ACTUARIAL SOCIETY OF SOUTH AFRICA

Quantifying Risk, Enabling Opportunity.

Covid-19 model sessional meeting

2020 05 06

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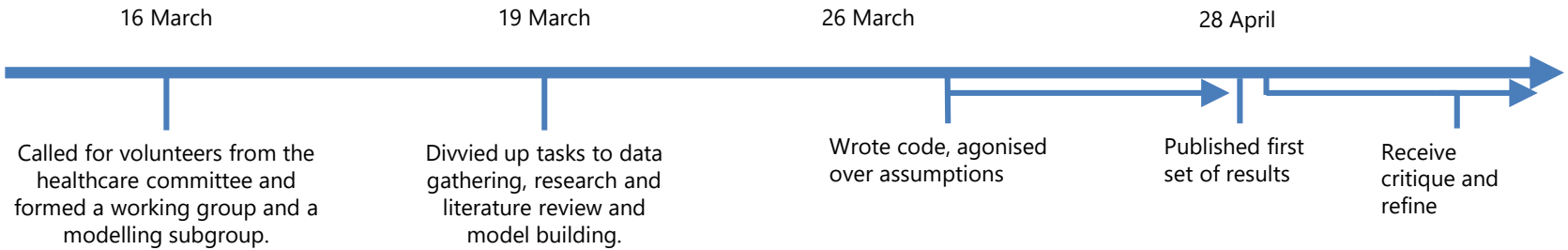
Quantifying Risk, Enabling Opportunity.

Update on ASSA Covid-19 model

Barry Childs



Approach is to produce a model for use by broader profession that is sound in its basis and provides guidance in its application.

Special thanks to:

Percept	NMG
Clinix	3One
Alexander Forbes	Discovery
Medscheme	Insight

Local national modelling efforts were driven by the NICD on behalf of the DOH, with competing models tabled by MASHA, HERO and SACEMA.

Other local models developed for different purposes.

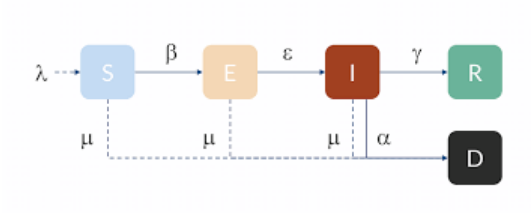
Internationally, research comes out almost as fast as viral spread. Imperial College London were among first internationally to produce estimates that shocked policymakers into action.

Data availability, the media, and easy to use data visualisation allowed dashboards to bloom and armchair epidemiologists everywhere to emerge.

Pandemic of data and opinions.

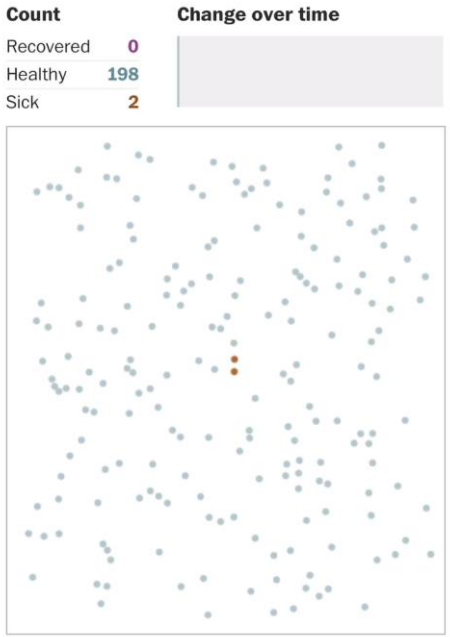
Primarily 2 model choices

Susceptible, Exposed, Infected, Removed

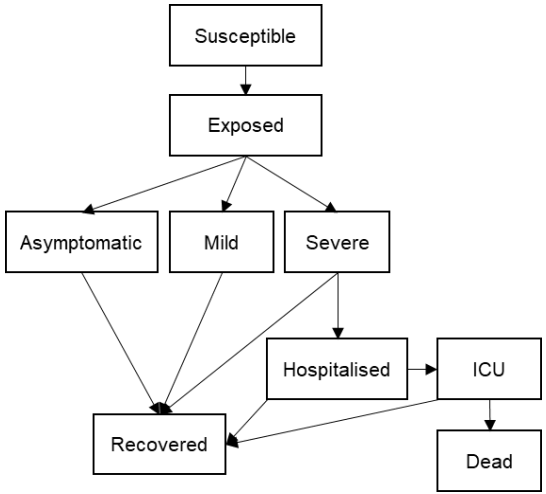


$$
\begin{aligned}
\frac{dS}{dt} &= \mu(N-S) - \beta\frac{SI}{N} - \nu S \\
\frac{dE}{dt} &= \beta\frac{SI}{N} - (\mu+\sigma)E \\
\frac{dI}{dt} &= \sigma E - (\mu+\gamma)I \\
\frac{dR}{dt} &= \gamma I - \mu R + \nu S \\
N &= S + E + I + R
\end{aligned}
$$

Agent Based Model



Model structure



Base parameters

- *R0 = 3*
- *Proportion of asymptomatic cases = 75%*
- *Relative Infectiousness of asymptomatic cases (to symptomatic cases) – 50%*
- *30% of mild cases detected, all severe and critical cases detected**
- *Lockdown effect = 60% x R0*
- *NPIs after lockdown = 75% x R0*
- *Infectiousness pre isolation: Asymptomatic 10 days, Mild 7 days, Severe 2.3 days,*
- *Severe isolated in hospital for 3.7 days*
- *Hospital stay: 10 days if not critical, 6 critical days if critical plus 10 days in ICU if recover or 6 if die*
- *Proportion of admissions ending in ICU =21.3%.*

Scenario 2 (else equal to base)
- *R0 = 2.6*
- *Asymptomatic proportion = 50%*

Scenario 3 (else equal to base)
- *Lockdown effect = 50% x R0*
- *NPIs after lockdown effect = 70% x R0*

Scenario 4 (else equal to base)
- *Lockdown effect = 70% x R0*
- *NPIs after lockdown effect = 80% x R0*

Challenges

Too much (often conflicting) information

Pace of information change

Missing pieces

Unknowns

Treatments
Vaccine
Immunity
Interventions
Long term morbidity
True IFR
Missing deaths

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ASSA Covid-19: Model detail

Dave Strugnell

"A SIMPLE SEIR MODEL"

Modeling our survival in a zombie apocalypse

João Paulo A. de Mendonça,* Leonardo M. V. Teixeira, and Fernando Sato
Dep. de Física, Universidade Federal de Juiz de Fora, Brazil

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Original Article

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ZombieApocalypse: Modeling the social dynamics of infection and rejection

Jan R Riebling[1] and Andreas Schmitz[2]

Abstract
In this article, we propose a model that we call ZombieApocalypse and that relies on agent-based simulation on a dynamic network topology. We simulate three strategies common to the zombie mythology and the sociology of figurational dynamics by Norbert Elias: cutting ties, being sentimental, and stigmatization. The simulation results are analyzed on two dimensions: the outcome for the populations of zombies and humans as well as the resulting changes in topology. We show that the introduction of social dynamics into these models leads to unexpected outcomes. Implications for more "serious" research on general models of infection and social dynamics are discussed.

Keywords
Infectious diseases, simulation, social networks, figurational dynamics, zombies

When zombies attack!: Mathematical modelling of an outbreak of zombie infection

Philip Munz[1], Ioan Hudea[2], Joe Imad[3], Robert J. Smith?[4*]

JOURNAL OF MICROBIOLOGY & BIOLOGY EDUCATION, March 2016, p. 137-142
DOI: http://dx.doi.org/10.1128/jmbe.v17i1.1066
Scientific Citizenship

Equations of the End: Teaching Mathematical Modeling Using the Zombie Apocalypse †

Eric T. Lofgren[1]*, Kristy M. Collins[2], Tara C. Smith[3], and Reed A. Cartwright[4]
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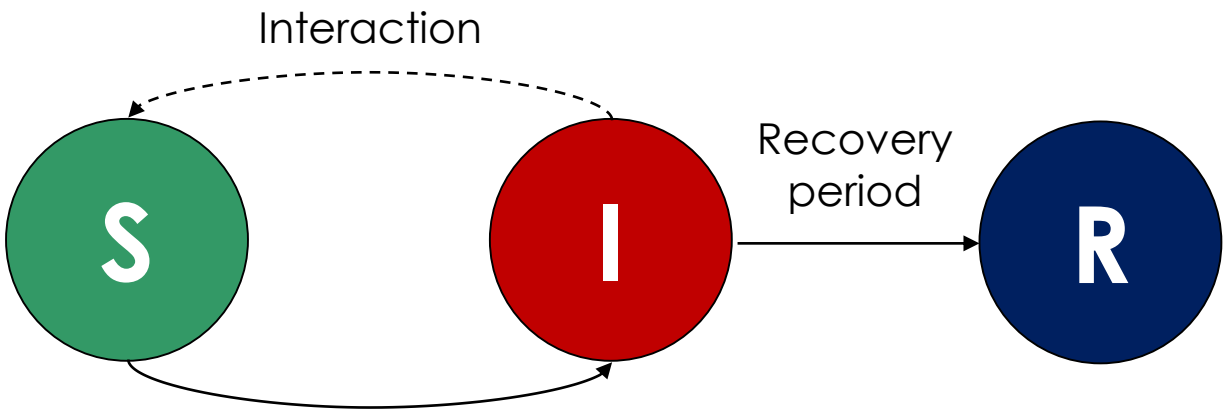
[3]*College of Public Health, Kent State University, Kent, OH 44242,*
[4]*School of Life Sciences and the Biodesign Institute, Arizona State University, Tempe, AZ 85287*

Mathematical models of infectious diseases are a valuable tool in understanding the mechanisms and patterns of disease transmission. It is, however, a difficult subject to teach, requiring both mathematical expertise and extensive subject-matter knowledge of a variety of disease systems. In this article, we explore several uses of zombie epidemics to make mathematical modeling and infectious disease epidemiology more accessible to public health professionals, students, and the general public. We further introduce a web-based simulation, White Zed (http://cartwrig.ht/apps/whitezed/), that can be deployed in classrooms to allow students to explore models before implementing them. In our experience, zombie epidemics are familiar, approachable, flexible, and an ideal way to introduce basic concepts of infectious disease epidemiology.

THE SIMPLEST SIR MODEL



Susceptible: $\frac{dS}{dt} = -\beta SI$

Infected: $\frac{dI}{dt} = \beta SI - \gamma I$

Removed: $\frac{dR}{dt} = \gamma I$

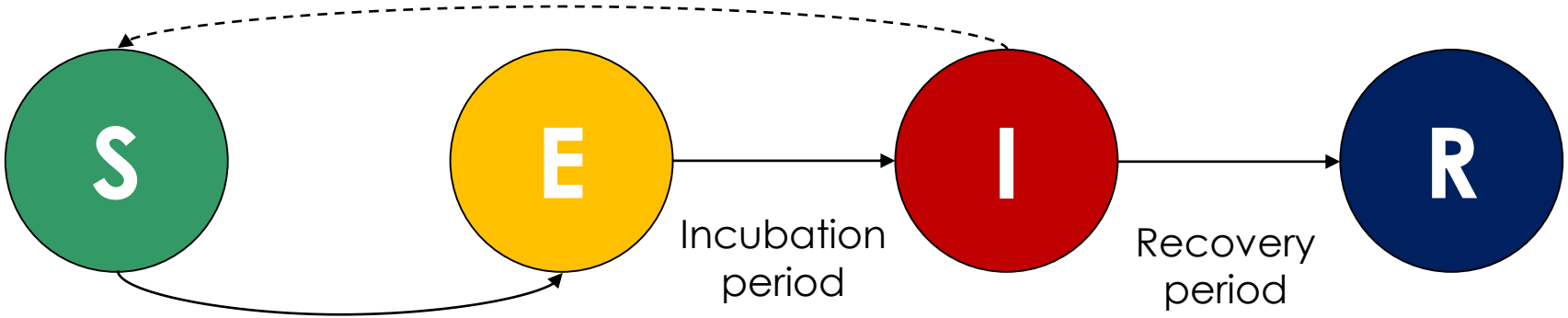
THE BASIC REPRODUCTION NUMBER

$$R_0 = \frac{\beta}{\gamma}$$

i.e. ratio of rate of infectious spread (essentially, mean number of contacts x probability of transmission per contact) to rate of recovery.

Measures the mean number of secondary infections caused by a single infected individual, *given an entirely susceptible population.*

A SIMPLE SEIR MODEL



Susceptible: $\frac{dS}{dt} = -\beta SI$

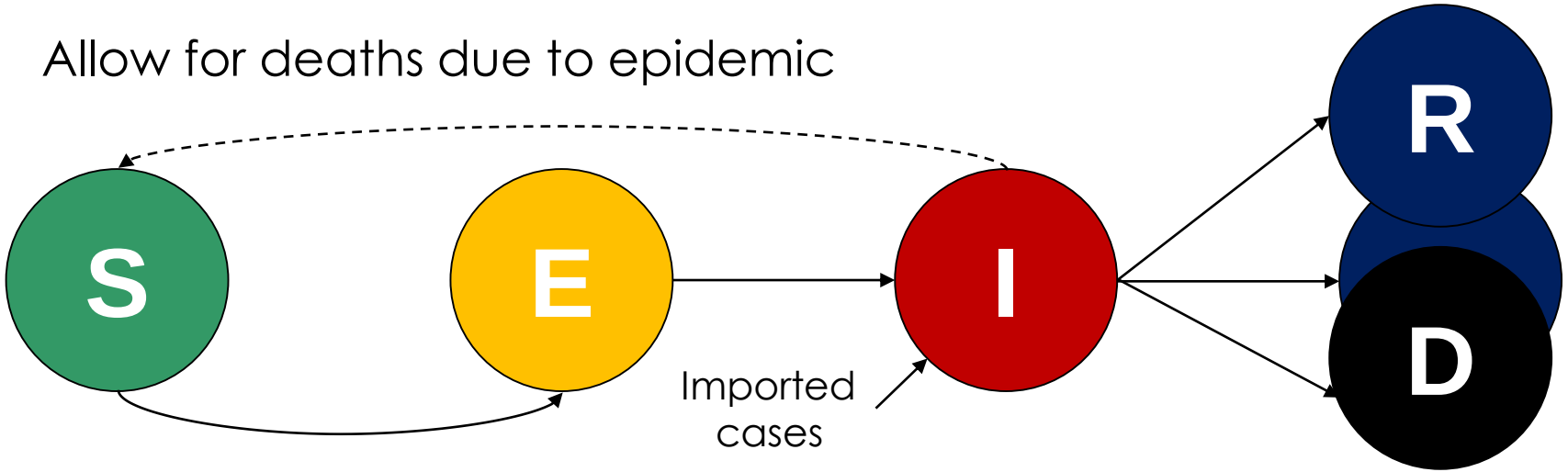
Infected: $\frac{dI}{dt} = \alpha E - \gamma I$

Exposed: $\frac{dE}{dt} = \beta SI - \alpha E$

Removed: $\frac{dR}{dt} = \gamma I$

ADDING SOME COMPLEXITY

- Allow for births/entrants to population
- Allow for non-epidemic deaths – not incorporated
- Allow for deaths due to epidemic



ASSA MODEL PURPOSE

- To contribute to national debate, though not to supplant work of epidemiological experts
- To provide a flexible framework to allow for the application of actuarial judgement
- To model the impact of Covid-19 on mortality as well as healthcare resource utilisation
- To allow for the modelling of select populations

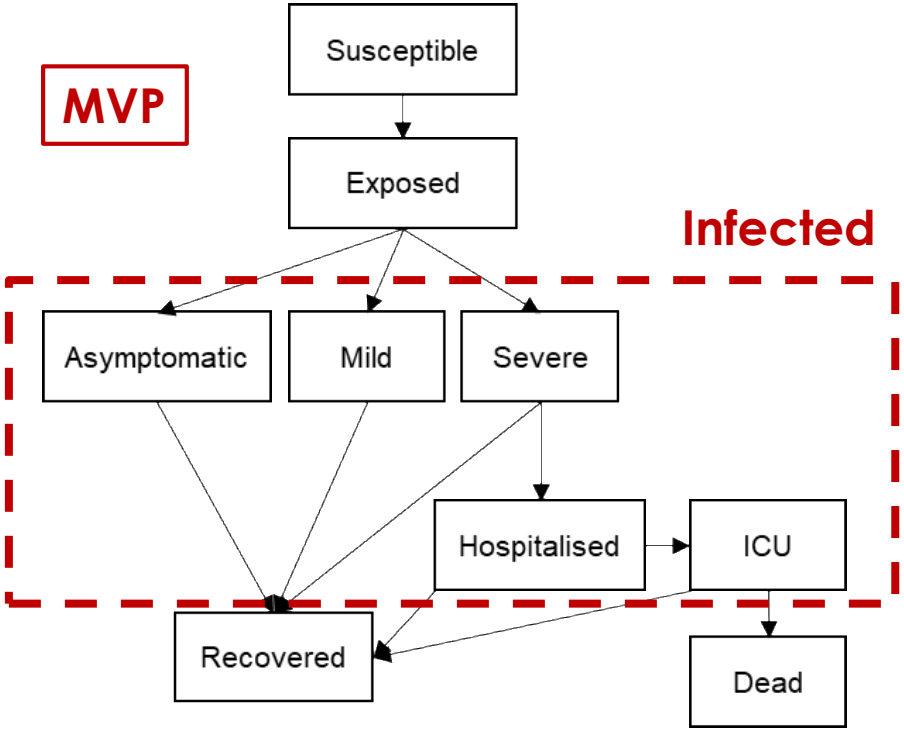
Remain part of conversation, not echo chamber

User-friendly front-end to Python back-end

Multiple infected states, including hospitalisations

Multiple sub-populations

ADDING MORE COMPLEXITY



Cases categorised by ultimate severity: asymptomatic, mild, severe.

Hospital utilisation from severe infections.

At present, one mortality pathway: via ICU.

ADDING MUCH MORE COMPLEXITY

Population sub-divided by:

- **Age**: currently allowed for by differential severity outcomes in 10-year age-bands, informed by Ferguson et al. (2020)
- **Sex**: not yet allowed for
- **Population density**: not yet allowed for (but allowance for differential infectious spread in different sub-populations is in development)
- **Co-morbidity risk**: not yet allowed for

THIS MUCH MORE COMPLEXITY

$$\vec{R}^{(g)}_{0,eff} = \vec{Q}_{SE} / \left[diag(\boldsymbol{Q}^{(g)}_{II}) \vec{\delta}^{(g)} + \vec{Q}^{(g)}_{IR} \odot (1 - \vec{\beta}^{(g)}) \odot (1 - \vec{\delta}^{(g)}) + \vec{Q}^{(g)}_{ID} \odot \vec{\beta}^{(g)} \odot (1 - \vec{\delta}^{(g)}) \right],$$

$$\begin{aligned}
\frac{d}{dt} S^{(g)} &= -\frac{1}{N} \left[\sum_m \left(\vec{s}(t) \odot \vec{Q}_{SE} \right) \cdot \vec{I}^{(m)} \right] S^{(g)} \\
\frac{d}{dt} E^{(g)} &= \frac{1}{N} \left(\sum_m \vec{Q}_{SE} \cdot \vec{I}^{(m)} \right) S^{(m)} - T^{-1}_{inc} E^{(g)} \\
\frac{d}{dt} \vec{I}^{(g)} &= \vec{\alpha}^{(g)} T^{-1}_{inc} E^{(g)} - \boldsymbol{Q}^{(g)}_{II} f_\delta(\vec{\delta}^{(g)}) \odot \vec{I}^{(g)} \\
&\quad - \vec{Q}^{(g)}_{IR} \odot (1 - f_\beta(\vec{\beta}^{(g)})) \odot (1 - f_\delta(\vec{\delta}^{(g)})) \odot \vec{I}^{(g)} \\
&\quad - \vec{Q}^{(g)}_{ID} \odot f_\beta(\vec{\beta}^{(g)}) \odot (1 - f_\delta(\vec{\delta}^{(g)})) \odot \vec{I}^{(g)} \\
&\quad + \vec{Z}^{(g)}(t) \\
\frac{d}{dt} \vec{R}^{(g)} &= \vec{Q}^{(g)}_{IR} \odot (1 - f_\beta(\vec{\beta}^{(g)})) \odot (1 - f_\delta(\vec{\delta}^{(g)})) \odot \vec{I}^{(g)} \\
\frac{d}{dt} \vec{D}^{(g)} &= \vec{Q}^{(g)}_{ID} \odot f_\beta(\vec{\beta}^{(g)}) \odot (1 - f_\delta(\vec{\delta}^{(g)})) \odot \vec{I}^{(g)}
\end{aligned}$$

$$R_0 = \frac{1}{N} \sum_g N^{(g)} \vec{\alpha}^{(g)} \cdot \vec{R}^{(g)}_{0,eff}.$$

Effective R_0 now a little more complex to determine.

Vector/matrix representation of system of ODEs.

KEY PARAMETERS

Parameter	Influence
Baseline R_0	Determines pace of spread as well as ultimate proportion infected at herd immunity threshold, given no intervention
Asymptomatic proportion	Determines how far infection has already spread, which influences future trajectory and associated mortality/healthcare impacts
Asymptomatic relative infectiousness	Since asymptomatic cases are less likely to isolate, determines extent of infectious spread from this key vector
Lockdown relative R_t	Impact on infectious spread due to Level 5 lockdown measures
Post-lockdown relative R_t	Impact on infectious spread due to post-Level 5 measures
Age-related rates of hospitalisation, ICU admission and mortality	Direct impact on outcomes of interest
Lengths of stay in states	Impact on spread and peak demand

TOP OF THE DEVELOPMENT PLAN

- Sampling Important Resampling approach to calibration and quantification of uncertainty
- Sub-population differentiation in infectious spread
- Review of parameters (literature and emerging data)
- Review of structure (e.g. non-ICU mortality pathways?)
- And response to the many considered, and appreciated, comments on the initial model release

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ASSA COVID-19: Literature Review

Adam Lowe

Types of Literature

A large amount of research is being conducted as the COVID-19 pandemic unfolds:

- Most of it is made available pre-peer review for timing reasons;
- It is often based on very low data volumes;
- Much of the initial research was focused on Wuhan and other regions of China, but newer research is coming out of Europe and the US almost daily; and
- Expectedly the range of results and potential assumptions reported is broad, and research can be found to support most assumption sets.

Key Assumptions Guided by Research

Initial Transmission Rate (R0)

- Number of contacts per infected life
  - Represents potential transfer of infection

Levels of Severity of Cases

- Proportion of Asymptomatic Cases
- Breakdown of Symptomatic Cases

Hospitalisation Rates and Lengths of Stay

- Proportion of Symptomatic Cases Hospitalised
- ICU Usage
- Days Spent per Ward

Infection and Case Fatality Rates

- Implied in the ASSA model
- Differ in the denominator – IFR uses all infections, CFR only reported confirmed cases

Potential Impact of Interventions

- Lockdown
- Case Isolation
- Social Distancing

Initial Transmission Rates (R0)

Study	Data Source	Central Estimate	95% CI
Wu, Leung and Leung	Wuhan, Dec ‘19 – Jan ‘20	2.68	2.47 - 2.86
Shen, Peng, Xiao and Zhang	Wuhan and Hubei Province, Dec ’19 – Jan ‘20	4.71 (initial) 2.08 (end)	4.50 – 4.92 1.99 – 2.18
Remuzzi and Remuzzi	Italy, Feb-Mar ‘20	3.0	2.76 – 3.25
Zhao et. al.	Diamond Princess	2.1	2.0 -2.2

Estimates range mostly from 2.0 to 3.5 – some studies even fall outside this.

Levels of Severity: Asymptomatic Cases

Study	Data Source	Central Estimate	95% CI
Li et. al.	Wuhan, Dec ‘19 – Jan ‘20	86%	82% - 90%
Kenji et. al.	Diamond Princess	17.9%	15.5% - 20.2%
Verity et. al.	Wuhan, repatriation data	45%	40% - 50%
Michael Day	China, NHC	78%	N/A
Kissler et. al.	Various, including previous SARS viruses	77.5%	75% - 80%
deCODE, Iceland National Health	Iceland live testing	50%	N/A

Researchers at Oxford University compiled a meta-study of reported proportions and found a range of 5% to 80% was reported – very dependent on definition of ‘asymptomatic’ and testing rates.

Levels of Severity: Symptomatic Cases

Most studies cite the WHO/China Joint Mission Report. Of reported cases:

- 80% are mild/moderate
- 14% severe; and
- 6% critical.

Most studies take this to mean 'severe' cases will require hospitalization and 'critical' cases will require ventilation/intensive care. ICL splits this by age band

Age-group (years)	% symptomatic cases requiring hospitalisation	% hospitalised cases requiring critical care	Infection Fatality Ratio
0 to 9	0.1%	5.0%	0.002%
10 to 19	0.3%	5.0%	0.006%
20 to 29	1.2%	5.0%	0.03%
30 to 39	3.2%	5.0%	0.08%
40 to 49	4.9%	6.3%	0.15%
50 to 59	10.2%	12.2%	0.60%
60 to 69	16.6%	27.4%	2.2%
70 to 79	24.3%	43.2%	5.1%
80+	27.3%	70.9%	9.3%

Levels of Severity: Duration of Infectiousness

Literature on asymptomatic/unreported cases is (obviously) limited, but generally assumes they don't specifically isolate. ICL assumptions: mild cases when diagnosed will isolate within a day, severe cases spend 8 days in hospital and critical cases 16 days, including 10 in ICU.

China data showed the following average time to specific outcomes based on a sample of cases:

Outcome	Mean (days)	S.D. (days)	Number of reports
First consultation	2.10	2.65	172
Hospitalised	5.76	4.22	267
Recovered/Discharged	20.51	6.69	65
Death	16.00	8.21	8
Hospitalised duration	14.51	7.36	57

Mortality Rates (IFRs and CFRs)

Study	Data Source	Type	Central Estimate
Verity et. al.	Wuhan, repatriation data	CFR IFR	1.38% 0.66%
WHO/China Joint Mission	China	CFR	0.7%
Dorigatti et. al.	Wuhan, Hubei and repatriation	IFR	0.8%
Wang et. al.	China, hospital data	CFR	2.9%

CFR is a lag indicator, many deaths happen a long time after infection. IFR may never be known unless entire populations are tested.

Effectiveness of Interventions

Studies into the effectiveness of interventions are limited by data. Early evidence is that:

- The shutdown of Wuhan reduced transmission rates by between 55% and 69% depending on the study;
- Italian data suggested a 30% impact of the restrictions imposed in Northern Italy;
- US researchers calculated a 50-60% impact from social distancing and 85% from lockdown in China, but noted a reduced social distancing impact of 35-40% in the US data.

Effectiveness of Interventions

ICL modelled a variety of scenarios:

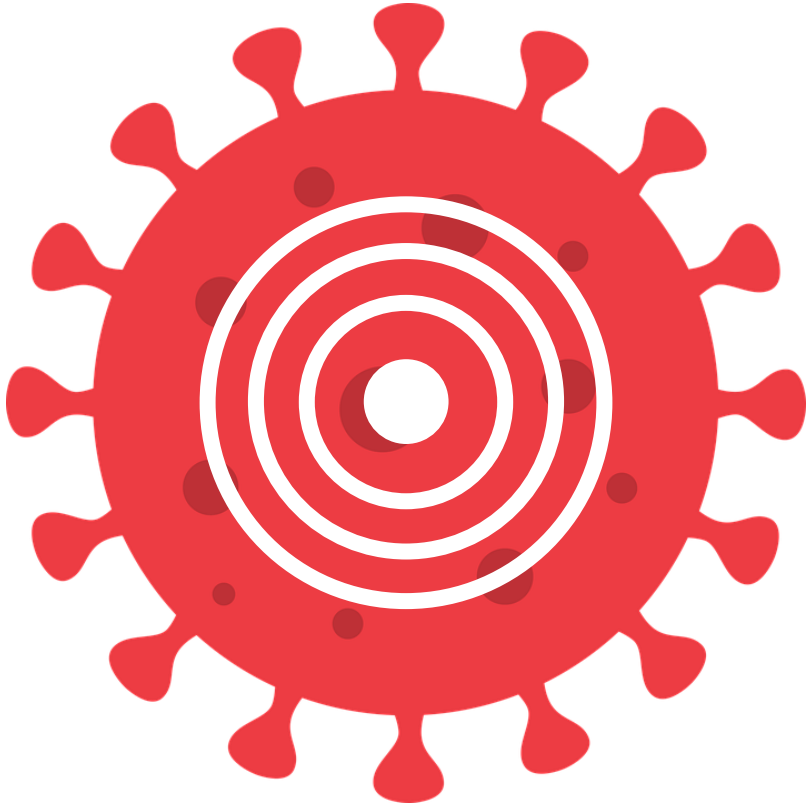
Table 3. Mitigation options for GB. Relative impact of NPI combinations applied nationally for 3 months in GB on total deaths and peak hospital ICU bed demand for different choices of cumulative ICU case count triggers. The cells show the percentage reduction in peak ICU bed demand for a variety of NPI combinations and for triggers based on the absolute number of ICU cases diagnosed in a county per week. PC=school and university closure, CI=home isolation of cases, HQ=household quarantine, SD=social distancing of the entire population, SDOL70=social distancing of those over 70 years for 4 months (a month more than other interventions). Tables are colour-coded (green=higher effectiveness, red=lower). Absolute numbers are shown in Table A1.

	Trigger (cumulative ICU cases)	PC	CI	CI_HQ	CI_HQ_SD	CI_SD	CI_HQ_SDOL70	PC_CI_HQ_SDOL70
R_0=2.4 Peak beds	100	14%	33%	53%	33%	53%	67%	69%
	300	14%	33%	53%	34%	57%	67%	71%
	1000	14%	33%	53%	39%	64%	67%	77%
	3000	12%	33%	53%	51%	75%	67%	81%
R_0=2.2 Peak beds	100	23%	35%	57%	25%	39%	69%	48%
	300	22%	35%	57%	28%	43%	69%	54%
	1000	21%	35%	57%	34%	53%	69%	63%
	3000	18%	35%	57%	47%	68%	69%	75%
R_0=2.4 Total deaths	100	2%	17%	31%	13%	20%	49%	29%
	300	2%	17%	31%	14%	23%	49%	29%
	1000	2%	17%	31%	15%	26%	50%	30%
	3000	2%	17%	31%	19%	30%	49%	32%
R_0=2.2 Total deaths	100	3%	21%	34%	9%	15%	49%	19%
	300	3%	21%	34%	9%	17%	49%	20%
	1000	4%	21%	34%	11%	21%	49%	22%
	3000	4%	21%	34%	15%	27%	49%	24%

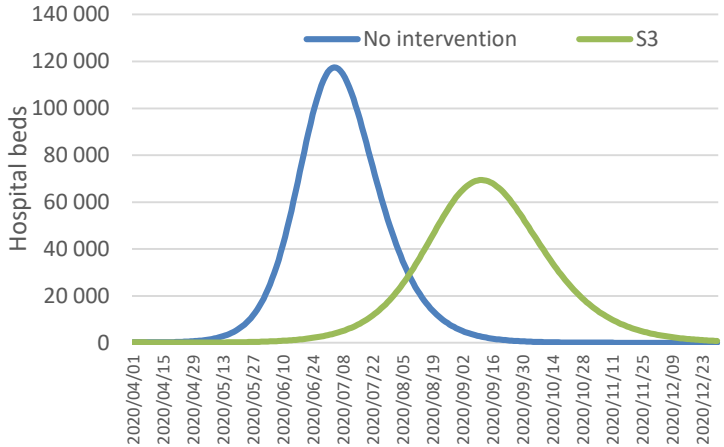
Other Assumptions / Research Areas

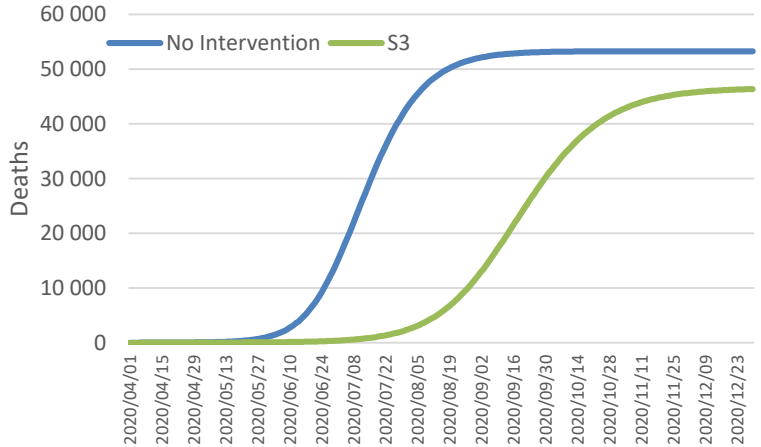
- Effect of population density (appears from research to be steep at lower densities and flat at high densities);
- Key co-morbidities
  - From research cardiovascular conditions and diabetes had greatest impact on mortality
  - HIV/TB weren't tested in the research – could be key for SA

Model results



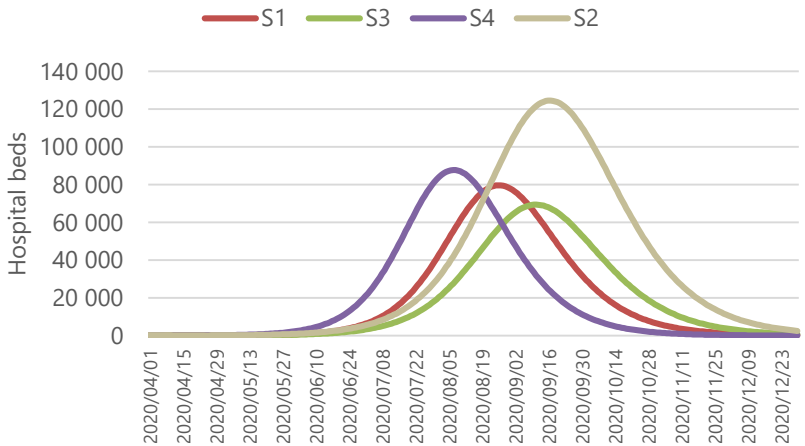
“Flatten the curve”

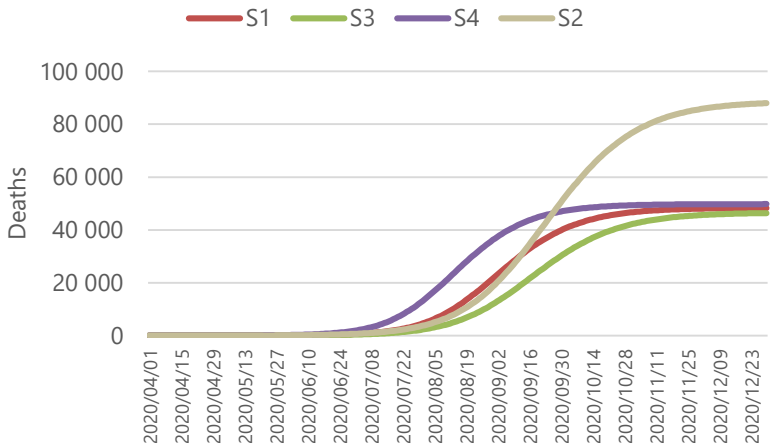




Non Pharmaceutical Interventions to slow the spread of disease aim to flatten the curve – that is, slow disease spread to allow time to build health system capacity and response, and improve suppression and mitigation efforts.

First set of scenarios





assacovid19.org.za

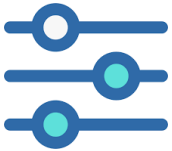
Online version of model
First report and scenarios
Technical model write-up

Planned next steps

Brace for critique

covid19@actuarialsociety.org.za

Online version for users, including code. Technical write up.



More scenarios and testing of key parameters

Mortality
Asymptomatic %
Treatment paths
Weather
Cycles
NPI effects

Refine model to allow for:

Comorbidities
Density
Regions
Movement