Briefing Document.

The 2019 novel Coronavirus - forward view

29th January 2020

Crystallise

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Summary

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As of the 29th of January 2020, the novel coronavirus 2019 (2019-nCov) outbreak had been known to have infected 6,065 people, of whom 132 had died.

How it evolves will be sensitive to:

- the degree of coordinated **international response** to the epidemic,
- whether there is any **seasonality** in the transmission rates, a characteristic of many human coronavirus infections,
- the **basic reproductive rate (R0)** and **case-fatality rate**,
- the rate of development, effectiveness, and distribution of a **vaccine** within a year.

Using SIRD modelling, we have explored optimistic, intermediate, and pessimistic scenarios. All scenarios make an assumption that three quarters of cases are asymptomatic, with a case fatality rate of 0.5%, a basic reproductive number (R0) of 2.5, and a seasonal pattern to transmissibility.

In the pessimistic scenario, with no control measures, the outbreak infects most of the World's population within 6 months and kills over 30 million people.

In the intermediate scenario, control measures halve transmissibility. In this case, we see 350 million cases within one year and over 1 million deaths.

The aggressive control scenario further reduces the number of infections to 8.5 million people, with over 30,000 deaths.

Background

The World Health Organisation (WHO) first became aware of a cluster cases of viral pneumonia in the city of Wuhan, the capital of Hubei province in the Peoples Republic of China, caused by a novel virus. On the 7th of January this novel virus was identified as a coronavirus. Coronaviruses are very common and are one cause of the common cold. However, other strains of coronaviruses are far more dangerous. In 2003, a strain of coronavirus was responsible for 8,096 cases of severe adult respiratory distress syndrome (SARS), and resulted in 774 deaths. Since 2012, the Middle East respiratory syndrome (MERS) has caused 2,494 laboratory confirmed cases, and has resulted in 858 deaths. Figure 1 shows a bubble map of cases globally.

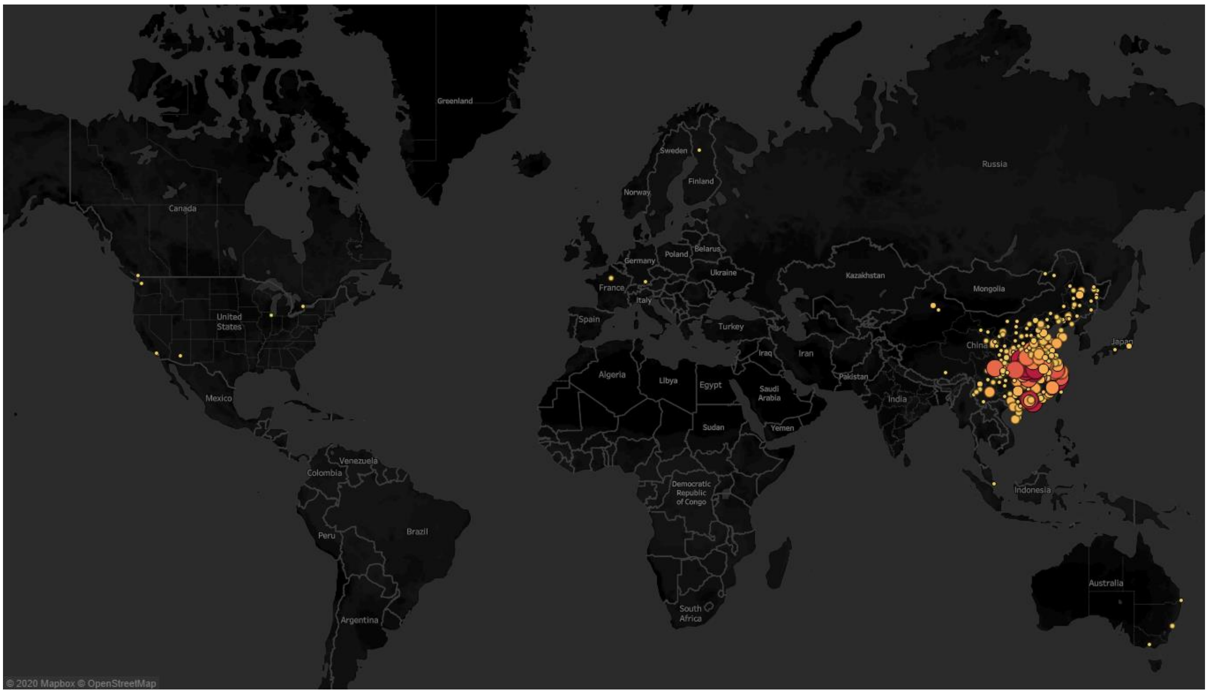

Figure 1 Bubble map of cases of 2019-nCoV showing the density of cases within China compared to the rest of the World.

The case fatality rate of 2019-nCoV appears to be about 3%. This is much less than the 11% rate for the SARS outbreak of 2003 and the crude case fatality rate of 34.5% for MERS(WHO, 2003, 2019; Wang *et al.*, 2020). However, 2019-nCoV does appear to be spreading faster than the 2003 SARS virus: within 5 weeks it has matched the number of cases 2003 SARS accrued over 7 months.

The current numbers of cases and deaths are shown in Table 1.

Table 1 Numbers of cases and deaths from the 2019-nCoV, from the WHO situation reports to the 29th January 2020. (WHO, 2020b)

Date	Deaths	Cases
12-Jan-20	1	41
20-Jan-20	9	282
21-Jan-20	10	314
23-Jan-20	11	581
24-Jan-20	12	846
25-Jan-20	13	1320
26-Jan-20	14	2014
27-Jan-20	15	2798
28-Jan-20	16	4593
29-Jan-20	17	6065

Methods

In this briefing document, the results from a simple naïve projection model and an epidemiological compartmental model of epidemics are presented. These models are used to project cases and deaths forward from the present, with multiple scenarios of control and seasonality to estimate the range of possible impacts. Details of the model parameterisation are given in an appendix.

The future dynamics of the epidemic have been simulated using a Susceptible, Infected, Recovered, and Died (SIRD) epidemiological compartmental model(Kermack and McKendrick, 1927). As it is very early in the development of this epidemic, parameterisation of this SIRD model is difficult. Estimates for the basic reproduction rate[1] (R0) vary from 1.5 to 7.1 with a widely quoted rate of 2.5 in the media, based on a report from Imperial College(Imai *et al.*, 2020; Read *et al.*, 2020; Zhao *et al.*, 2020).

A series of scenarios are modelled with varying estimates of the R0, two case fatality rates (2% and 0.5%), different degrees of infection control interventions and with and without seasonal variation in transmissibility.

[1] The number of additional infections caused by each case when there is no immunity at all in the population.

Results

Naïve projection model

Firstly, a simple naïve projection of the current trends may give some idea of the expected outcomes over the next couple of weeks. Plotting the numbers of cases and deaths against time on a logarithmic y-axis scale, we can see a log-linear trend. If this is projected forwards to the 17th of February (nearly 3 weeks), we can see this would suggest a global number of cases of over 2.5 million, with over 34,000 deaths (Figure 2 and Figure 3).

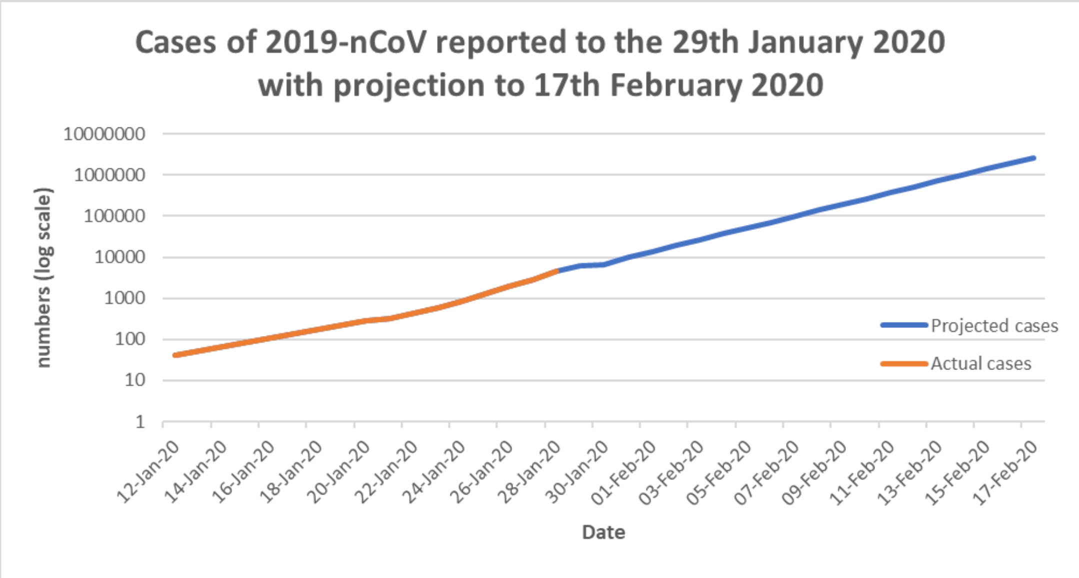

Figure 2 The recorded number of cases up to the 29th January 2020 with a log-linear projection to the 17th February(WHO, 2020b).

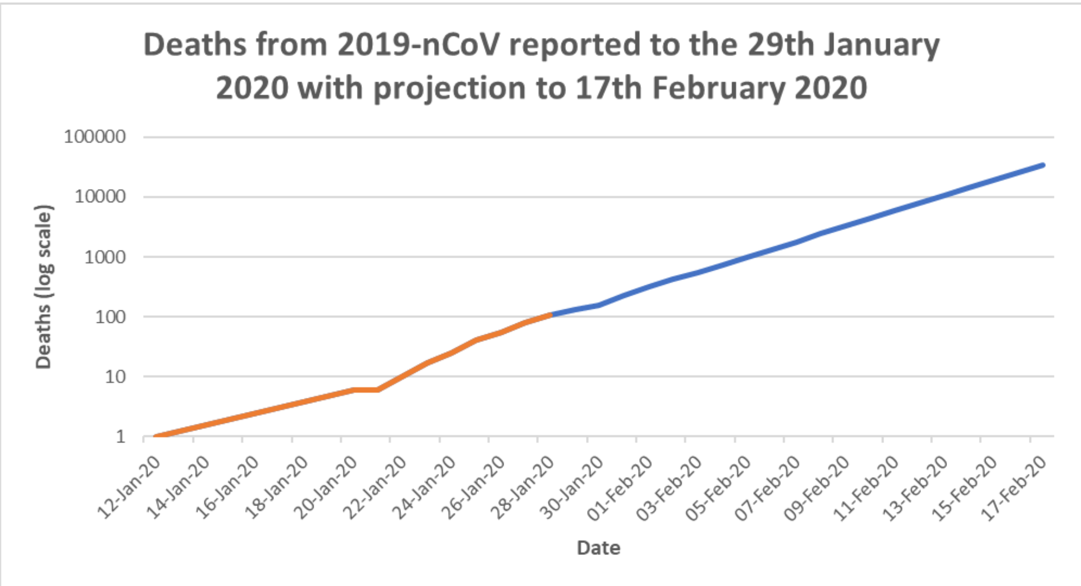

Figure 3 The number of reported deaths from 2019-nCoV up to the 29th January with a log-linear projection to the 17th of February(WHO, 2020b).

SIRD model

Figure 4 shows the results of the SIRD model using an R0 of 2.5, with no subsequent action taken to reduce that number.

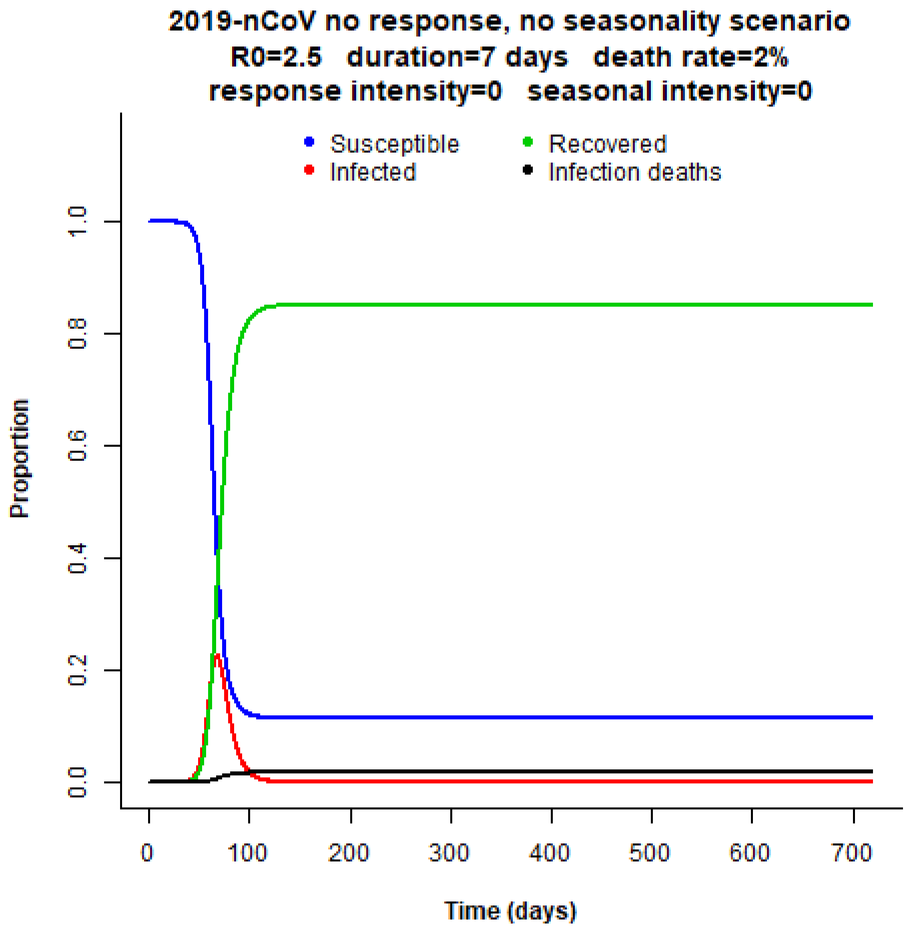

Figure 4 The spread of 2019-nCoV that would be expected with an R0 of 2.5, a duration of 7 days for infectivity, a 2.5% death rate, and with no subsequent modification of the R0 or death rate.

According to this 'do nothing' scenario, in 100 days 6.9 billion people will have been infected and nearly 129 million people will have died globally. The crude case fatality rate of 2% may well be over-estimated, as it is common for respiratory viruses to result in asymptomatic infection, and at least one estimate is that over 70% are asymptomatic(Galanti *et al.*, 2019). If we make an assumption that the true rate of infection is four times the observed number of cases, then we would have a true death rate of about 0.5%. Re-simulation with this figure would suggest that about 33 million would die globally, which is lower than the 1918 global influenza pandemic which killed about 50 million people globally, but in a much shorter time-frame.(Morens and Fauci, 2007)

Fortunately, it is simply not plausible that there would be no reduction of the R0 over time as individuals take steps to avoid infection, and institutions and governments take steps to avoid disease spread. These very alarming projections make an assumption that any efforts to control the spread of the disease are no more effective than they have been up to now, which is an unrealistic assumption. As of the 29th January, the Chinese Lunar holiday has been extended, many cities in

China are in relative quarantine, some major airlines are suspending flights in and out of mainland China, and procedures are in place for handling infected cases in ways that reduce transmission.

We have re-simulated the epidemic with an aggressive response that reduces transmissibility by 10% each week from the second week to a floor of 10%, which is maintained for two weeks before being removed in steps over 3 weeks.

This response would include things like shutting down transport hubs, quarantining affected districts, and closing schools and business, all actions that would be very difficult to maintain for prolonged periods. With this aggressive response, the scale of the outbreak changes very little, but is shifted later into the year with a peak at around 149 days instead of 69 days. This would potentially be a very important achievement, as coronaviruses are typically, but not always, seasonal, and so its impact would be expected to be far lower when most of the global population is experiencing summer. It is hard to estimate the scale of the impact of these measures on transmissibility, but a modelling study from the University of Lancaster estimates that a 99% reduction in all travel, what is effectively a complete, nation-wide travel-ban, would reduce transmissibility by only 25%(Read *et al.*, 2020 - version from 24/1/20). However, closing schools in Japan during the 2009 influenza pandemic was thought to reduce child to child transmissibility about 70%. This suggests that closing workplaces, schools, and collective recreational events could possibly achieve the aggressive 90% reduction when applied in combination with the travel ban. However, this approach is very difficult to achieve and maintain, and is economically very damaging. The evidence for the wearing of standard face masks in public does not suggest any significant impact(Canini *et al.*, 2010).

The SARS epidemic began to decline rapidly in May 2003 and was gone by the end of July. This may have been due to public health measures, but it seems likely that seasonality played a part(Dowell and Shang Ho, 2004). If we repeat this scenario by applying a seasonal reduction in the transmission of the coronavirus with a decline beginning in mid-March, reaching a 90% reduction by mid-May, and then rising again from the beginning of October, then we get the results shown in Figure 5.

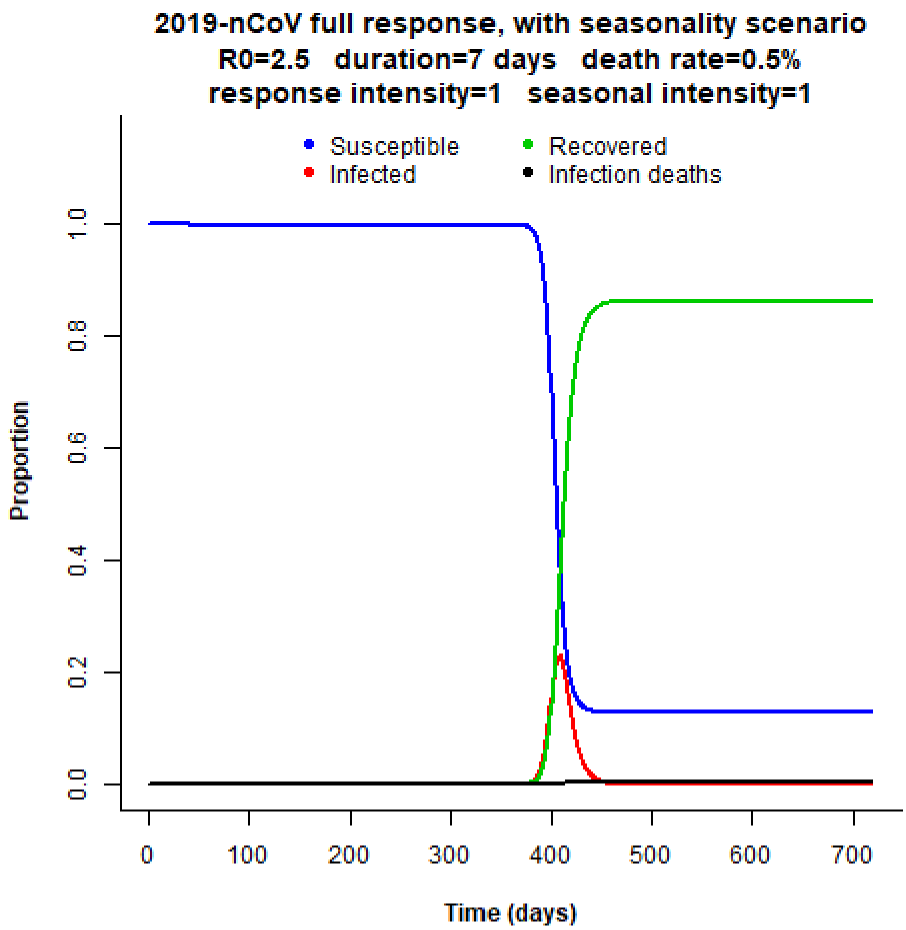

Figure 5 Modelling the epidemic with an assumption of an aggressive response to the outbreak and a seasonal pattern to the transmission.

Again, the scale of the epidemic does not change, it is just pushed back to the late winter of 2020/21. Even an intermediate response that merely halves transmissibility would have a similar effect, delaying the outbreak to mid-winter 2020/21. This buys time for the development of a 2019 novel coronavirus vaccine and does not preclude the option to apply aggressive infection control measures at that time as well. Under this scenario, at one year, the total number of people infected globally would be about 350 million with 1.3 million deaths. Put into perspective, this compares to between 300,000 and 800,000 deaths from seasonal influenza globally every year(Iuliano *et al.*, 2018). As a best-case scenario, a globally coordinated, aggressive programme of infection control measures that reduces transmissibility by 90% would reduce the number of infections at one year to about 8.5 million globally with about 32,000 deaths.

If the true R0 is slightly lower, at 2 further infections per case, then even the intermediate response can dramatically reduce the impact. A 50% reduction in transmission reduces the R0 to 1, stopping the growth of the epidemic. This scenario would result in just over half a million infected, and less than 11,000 deaths.

Weaknesses in model projections

We are still very early in the evolution of this epidemic and there is still a great deal of uncertainty around the assumptions used to parameterise these models. These include the R0, the crude case fatality rate, the rate of asymptomatic infection and the seasonality of the 2019-nCoV (if any). There are also considerable uncertainties around the effectiveness of global infection control responses.

As well as uncertainty in the values used to parameterise the models, the model's structure makes assumptions that are likely to be unrealistic, or at least overly-simplistic:

1) The analysis was deterministic, meaning that it was not possible to generate distributions for the uncertainty of the results. A stochastic model would allow the effects of randomness to be considered.
2) The R0 is assumed to be constant throughout the duration of an individual infection, which would not be the case.
3) The fatality rate is assumed to be constant throughout the duration of an individual infection, which would not be the case.
4) There has been suggestions in the media that the infection can be transmitted before symptoms occur(WHO, 2020a). If true this could reduce the effectiveness of containment measures. The models presented here do not consider this possibility.
5) The compartments in this model are limited to Susceptible, Infected, Recovered and Dead from infection, and does not include compartments for exposure, asymptomatic infection and successful vaccination, which could carry alternative assumptions for the R0.
6) The model treats the global population as homogeneous and freely mixing, without consideration for national or geographical borders, or the effects of age on mortality and transmission.
7) The model does not consider the possibility of further genetic mutation of the coronavirus, which could alter it's transmissibility or virulence.

Conclusion

This epidemic continues to evolve at an alarming rate. This modelling, with an assumption of an R0 of 2.5 and a death rate of 0.5%, would suggest that this epidemic could infect the majority of the World's population within 6 months and kill over 100 million people if it were left completely unchecked. In the most optimistic scenario presented here, which includes an assumption of a seasonal reduction of transmission in summer and an aggressive coordinated global programme of measures to reduce transmission, the number of people infected globally would be kept below 10 million and the number of deaths in the tens of thousands. The intermediate scenario with a 50% reduction in transmission from public health measures would result in a few hundred million infections and over 1 million deaths within a year.

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Appendix

Modelling assumptions

Basic reproductive number scenarios were applied with R0 values of 1.5, 2.0, 2.5, 3.0 and 4.0.

The duration of infectiousness was fixed at 7 days.

Two death rates of 2% and 0.5% were explored based on an assumption that the observed number of cases is one quarter of the total number because of asymptomatic infections.

A death rate of 1% from causes other than 2019-nCoV and a birth rate of 1% per annum were applied, though over a 2-year time horizon, this will have little impact on results.

The model presented here was deterministic with predefined parameter values. To simulate changes in R0 due to seasonality and infection control response, vectors were applied for modifying R0 over time. The impact of infection control measures was applied using the vector shown in Figure 6 that runs from the beginning of the simulation and is applied to the R0 values.

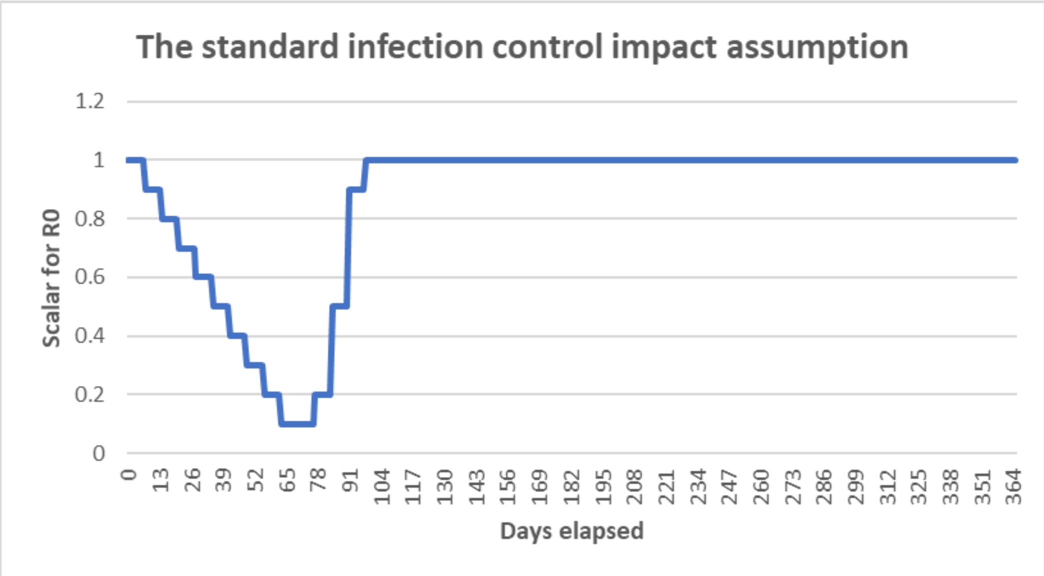


Figure 6 The standard infection control impact scenario. The scalar is used to modify the R0. The scenario lasts 100 days on the assumption this is sufficient to control the infection, or is abandoned as it has failed and is too difficult to sustain.

The assumption is that the full impact of infection control measures on R0 is the most optimistic control scenario, but an additional 'intermediate' impact scenario was also used with a 50% reduction in the impact.

Seasonality was assumed to be present or not present. The impact of seasonality was represented by the vector show in Figure 7 and was linked to the calendar year.

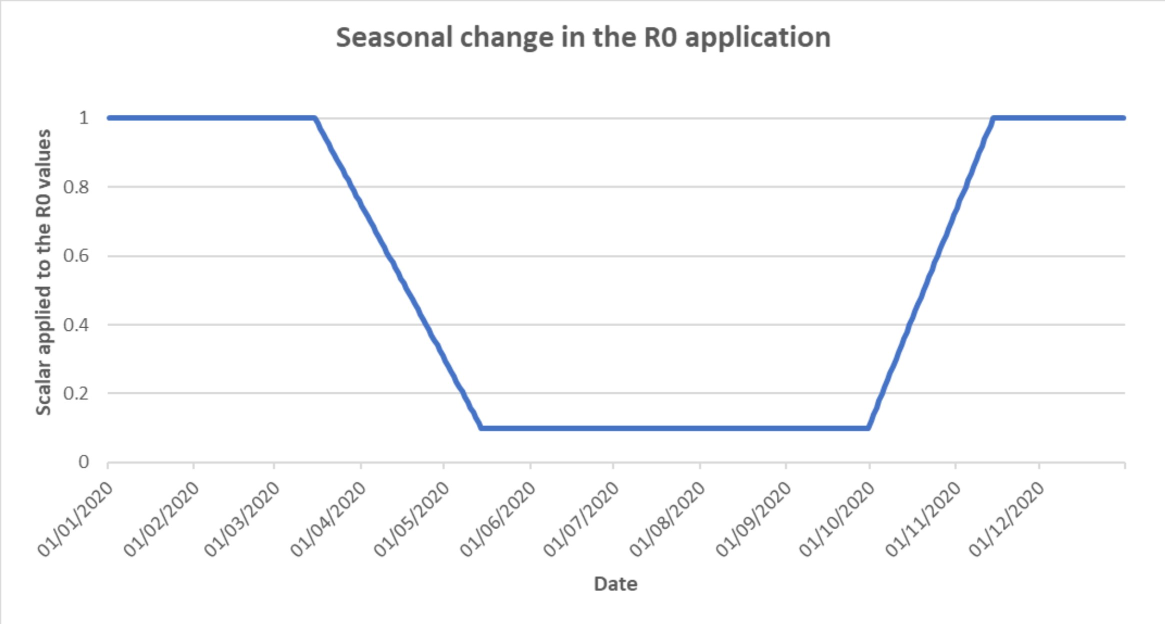
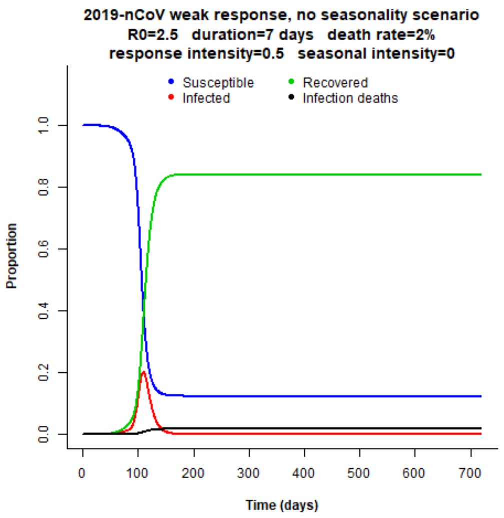
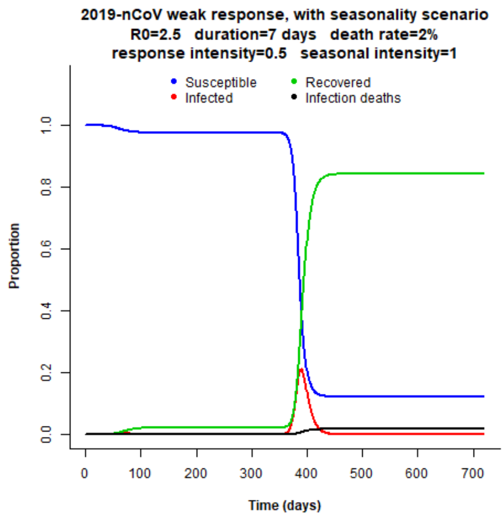
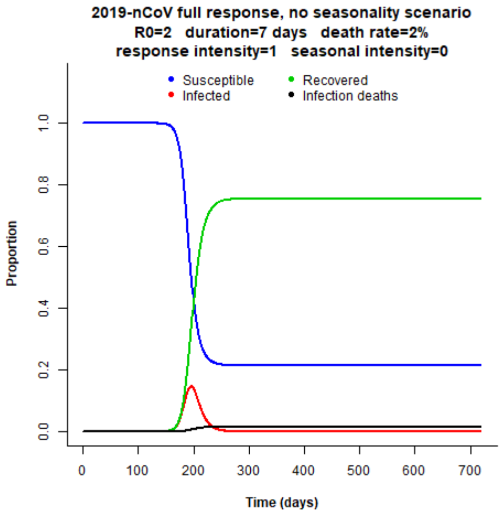


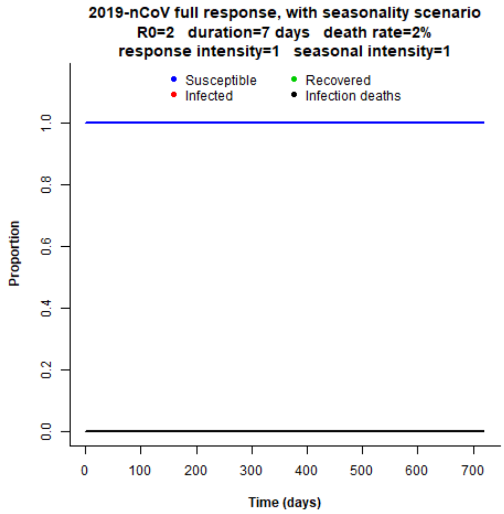
Figure 7 The R0 scaling vector used to simulate the season variation in transmissibility.

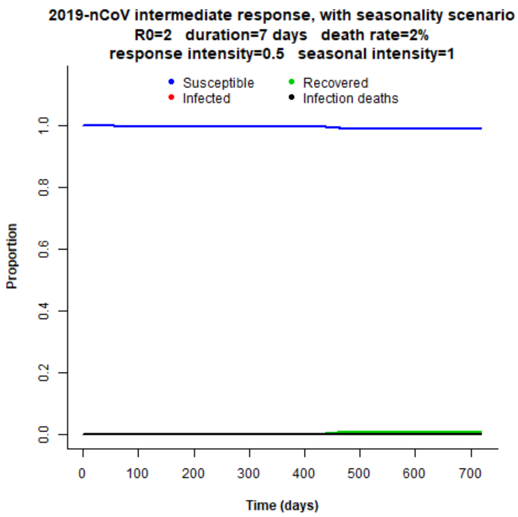
Results from simulations

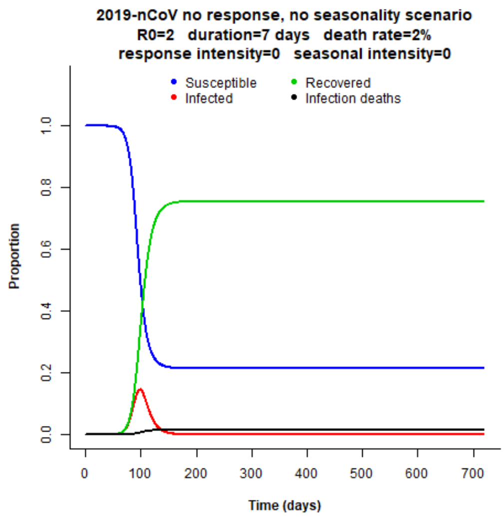


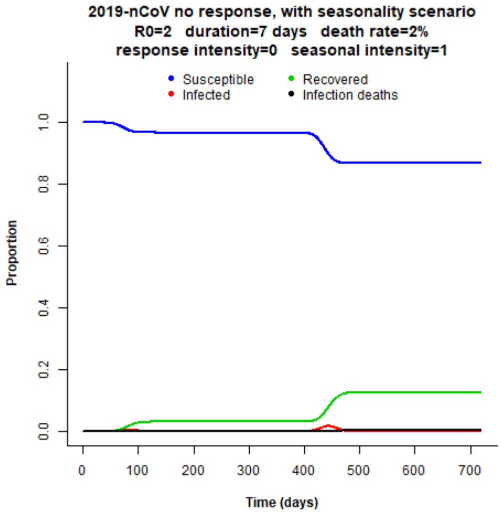








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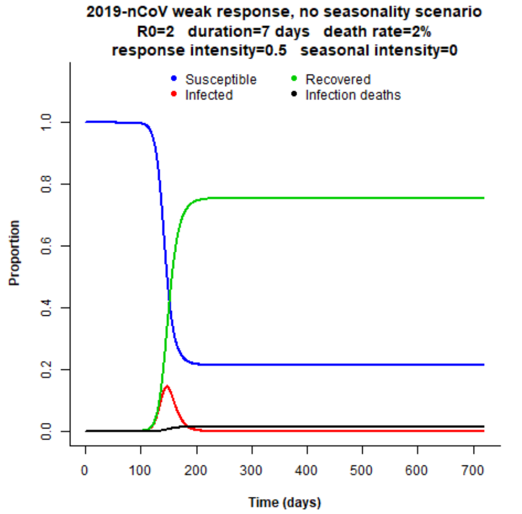
Susceptible
Infected
Recovered
Infection deaths
Proportion
0.0 0.2 0.4 0.6 0.8 1.0
0 100 200 300 400 500 600 700
Time (days)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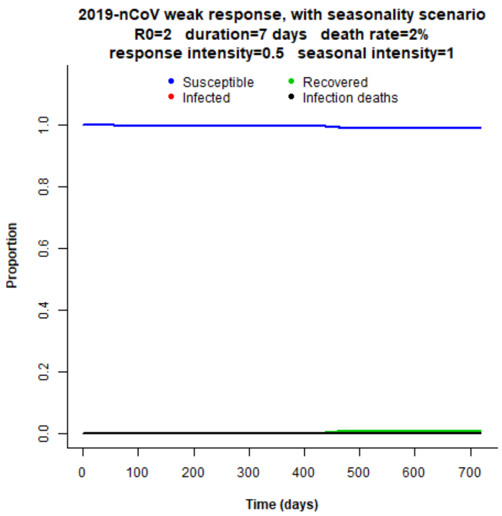
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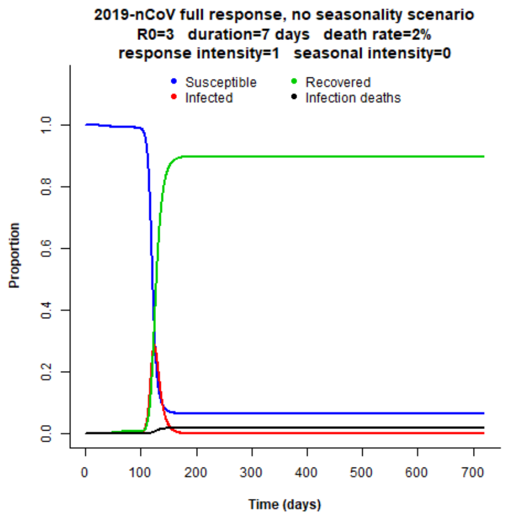
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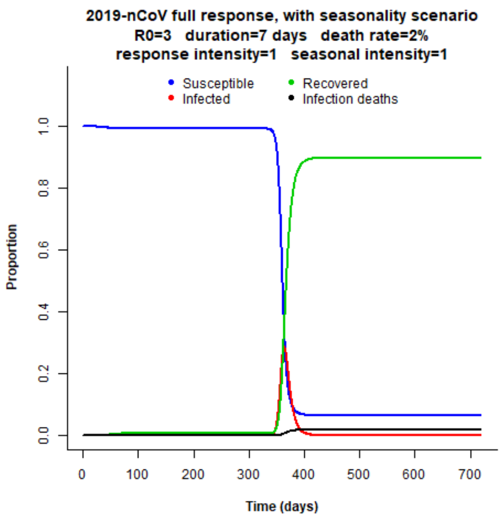
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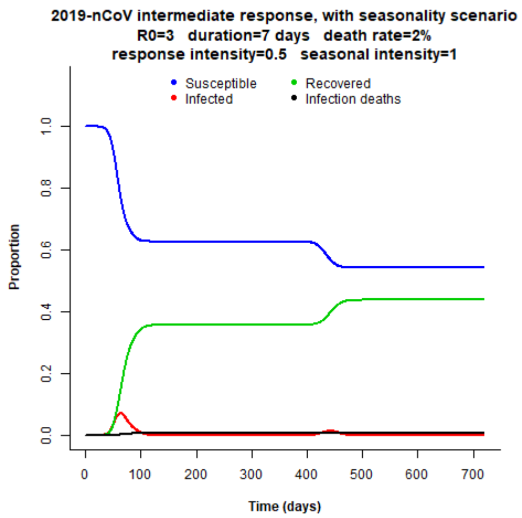
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Recovered
Infection deaths
Proportion
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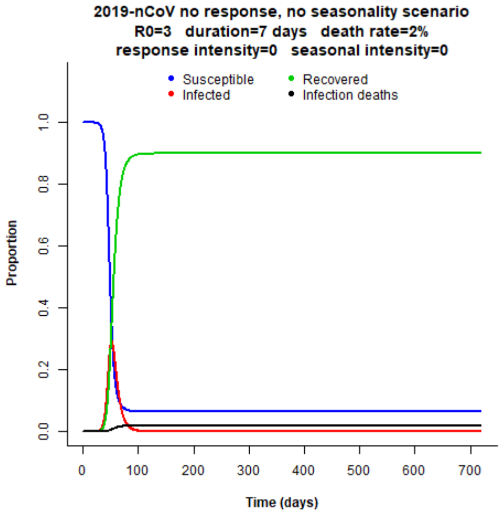
Time (days)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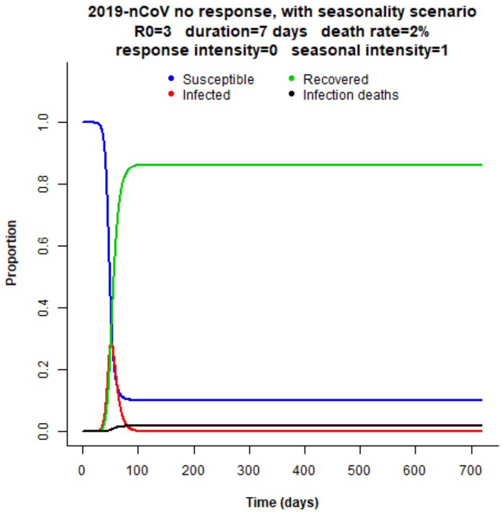
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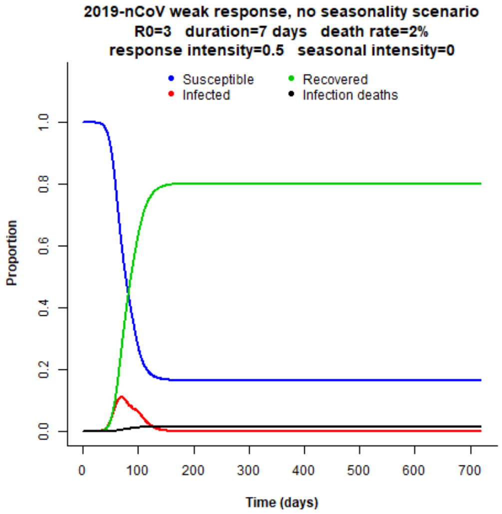
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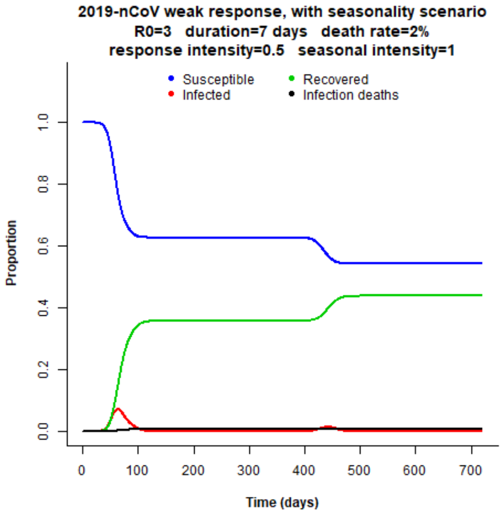
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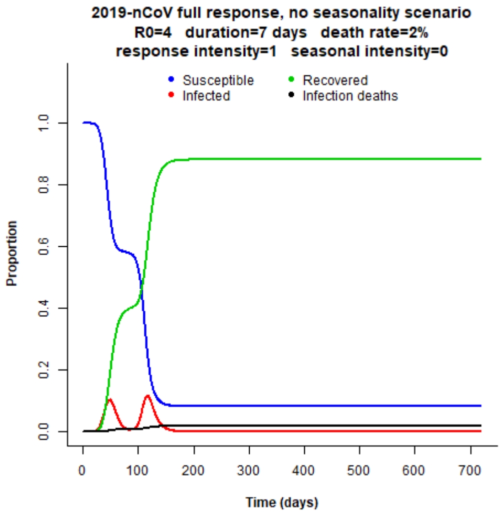
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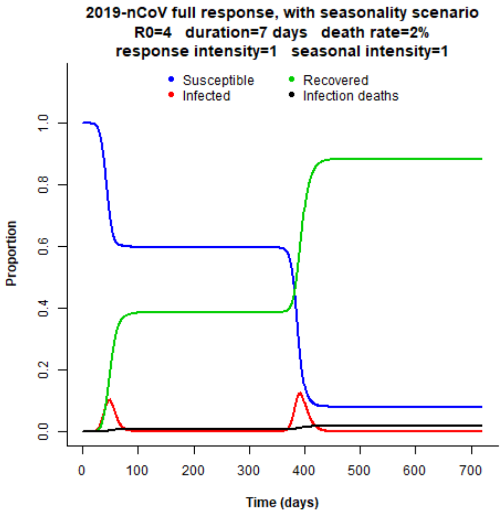
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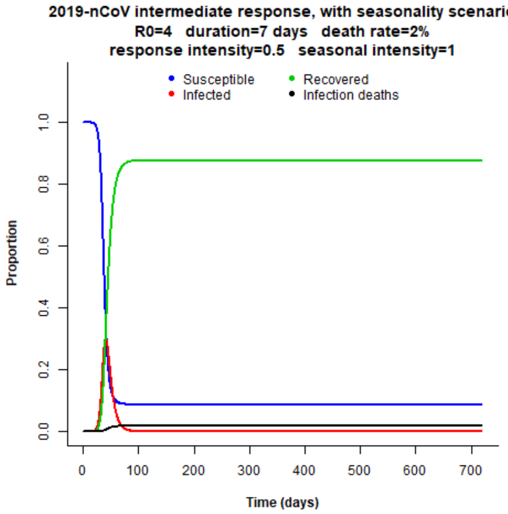
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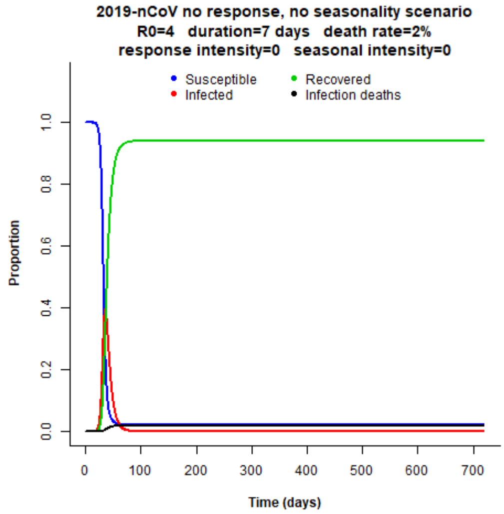
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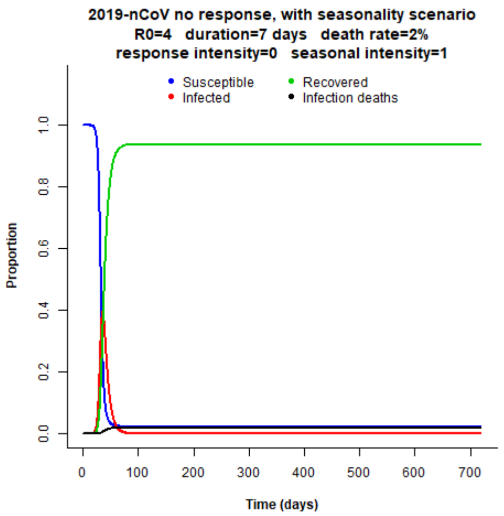
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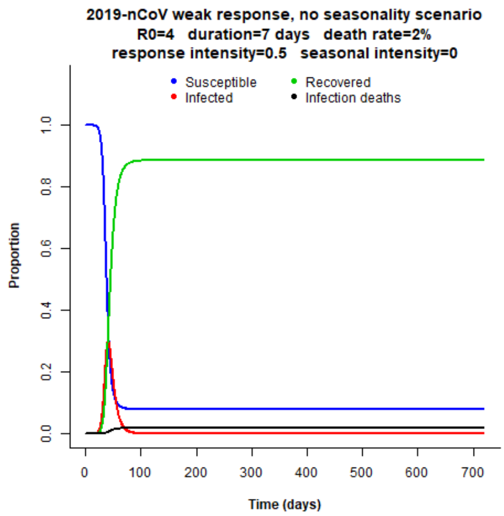
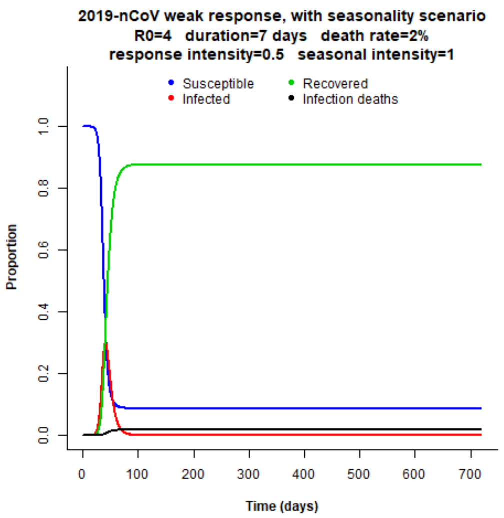
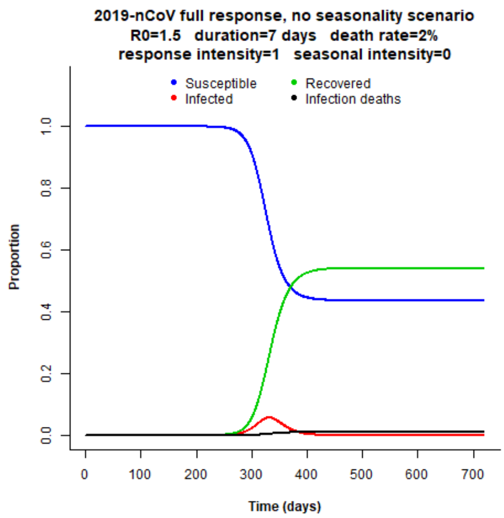
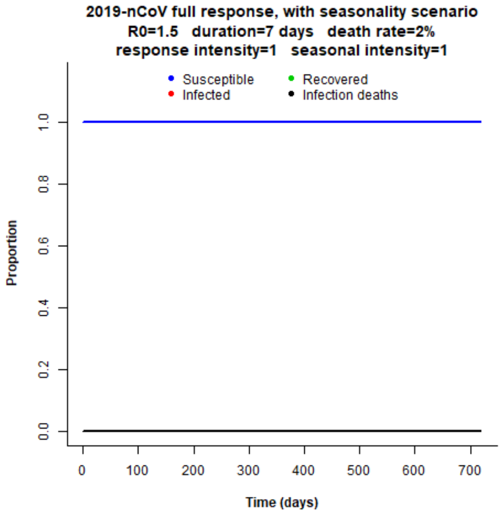
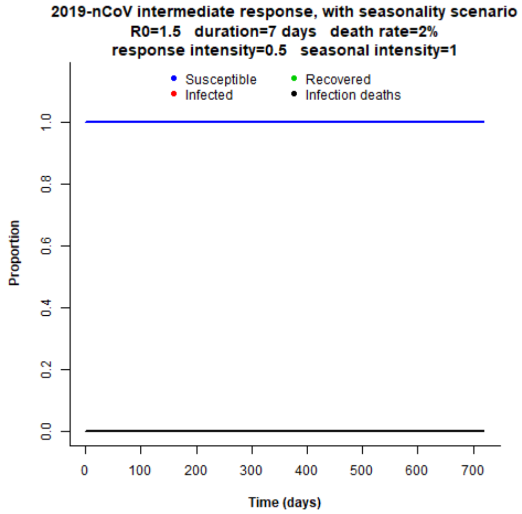
Recovered
Infection deaths
Proportion
Time (days)

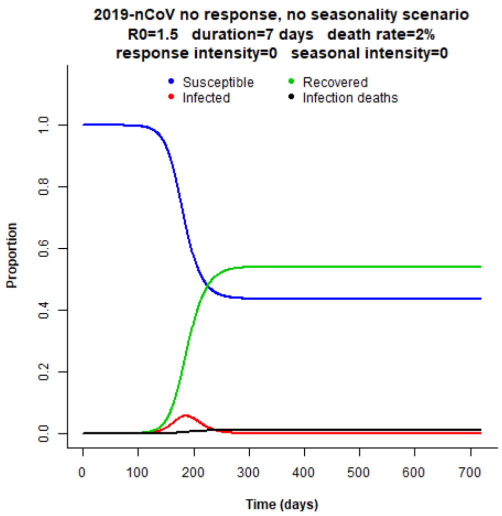

2019-nCoV weak response, no seasonality scenario
R0=4 duration=7 days death rate=2%
response intensity=0.5 seasonal intensity=0
Susceptible
Infected
Recovered
Infection deaths
Proportion
Time (days)


2019-nCoV weak response, with seasonality scenario
R0=4 duration=7 days death rate=2%
response intensity=0.5 seasonal intensity=1
Susceptible
Infected
Recovered
Infection deaths
Proportion
Time (days)


2019-nCoV full response, no seasonality scenario
R0=1.5 duration=7 days death rate=2%
response intensity=1 seasonal intensity=0
Susceptible
Infected
Recovered
Infection deaths
Proportion
Time (days)


2019-nCoV full response, with seasonality scenario
R0=1.5 duration=7 days death rate=2%
response intensity=1 seasonal intensity=1
Susceptible
Infected
Recovered
Infection deaths
Proportion
Time (days)


2019-nCoV intermediate response, with seasonality scenario
R0=1.5 duration=7 days death rate=2%
response intensity=0.5 seasonal intensity=1
Susceptible
Infected
Recovered
Infection deaths
Proportion
Time (days)


2019-nCoV no response, no seasonality scenario
R0=1.5 duration=7 days death rate=2%
response intensity=0 seasonal intensity=0
Susceptible
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Infection deaths
Proportion
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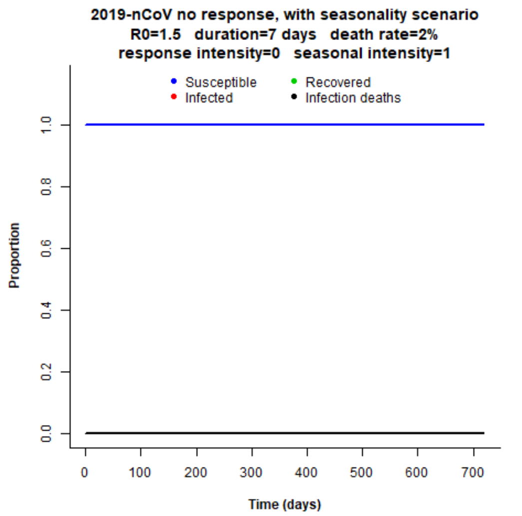
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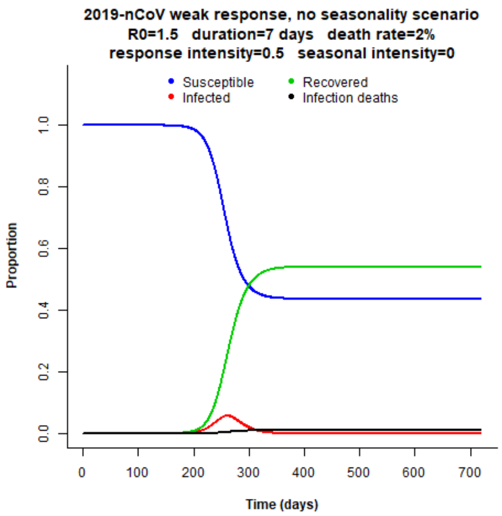
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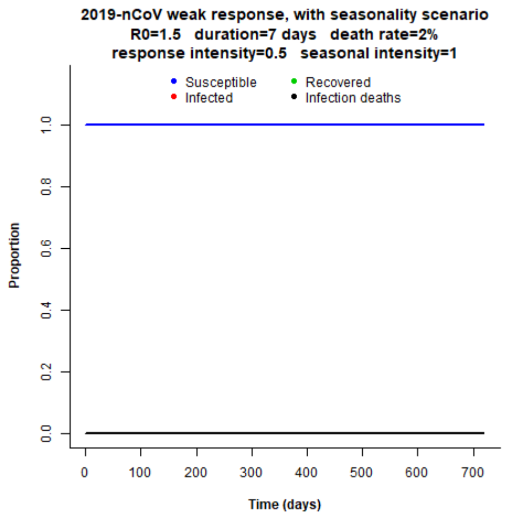
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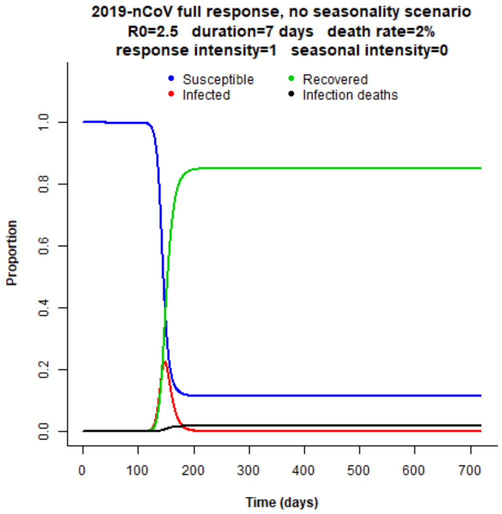
2019-nCoV full response, no seasonality scenario
R0=2.5 duration=7 days death rate=2%
response intensity=1 seasonal intensity=0
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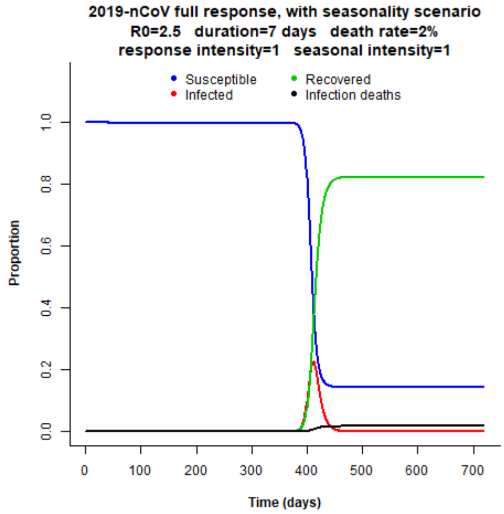
Infection deaths
Proportion
Time (days)


2019-nCoV full response, with seasonality scenario
R0=2.5 duration=7 days death rate=2%
response intensity=1 seasonal intensity=1
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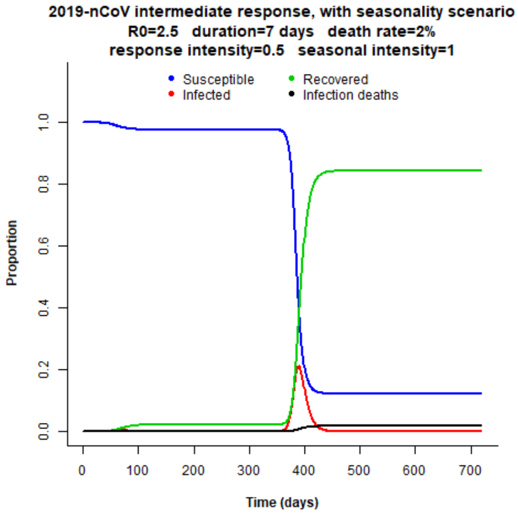
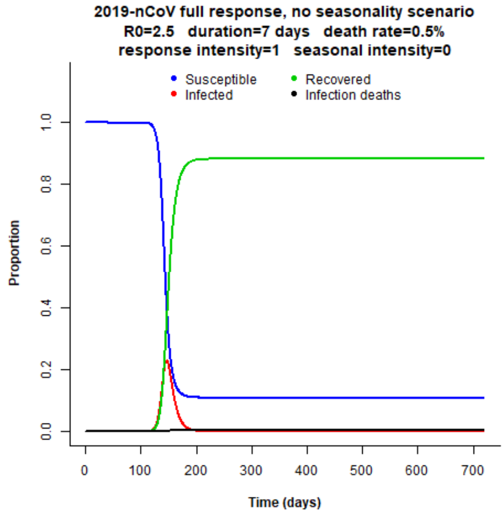
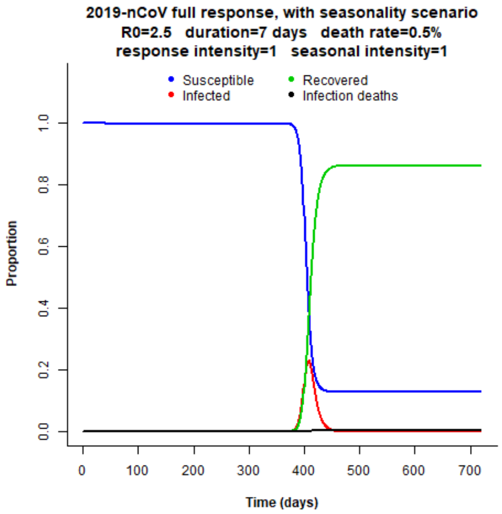
Infection deaths
Proportion
Time (days)


2019-nCoV intermediate response, with seasonality scenario
R0=2.5 duration=7 days death rate=2%
response intensity=0.5 seasonal intensity=1
Susceptible
Recovered
Infected
Infection deaths
Proportion
Time (days)


2019-nCoV full response, no seasonality scenario
R0=2.5 duration=7 days death rate=0.5%
response intensity=1 seasonal intensity=0
Susceptible
Recovered
Infected
Infection deaths
Proportion
Time (days)


2019-nCoV full response, with seasonality scenario
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response intensity=1 seasonal intensity=1
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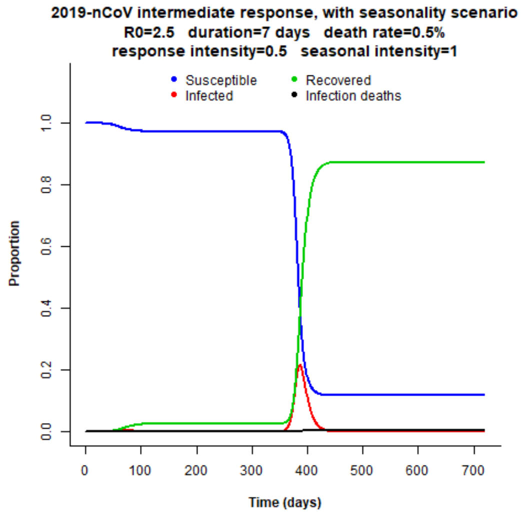
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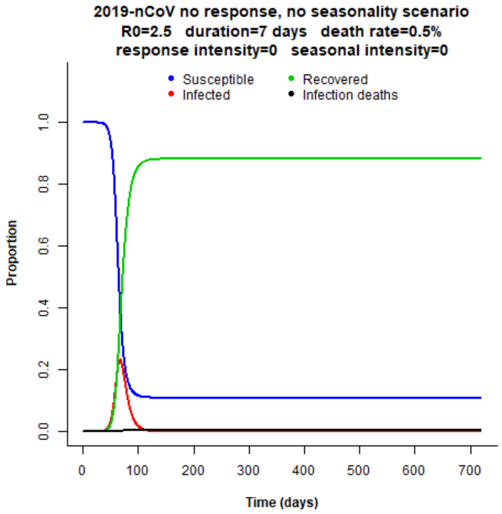
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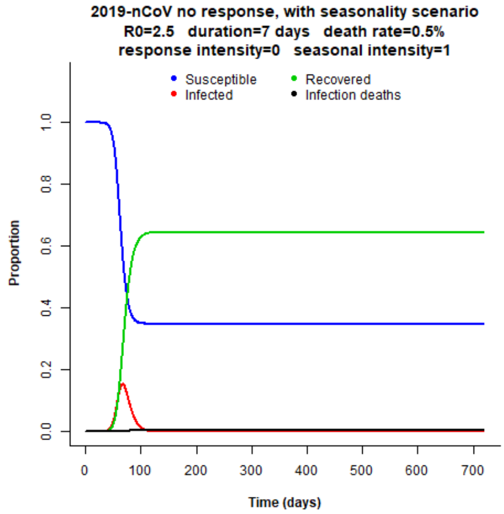
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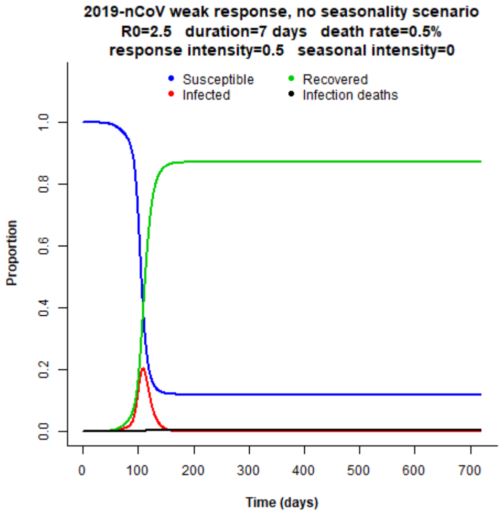
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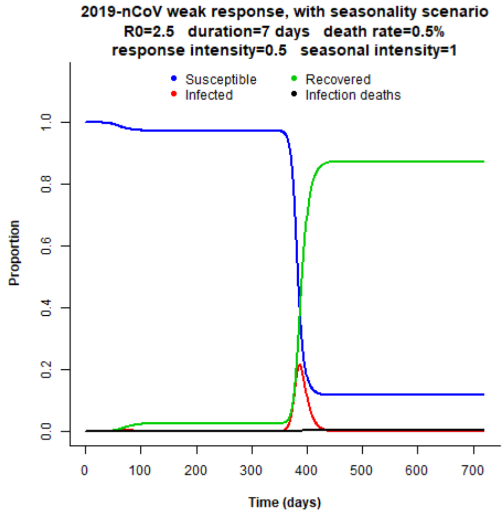
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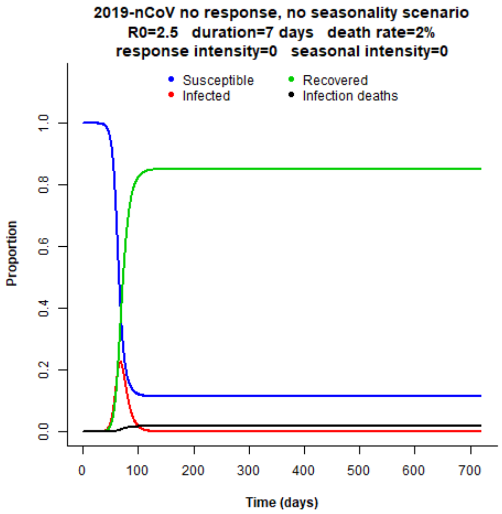
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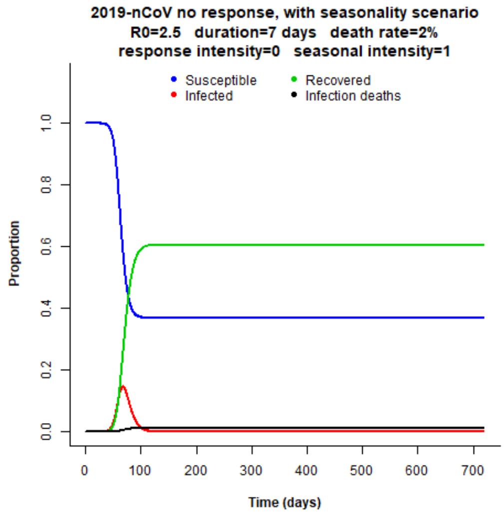
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