ Deaths\ (Natural) to\ COVID-19\ Death\ Ratio} \times \mu_1 \quad \textbf{Equation 48}$$

Determining the Admission Status

The average admission status for COVID-19 patients was calculated using the Number of patients Currently in Hospital (n), General Ward (n), High Care (n), Intensive Care Unit (n), Isolation Ward (n), On Oxygen (n) and On Ventilator (n) Data in the NICD DATCOV surveillance system from 24 May-17 August 2020. The average admission Status was calculated using Equation 49-54:

$$\text{General Ward (\%)} = \overline{\frac{\text{General Ward (n)}_t}{\text{Currently in Hospital (n)}_t}} \times 100 \quad \textbf{Equation 49}$$

$$\text{High Care (\%)} = \overline{\frac{\text{High Care (n)}_t}{\text{Currently in Hospital (n)}_t}} \times 100 \quad \textbf{Equation 50}$$

$$\text{Intensive Care Unit (\%)} = \overline{\frac{\text{Intensive Care Unit (n)}_t}{\text{Currently in Hospital (n)}_t}} \times 100 \quad \textbf{Equation 51}$$

$$\text{Isolation Ward (\%)} = \overline{\frac{\text{Isolation Ward (n)}_t}{\text{Currently in Hospital (n)}_t}} \times 100 \quad \textbf{Equation 52}$$

$$\text{On Oxygen (\%)} = \overline{\frac{\text{On Oxygen (n)}_t}{\text{Currently in Hospital (n)}_t}} \times 100 \quad \textbf{Equation 53}$$

$$\text{On Ventilator (\%)} = \overline{\frac{\text{On Ventilator (n)}_t}{\text{Currently in Hospital (n)}_t}} \times 100 \quad \textbf{Equation 54}$$

The admission status was then calculated using the Hospitalised Cases in the model with Equation 55:

$$\text{Admitted (n)} = Admitted(\%) \times H \quad \textbf{Equation 55}$$

Where the Admitted (%) is the General Ward (%), High Care (%), Intensive Care Unit (%), Isolation Ward (%), On Oxygen (%) and Ventilator (%) respectively.

Seeding the Model

Reported Case Data

The ARI COVID-19 Dashboard/Server is based on a Ms Excel Data Model using Queries as inputs. The COVID-19 Johns Hopkins Data is downloaded from their website automatically and periodically into the ARI Google Drive through the Server. This data then forms the input into the ARI COVID-19

Dashboard as Queries. The Queries are merged to create an Excel Data Model which then produces pivot outputs.

The Queries are based on the following CSV files on the ARI Google Drive which are automatically updated every day by the server from the COVID-19 Johns Hopkins Database:

Cases: Google Drive African Research Initiative\Research Projects\COVID-19 in Africa\Datasets\COVID-19\Johns Hopkins CSSE\Data\time_series_covid19_confirmed_global

Deaths: Google Drive African Research Initiative\Research Projects\COVID-19 in Africa\Datasets\COVID-19\Johns Hopkins CSSE\Data\ time_series_covid19_deaths_global

Recovered: Google Drive African Research Initiative\Research Projects\COVID-19 in Africa\Datasets\COVID-19\Johns Hopkins CSSE\Data\ time_series_covid19_recovered_global

The outputs are the Cumulative Cases, Cumulative Recovered Cases and Cumulative Deaths due to COVID-19 per day. This data forms the feed into the Reported Cases. Reported Cases can be assumed to be cases which develop symptoms (as they are most likely to be reported for clinical diagnosis) and those which have been identified via contact tracing from primary infections. However, this assumption can be assumed if testing protocols and procedures in a country are relatively ineffective. If the testing protocol and procedure of a country is good particularly if they conduct contact tracing of reported cases and clinical diagnosis of traced cases. Then there is a probability of identifying asymptomatic cases. Since reported cases come after a period of clinical diagnosis, reported case dates thus are lagged from the Average Date of infection. Therefore, an Average Date of infection date (real-time cases) was estimated based on Equation 56 below:

$$Average\ Date\ of\ Infection = Reported\ Case\ Date - Average\ Time\ for\ Clinical\ Diagnosis$$

Equation 56

Where the Average time for Clinical diagnosis ($T_{testing}$) is the average time taken for an infected person to be diagnosed and the diagnosis outcome to be classified and reported as a COVID-19 case.

Each country will have its own ARI COVID-19 Server/Dashboard. In this example, the ARI COVID-19 Server/Dashboard for South Africa can be found in the following address:

Google Drive\African Research Initiative\Research Projects\COVID-19 in Africa\Risk Assessment Model Design\South Africa\ South Africa ARI COVID-19 Dashboard

The Report Cases sheet in the model carries information on COVID-19 cases reported for a country. It has data on COVID-19 Sum of Cases, Sum of Recovered Cases, Sum of Deaths, Active Cases, Daily New Cases, Daily Deaths, Daily Recovered Cases, Daily Death, Average Date of Infection, Day Count since Initial Reported Case, and Country Activity. Country Activities such as National Lockdowns have a great impact on daily contacts thus each period of Country Activity in the pandemic will be modelled as a scenario respectively.

Active Cases are giving by Equation 57:

$$Active\ Cases = Sum\ of\ Cases - Sum\ of\ Recovered\ Cases - Sum\ of\ Deaths$$ **Equation 57**

To seed the model in each scenario, initial conditions were defined using the Active Cases taken as the total symptomatic cases at the reported case date.

Regression and Statistical Analysis

To seed the models, a Non-linear regression analysis was conducted between the Reported COVID-19 Deaths and Death due to COVID-19 (D) from the model for the period in the Country Activity. This was done in the Statistical Analysis Sheets. Seeding the Models with points that are oversensitive results in large deviations between modelled data versus reported case data. This deviation or noise introduced by "over-sensitive" data points creates a significant error in the model results. Thus, it was important to decide which Data points can be used in the Regression Analysis. For our current modelling, this was particularly important at the start of the pandemic. To decide this, ARI used a Data Point Sensitivity term described by Equation 58:

$$\text{Data Point Sensitivity} = \frac{\text{Active Case or Reported COVID}-19\text{ Deaths}}{\textit{Lowest Possible Data Unit}} \qquad \textbf{Equation 58}$$

Where the Lowest Possible Data unit is the lowest possible unit of measurement for that data. In this case, it is 1 COVID-19 Reported Case. Data points with a Data Point Sensitivity greater than 5 % were ignored in the Regression Analysis. To conduct the Regression Analysis, the Residual and Normalised Error was determined using Equation 59 and Equation 60:

$$Residual = Modelled\ Data - \text{Active Case Data/Reported COVID-19 Deaths} \qquad \textbf{Equation 59}$$

$$Normalised\ Error = \frac{Residual}{Active\ Cases\ or\ Reported\ COVID-19\ Deaths} \qquad \textbf{Equation 60}$$

To allow the goodness of fit of Modelled data to Active Case or Reported COVID-19 Deaths Data, the Average Normalised Error of all Data points used in the Regression Analysis was reduced to 0 by changing the Effective Daily Contact Number (β) using the What-If Analysis Function. The pooled sample variance (s^2) was then calculated using Equation 61:

$$s^2 = \frac{\sum_{i=1}^{n1}(xi-\overline{x1})^2+\sum_{i=1}^{n1}(xj-\overline{x2})^2}{n1+n2-2} \qquad \textbf{Equation 61}$$

Where xi is the Reported Case Data points, $\overline{x1}$ is the Reported Case Data Points Mean, xj is the Model Data points, $\overline{x2}$ is the Model Data Points Mean, n1 and n2 are the samples sizes. The T-value: Two-Sample Assuming Equal Variance was used to calculate the t-value using Equation 62

$$t = \frac{\overline{x1}-\overline{x2}}{\sqrt{s^2\left(\frac{1}{n1}+\frac{1}{n2}\right)}} \qquad \textbf{Equation 62}$$

For the 1st Model Scenario (South Africa No lockdown), there were no reported COVID-19 deaths therefore reported active cases were used to seed this Model Scenario. To do this a sensitivity analysis was run to determine the fraction of reported cases that are Presymptomatic, Mild, Asymptomatic and Critical & Severe. This was done using a VBA code following the computational steps outlined in Figure 3

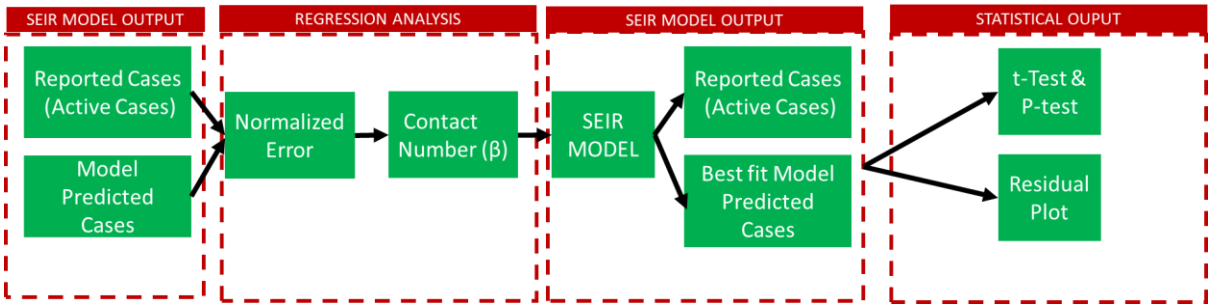


Figure 3: ARI COVID-19 SEIR Model Scenario 1Statistical Analysis Computational Steps

The combination of the Φ_1 Φ_2 Φ_3 Φ_4 that resulted in the lowest T-value are shown in Table 2 and was chosen to seed the Base Case Model Scenario 1.

Table 2: Fraction of Pre-symptomatic, Mild, Asymptomatic and Critical & Severe in Reported Cases

Φ_1 (Fraction of Mild Cases Reported)	0.5
Φ_2 (Fraction of Presymptomatic Cases Reported)	1
Φ_3(Fraction of Asymptomatic Cases Reported)	0.1
Φ_4(Fraction of Critical & Severe Cases Reported)	1

For other Model Scenarios (South Africa National Lockdown Alert Level 5, 4 and 3), Reported COVID-19 Deaths were used to seed the Models. For National Lockdown Alert Level 3 the reported COVID-19 deaths were adjusted to include unreported COVID-19 Deaths using Equation 63:

$$Reported\ COVID-19\ Deaths\ (Seed) = Reported\ COVID-19\ Deaths + Reported\ COVID-19\ Deaths \times \overline{Unreported\ Excess\ Deaths\ (Natural) to\ COVID-19\ Death\ Ratio} \qquad \textbf{Equation 63}$$

A sensitivity analysis was conducted on each variable used in the model and this is shown in the Variable Analysis 1 Sheet in the Base Case Model. A VBA code was used to run this analysis.

Modelling the Extended Cases

Extended Cases refer to African Countries other than South Africa. Figure 4 shows that most African countries had reported less than 100 000 cases as of 28 August 2020. Considering the date of initially reported cases in Africa and the Basic Reproductive Number of COVID-19, reported cases in Africa are likely not a good representation of the COVID-19 epidemic in Africa. African countries general have shown low COVID-19 testing statistics and lack COVID-19 surveillance programs (Dzinamarira, Dzobo & Chitungo, 2020). ARI, therefore, will be adapting its Base Case COVID-19 Model for South Africa (a country with relatively better COVID-19 testing statistics and surveillance programs) to other African Countries. To achieve this we will use **Adjustment factors** on model parameters. The Adjustment Factors can be found in the ARI Parameters Sheet in the Model.

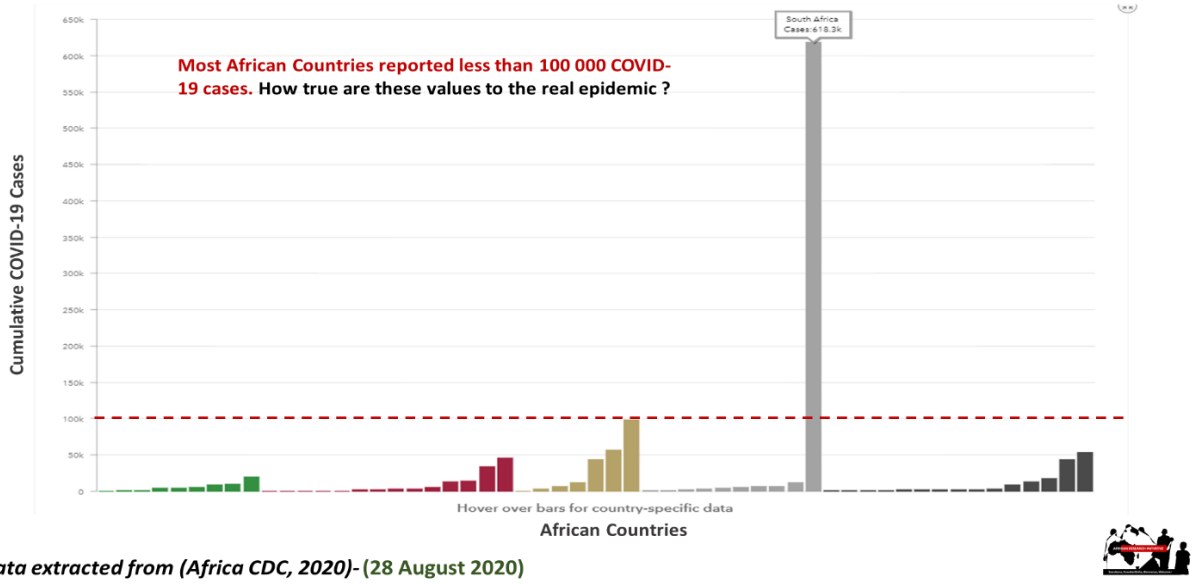


Figure 4: African Reported Cumulative COVID-19 Cases as of 28 August 2020

Adjustment of the Effective Daily Contact Number (β)

To adjust the effective Daily Contact Number, an assessment of the country activity was made particularly Lockdown measures implemented in the Country Activities and these measure/conditions will be compared to Table 3. This factor in the model is referred to as the Lockdown Factor (L_f). A Lockdown Factor (L_f) will be determined from the comparison.

Table 3: Reduction in the Effective Daily Contact Number (Lockdown Factor (L_f)) in the different National Lockdown Alert Levels in South Africa compared to the No-lockdown Scenario

COVID-19 Preventative Measure	Alert Lockdown Level	Reduction in β (day-1) (Base on South Africa)	Lockdown Measures/Conditions
National Lockdown	5	71.1	Movement Restrictions; Limited Services to Essential Services; Border and Air Space Closure; Enforcement of strick non-essential movement.
National Lockdown	4	65.4	Movement Restrictions; Border and Air Space Closure; Limited Services to Essential Services and slight allowance for some services.
National Lockdown	3	57.0	Border and Air Space Closure; Interprovincial travel limited to essential business, relocation and funerals. Operations of all businesses with the condition of Strict Hygiene Protocols.

Adjustment of the Proportion of Symptomatic Cases (ξ_2)

The risk of Age and disease in the development of COVID-19 symptoms was determined using ARI's COVID-19 Age-Disease Risk factor Calculator. The risk factor accounts for Age, HIV, TB, Hypertension and Diabetes in the development of symptoms in the extended country. The proportion of symptomatic cases (ξ_2) will be adjusted using the risk ratio (RR), AGE, DISEASE COVID-19 obtained from (ARI, 2020) and **calculated** in the **Age & Co-morbidity Risk Sheet** and **final input** found in the **ARI Parameters Sheet** using Equation 64:

$$Adjusted\ \xi_2 = \frac{\sum(AGE,Disease\ COVID-19\ RF,Symptoms,A \times Estimated\ Disease\ \ Prevalance\ in\ COVID-19\ Reported\ Cases\ (n),A,i)}{\sum(AGE,Disease\ COVID-19\ RF,Symptoms,SA \times Estimated\ Disease\ \ Prevalance\ in\ COVID-19\ Reported\ Cases\ (n),SA,i)} \times \xi_{2,SA}$$

Equation 64

The Adjusted ξ_2 will then be used as the input in the extended country.

Adjustment of the Proportion of Severe and Critical Cases (ξ_4)

The risk of Age and disease in the development of COVID-19 severe & critical symptoms was determined using ARI's COVID-19 Age-Disease Risk factor Calculator. The risk factor accounts for Age, HIV, TB, Hypertension and Diabetes in the development of severe and critical symptoms in the extended country. The proportion of severe and critical cases (ξ_4) will be adjusted using the risk ratio AGE, DISEASE COVID-19 RR Severe & Critical Symptoms obtained from (ARI, 2020) and **calculated** in the **Age & Co-morbidity Risk Sheet** and **final input** found in the **ARI Parameters Sheet** using Equation 65:

$$Adjusted\ \xi_4 = \frac{\sum(AGE,Disease\ COVID-19\ RF,SEVERE\ \&CRITICAL\ Symptoms,A \times Estimated\ Disease\ \ Prevalance\ in\ COVID-19\ Hospitalised\ Cases\ (n),A,i)}{\sum(AGE,Disease\ COVID-19\ RF,SEVERE\ \&CRITICAL\ Symptoms,SA \times Estimated\ Disease\ \ Prevalance\ in\ COVID-19\ Hospitalised\ Cases\ (n),SA,i)} \times \xi_{4,SA}$$

Equation 65

The Adjusted ξ_4 will then be used as the input in the extended country.

Adjustment of the Death Rate in Hospitalised Cases (μ_1)

The risk of Age and disease in the death of Hospitalised COVID-19 cases was determined using ARI's COVID-19 Age-Disease Risk factor Calculator. The risk factor accounts for Age, HIV, TB, Hypertension and Diabetes in the death of Hospitalised COVID-19 cases in the extended country. The death of Hospitalised COVID-19 cases (μ_1) will be adjusted using the risk ratio AGE, DISEASE COVID-19 RR COVID-19 Deaths obtained from (ARI, 2020) and **calculated** in the **Age & Co-morbidity Risk Sheet** and **final input** found in the **ARI Parameters Sheet** using Equation 66:

$$Adjusted\ \mu_1 = \frac{\sum(AGE,Disease\ COVID-19\ RF,Deaths,A \times Estimated\ Disease\ \ Prevalance\ in\ COVID-19\ Death\ Cases\ (n),A,i)}{\sum(AGE,Disease\ COVID-19\ RF,Deaths,SA \times Estimated\ Disease\ \ Prevalance\ in\ COVID-19\ Death\ Cases\ (n),SA,i)} \times \mu_{1,SA}$$

Equation 66

The Adjusted μ_1 will then be used as the input in the extended country.

Adjustment of the Hospitalisation Rate (h)

To account for the difference in Health care systems between the base and extended cases. The hospitalisation rate will be adjusted based on the number of hospitals, population and the percentage of the population outside 2-h travel time (UI) from hospitals using **Equation 67**:

$$Adjustment\ in\ h = \frac{Hospitals,Country}{Hospitals,SA} \times \frac{Population,SA}{Population,Country} \times \frac{UI,SA}{UI,Country} \times h$$

Equation 67

The Adjusted h will then be used as the input in the extended country.

Limitations

The major limitation of the ARI Model is accurate data in seeding the models and uncertainty of parameter values as COVID-19 is a relatively new disease with limited information. The risk factors in the model are limited to Age, HIV, TB, Diabetes and Hypertension due to limited data in disease prevalence which is required to calculate the risk factors. The limitation with the risk factor will most likely have a significant effect where other diseases are of high prevalence such as Malaria in Western Africa. The models will be adjusted continuously as new information about COVID-19 or data on other factors or diseases in Africa is obtained.

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