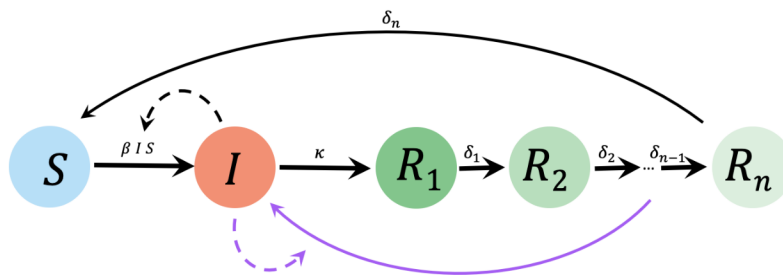


Impact of variants and NPI measures: SIR_n model

Model includes n waning classes, corresponding to reducing antibody levels over time.



Results for the SIR model

Assume a standard SIR model with waning at rate δ and transmission at rate β per day, as described by the differential equations:

```

In[ ]:= eqns = {D[S[t], t] == δ R[t] - β S[t] × I1[t],
               D[I1[t], t] == β S[t] × I1[t] - κ I1[t],
               (*We use I1 to differentiate from Mathematica's I=
               √-1 and to emphasize that this refers
               to the resident when considering a second variant infection below. *)
               D[R[t], t] == κ I1[t] - δ R[t]};
    
```

While the SIR_n accounts for declines in neutralizing antibodies over time by allowing for multiple recovered classes, both models have the same equilibrium number of individuals in the susceptible and infected classes, all else being equal. Thus the basic equilibrium properties of the SIR model provide insight into the SIR_n model as well.

As each infection lasts on average $1/\kappa$ days, the number of new infections per case is given by $\tilde{R}_0 = \frac{\beta}{\kappa}$ if everybody were in the susceptible class. Importantly, we are considering spread within a population that has been previously exposed to the disease, so that transmission may be lower due to cellular immunity and any residual humoral immunity among susceptible individuals and due to behavioural changes (including better masking and ventilation practices). We thus denote the reproductive number with a tilde and emphasize that this may differ from the R_0 that would have been observed in completely immunological and behaviorally naïve population.

Measuring the variables as a fraction of the full population, we have:

$$\begin{aligned} \text{In[]:= eqns} &= \{D[S[t], t] == \delta (1 - S[t] - I1[t]) - \beta S[t] \times I1[t], \\ &D[I1[t], t] == \beta S[t] \times I1[t] - \kappa I1[t]\}; \end{aligned}$$

This system has two equilibria (disease absent and disease endemic):

$$\text{In[]:= equil} = \text{Solve}[\{0 == \delta (1 - S - I1) - \beta S I1, \\ 0 == \beta S I1 - \kappa I1\}, \{S, I1\}]$$

$$\text{Out[]:=} \left\{ \left\{ S \rightarrow 1, I1 \rightarrow 0 \right\}, \left\{ S \rightarrow \frac{\kappa}{\beta}, I1 \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} \right\} \right\}$$

Also note that the disease-present equilibrium is identical to that described by Hethcote et al. (1981),

$$\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} = \frac{(1 - 1/\sigma)}{(1 + n \alpha)}, \text{ where } \sigma \rightarrow \beta/\kappa \text{ and } \alpha \rightarrow \kappa/(n \delta) \text{ [their } \gamma \text{ is our } \kappa \text{ and their } \epsilon \text{ is our } n \delta].$$

$$\text{In[]:=} \frac{(1 - 1/\sigma)}{(1 + n \alpha)} /. \sigma \rightarrow \beta/\kappa /. \alpha \rightarrow \kappa/(n \delta) // \text{Factor}$$

$$\text{Out[]:=} \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}$$

The disease-absent equilibrium is stable when $\beta > \kappa$, so public health measures that are so strong that $\tilde{R}_0 = \frac{\beta}{\kappa} < 1$ would lead to the disappearance of COVID and no infections. We assume that such measures are not in place:

$$\begin{aligned} \text{In[]:= eqns} &= \delta (1 - S - I1) - \beta S I1; \\ \text{eqni} &= \beta S I1 - \kappa I1; \\ \text{stabmat} &= \{\{D[eqns, S], D[eqns, I1]\}, \\ &\{D[eqni, S], D[eqni, I1]\}\} /. \text{equil}[[1]] // \text{Eigenvalues} \end{aligned}$$

$$\text{Out[]:=} \{-\delta, \beta - \kappa\}$$

The stability matrix for the disease-present equilibrium:

$$\text{In[]:= stabmat} = \{\{D[eqns, S], D[eqns, I1]\}, \\ \{D[eqni, S], D[eqni, I1]\}\} /. \text{equil}[[2]] // \text{Simplify}$$

$$\text{Out[]:=} \left\{ \left\{ -\frac{\delta (\beta + \delta)}{\delta + \kappa}, -\delta - \kappa \right\}, \left\{ \frac{\delta (\beta - \kappa)}{\delta + \kappa}, 0 \right\} \right\}$$

For stability (the real part of both eigenvalues are negative), the determinant of this 2x2 matrix must be positive and its trace must be negative, which will always be satisfied when the disease-absent equilibrium is unstable:

$$\text{In[]:= Det[stabmat] // Factor}$$

$$\text{Out[]:=} \delta (\beta - \kappa)$$

$$\text{In[]:= Tr[stabmat] // Factor}$$

$$\text{Out[]:=} -\frac{\delta (\beta + \delta)}{\delta + \kappa}$$

In[]:= **I1 /. equil[[2]] /. $\beta \rightarrow \tilde{R}_0 \kappa$ // Factor**

$$\text{Out[]} = \frac{\delta (-1 + \tilde{R}_0)}{(\delta + \kappa) \tilde{R}_0}$$

with the recovered class at frequency:

In[]:= **1 - S - I1 /. equil[[2]] /. $\beta \rightarrow \tilde{R}_0 \kappa$ // Factor**

$$\text{Out[]} = \frac{\kappa (-1 + \tilde{R}_0)}{(\delta + \kappa) \tilde{R}_0}$$

Accordingly, when $\tilde{R}_0 = \frac{\beta}{\kappa} > 1$, we expect case numbers to stabilize around $\hat{I} = \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}$ (granted that the real world case will have more complexity). This endemic equilibrium can be rewritten in terms of $\tilde{R}_0$ as $\hat{I} = \frac{(\tilde{R}_0 - 1) \delta}{\tilde{R}_0 (\delta + \kappa)}$.

Seroconversion: We will also consider the possibility that only a fraction q seroconvert and gain immunity after infection. In which case, the equilibrium changes to:

In[]:= **Solve[{ $\theta == \delta (1 - S - I1) - \beta S I1 + (1 - q) \kappa I1$,
 $\theta == \beta S I1 - \kappa I1$ }, {S, I1}]**

$$\text{Out[]} = \left\{ \left\{ S \rightarrow 1, I1 \rightarrow 0 \right\}, \left\{ S \rightarrow \frac{\kappa}{\beta}, I1 \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)} \right\} \right\}$$

In the selection coefficients computed for variants (see simulated transients), we'll need the fraction in the recovered class at the endemic equilibrium:

In[]:= **1 - S - I1 /. %[2]] // Factor**

$$\text{Out[]} = \frac{q (\beta - \kappa) \kappa}{\beta (\delta + q \kappa)}$$

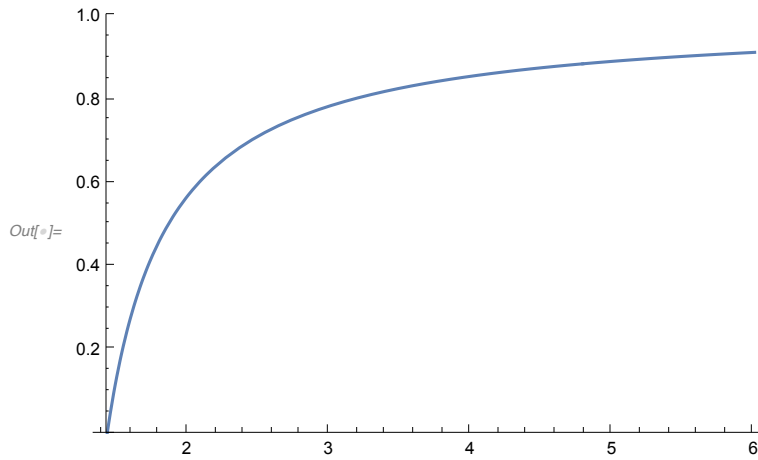
NPIs: Consider the claim that COVID is so rampant that people are exposed all the time and so NPI measures, such as masking, would make no difference. This effectively assumes that $\tilde{R}_0$ is very large so that the number of infected individuals $\hat{I} = \frac{(\tilde{R}_0 - 1) \delta}{\tilde{R}_0 (\delta + \kappa)}$ is nearly $\frac{\tilde{R}_0 \delta}{\tilde{R}_0 (\delta + \kappa)} = \frac{\delta}{(\delta + \kappa)}$ and so independent of efforts to reduce transmission (β is contained in $\tilde{R}_0$).

Generally, if NPI measures protect by an amount p (reducing transmission by a factor $1-p$), we can achieve the following reduction in cases per unit time at the endemic equilibrium:

$$\text{In[]} = \frac{\left(\frac{(\tilde{R}_0 - 1) \delta}{\tilde{R}_0 (\delta + \kappa)} \right) / . \tilde{R}_0 \rightarrow (1 - p) * \tilde{R}_0}{\left(\frac{(\tilde{R}_0 - 1) \delta}{\tilde{R}_0 (\delta + \kappa)} \right)}$$

$$\text{Out[]} = \frac{-1 + (1 - p) \tilde{R}_0}{(1 - p) (-1 + \tilde{R}_0)}$$

```
In[ ]:= Plot[ $\frac{(1-p) \tilde{R}_0 - 1}{(1-p) (\tilde{R}_0 - 1)}$  /. p -> 0.3, { $\tilde{R}_0$ , 1 / 0.7, 6}, PlotRange -> {Automatic, {0, 1}}]
```



Vaccination: We'll also allow a fraction of the entire population to vaccinate at rate v per day, assuming that the policy is such that all of these individuals would be in the susceptible class, allowing them to move to the first recovered class:

```
In[ ]:= eqns = {D[S[t], t] ==  $\delta (1 - S[t] - I1[t]) - \beta S[t] \times I1[t] - v$ ,  
D[I1[t], t] ==  $\beta S[t] \times I1[t] - \kappa I1[t]$ };
```

This system has two equilibria (disease absent and disease endemic):

```
In[ ]:= equilv = Solve[{0 ==  $\delta (1 - S - I1) - \beta S I1 - v$ ,  
0 ==  $\beta S I1 - \kappa I1$ }, {S, I1}]
```

```
Out[ ]:= {{S ->  $\frac{-v + \delta}{\delta}$ , I1 -> 0}, {S ->  $\frac{\kappa}{\beta}$ , I1 ->  $\frac{-v \beta + \beta \delta - \delta \kappa}{\beta (\delta + \kappa)}$ }}
```

The endemic equilibrium can be written as:

```
In[ ]:=  $\hat{I} = \frac{v}{\delta + \kappa}$ ;  
%- I1 /. equilv[[2]] /.  $\hat{I} \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}$  // Factor
```

```
Out[ ]:= 0
```

```
In[ ]:=  $\hat{I} \left( 1 - \frac{v \tilde{R}_0}{\delta (\tilde{R}_0 - 1)} \right)$ ;  
%- I1 /. equilv[[2]] /.  $\hat{I} \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}$  /.  $\tilde{R}_0 \rightarrow \beta / \kappa$  // Factor
```

```
Out[ ]:= 0
```

Note that there may ($v < \delta$) or may not ($v > \delta$) be any susceptibles remaining in the population at the disease-absent equilibrium, depending on how fast vaccination is relative to waning.

The endemic equilibrium becomes $\hat{I} = \frac{v}{\delta + \kappa}$ or equivalently $\hat{I} \left(1 - \frac{v \tilde{R}_0}{\delta (\tilde{R}_0 - 1)} \right)$. Given that $\delta < \kappa$, this means that $\hat{I}$ is reduced by the number of vaccines per recovery period.

We consider two vaccination rates, 0.012% corresponding to the low summer rate (May-July 2023) and 0.174% corresponding to the high fall rate (Sept-Dec 2022) in Canada (see vaccination-administration.xlsx from <https://health-infobase.canada.ca/covid-19/vaccine-administration/>).

```
In[ ]:= TRYvLOW = 1 / 8333; (* 0.00012 vaccinations per person per day*)
TRYvHIGH = 1 / 575; (* 0.00174 vaccinations per person per day*)
```

The population-level reduction in incidence for the nominal parameter rates:

```
In[ ]:=  $\frac{v}{\delta + \kappa}$  /.  $\delta \rightarrow 1 / 125$  /.  $\kappa \rightarrow 1 / 5$  /.  $v \rightarrow \{ \text{TRYvLOW}, \text{TRYvHIGH} \}$  // N
```

```
Out[ ]:= {0.000576946, 0.0083612}
```

leading to an overall incidence of:

```
In[ ]:=  $0.02 - \frac{v}{\delta + \kappa}$  /.  $\delta \rightarrow 1 / 125$  /.  $\kappa \rightarrow 1 / 5$  /.  $v \rightarrow \{ \text{TRYvLOW}, \text{TRYvHIGH} \}$  // N
```

```
Out[ ]:= {0.0194231, 0.0116388}
```

and a proportional decline in incidence of:

```
In[ ]:=  $1 - \frac{0.02 - \frac{v}{\delta + \kappa}}{0.02}$  /.  $\delta \rightarrow 1 / 125$  /.  $\kappa \rightarrow 1 / 5$  /.  $v \rightarrow \{ \text{TRYvLOW}, \text{TRYvHIGH} \}$  // N
```

```
Out[ ]:= {0.0288473, 0.41806}
```

With the high vaccination rate:

```
incidenceTAB = {0.02, 0.005, 0.04};
```

```
 $\delta$ TAB = {1 / 125, 1 / 100, 1 / 180};
```

```
 $\kappa$ TAB = {1 / 5, 1 / 3, 1 / 10};
```

```

In[ ]:= Flatten[
  Table[ {incidence,  $\delta$ ,  $\kappa$ , 100 If[  $\text{incidence} - \frac{v}{\delta + \kappa} > 0$ ,  $1 - \frac{\text{incidence} - \frac{v}{\delta + \kappa}}{\text{incidence}}$ , 1]} /. v ->
    TRYvHIGH /. incidence -> incidenceTAB[[i]] /.  $\delta$  ->  $\delta$ TAB[[j]] /.
     $\kappa$  ->  $\kappa$ TAB[[k]], {i, 1, 3}, {j, 1, 3}, {k, 1, 3}] // N, 2];
  Join[{"Incidence",  $\delta$ ,  $\kappa$ , "% reduction in incidence"}], (Round[1000  $\times$  %] / 1000.)] /.
  (0.001` Round[1000 "NA"]) -> "NA" // MatrixForm

```

Out[]:=/MatrixForm=

Incidence	δ	κ	% reduction in incidence
0.02	0.008	0.2	41.806
0.02	0.008	0.333	25.476
0.02	0.008	0.1	80.515
0.02	0.01	0.2	41.408
0.02	0.01	0.333	25.327
0.02	0.01	0.1	79.051
0.02	0.006	0.2	42.303
0.02	0.006	0.333	25.659
0.02	0.006	0.1	82.38
0.005	0.008	0.2	100.
0.005	0.008	0.333	100.
0.005	0.008	0.1	100.
0.005	0.01	0.2	100.
0.005	0.01	0.333	100.
0.005	0.01	0.1	100.
0.005	0.006	0.2	100.
0.005	0.006	0.333	100.
0.005	0.006	0.1	100.
0.04	0.008	0.2	20.903
0.04	0.008	0.333	12.738
0.04	0.008	0.1	40.258
0.04	0.01	0.2	20.704
0.04	0.01	0.333	12.664
0.04	0.01	0.1	39.526
0.04	0.006	0.2	21.152
0.04	0.006	0.333	12.83
0.04	0.006	0.1	41.19

In[]:= {Min[%], Max[%]}

Out[]:= {0.126636, 1.}

The probability of leaving the susceptible class by vaccination for the population is then:

$$\text{In[]:= } \frac{v}{\beta \hat{S} \hat{I} + v} /. \hat{S} \rightarrow \frac{\kappa}{\beta} /. \hat{I} \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} // \text{Factor}$$

$$\text{Out[]:= } \frac{v \beta (\delta + \kappa)}{v \beta \delta + v \beta \kappa + \beta \delta \kappa - \delta \kappa^2}$$

```

In[ ]:= % /. Flatten[Solve[ $\left(\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}\right) = \text{incidence}, \beta]$ ] /.  $\delta \rightarrow 1 / 125$  /.  $\kappa \rightarrow 1 / 5$  /.
      v  $\rightarrow \{0, \text{TRYvLOW}, \text{TRYvHIGH}\}$  /. incidence  $\rightarrow 0.02$  // N
Out[ ]:= {0., 0.0291273, 0.30303}

```

For an individual that is vaccinated at regular intervals (every T days), we can model the probability that their immunity wanes at time t and that they are then infected before their next dose. Assuming an exponentially distributed waning time, this equals:

```

In[ ]:= Integrate[ $\delta \text{Exp}[-\delta t] (1 - \text{Exp}[-\beta \text{incidence} (T - t)])$ , {t, 0, T}] // Simplify
Out[ ]:= 
$$\frac{\text{incidence} (\beta - e^{-T \delta} \beta) + (-1 + e^{-\text{incidence} T \beta}) \delta}{\text{incidence} \beta - \delta}$$


```

The first part ($\delta \text{Exp}[-\delta t]$) is the probability density function for waning at time t , and the second part is the probability of being infected, given that individuals would have a chance of $\text{Exp}[-\beta \hat{I}(T-t)]$ of remaining susceptible by the time of receiving their next vaccination. This assumes that if they do not remain susceptible, they get one (but only one) infection during this time interval, which is reasonable for the low rates of infection and long subsequent waning times considered under the nominal parameter values.

This can be written as

```

In[ ]:= 1 - 
$$\frac{e^{-T \delta} \text{incidence} \beta - e^{-\text{incidence} T \beta} \delta}{\text{incidence} \beta - \delta}$$
;
% - %% // Simplify
Out[ ]:= 0

```

Annually, the number of infections is:

$$\frac{365}{T} \left(1 - \frac{e^{-T \delta} \text{incidence} \beta - e^{-\text{incidence} T \beta} \delta}{\text{incidence} \beta - \delta} \right);$$

and that relative to individuals not receiving vaccinations would be:

```

In[ ]:= 
$$\frac{\frac{365}{T} \left( 1 - \frac{e^{-T \delta} \text{incidence} \beta - e^{-\text{incidence} T \beta} \delta}{\text{incidence} \beta - \delta} \right)}{365 \kappa \text{incidence}}$$
 /. T  $\rightarrow 365 / 2$  /.  $\beta \rightarrow 0.42$  /.  $\delta \rightarrow 1 / 125$  /.  $\kappa \rightarrow 1 / 5$  /.
      incidence  $\rightarrow 0.02$  // Factor
Out[ ]:= 0.603807

```

But this depends strongly on the parameters (dropping to a nearly 100% chance of remaining susceptible [0% chance of infection before vaccination] if waning is a lot longer and vice versa) and does not account for variation in waning process:

```

In[ ]:= incidenceTAB = {0.02, 0.005, 0.04};
       $\delta$ TAB = {1 / 125, 1 / 100, 1 / 180};
       $\kappa$ TAB = {1 / 5, 1 / 3, 1 / 10};

```

```

In[ ]:= Flatten[
  Table[{{incidence,  $\delta$ ,  $\kappa$ , If[ $\frac{\delta \kappa}{\delta - \text{incidence} (\delta + \kappa)} > 0$ ,  $\frac{\delta \kappa}{\delta - \text{incidence} (\delta + \kappa)}$ , "NA"],
    If[ $\frac{\delta \kappa}{\delta - \text{incidence} (\delta + \kappa)} > 0$ ,  $\frac{365}{T} \left( 1 - \frac{e^{-T \delta} \text{incidence} \beta - e^{-\text{incidence} T \beta} \delta}{\text{incidence} \beta - \delta} \right)$ , "NA"],
    If[ $\frac{\delta \kappa}{\delta - \text{incidence} (\delta + \kappa)} > 0$ ,  $365 \kappa \text{incidence}$ , "NA"],
    If[ $\frac{\delta \kappa}{\delta - \text{incidence} (\delta + \kappa)} > 0$ ,  $\frac{\frac{365}{T} \left( 1 - \frac{e^{-T \delta} \text{incidence} \beta - e^{-\text{incidence} T \beta} \delta}{\text{incidence} \beta - \delta} \right)}{365 \kappa \text{incidence}}$ , "NA"]}], /.
     $\beta \rightarrow \frac{\delta \kappa}{\delta - \text{incidence} (\delta + \kappa)}$  /.  $T \rightarrow 365 / 2$  /.  $\text{incidence} \rightarrow \text{incidenceTAB}[[i]]$  /.
     $\delta \rightarrow \delta \text{TAB}[[j]]$  /.  $\kappa \rightarrow \kappa \text{TAB}[[k]]$ , {i, 1, 3}, {j, 1, 3}, {k, 1, 3}], 2];
Join[{"Incidence",  $\delta$ ,  $\kappa$ ,  $\beta$ , "Annual inf vac", "Annual inf unvac", "Ratio"}],
  (Round[1000  $\times$  %] / 1000.)] /. (0.001` Round[1000 "NA"])  $\rightarrow$  "NA" // MatrixForm

```

Out[]:=MatrixForm=

Incidence	δ	κ	β	Annual inf vac	Annual inf unvac	Ratio
0.02	0.008	0.2	0.417	0.878	1.46	0.601
0.02	0.008	0.333	2.273	1.436	2.433	0.59
0.02	0.008	0.1	0.137	0.397	0.73	0.544
0.02	0.01	0.2	0.345	0.886	1.46	0.607
0.02	0.01	0.333	1.064	1.428	2.433	0.587
0.02	0.01	0.1	0.128	0.427	0.73	0.585
0.02	0.006	0.2	0.769	0.932	1.46	0.639
0.02	0.006	0.333	NA	NA	NA	NA
0.02	0.006	0.1	0.161	0.358	0.73	0.49
0.005	0.008	0.2	0.23	0.184	0.365	0.505
0.005	0.008	0.333	0.424	0.319	0.608	0.525
0.005	0.008	0.1	0.107	0.09	0.182	0.491
0.005	0.01	0.2	0.223	0.204	0.365	0.56
0.005	0.01	0.333	0.402	0.347	0.608	0.57
0.005	0.01	0.1	0.106	0.101	0.182	0.552
0.005	0.006	0.2	0.245	0.154	0.365	0.421
0.005	0.006	0.333	0.48	0.279	0.608	0.459
0.005	0.006	0.1	0.11	0.072	0.182	0.396
0.04	0.008	0.2	NA	NA	NA	NA
0.04	0.008	0.333	NA	NA	NA	NA
0.04	0.008	0.1	0.217	0.899	1.46	0.616
0.04	0.01	0.2	1.25	1.597	2.92	0.547
0.04	0.01	0.333	NA	NA	NA	NA
0.04	0.01	0.1	0.179	0.905	1.46	0.62
0.04	0.006	0.2	NA	NA	NA	NA
0.04	0.006	0.333	NA	NA	NA	NA
0.04	0.006	0.1	0.417	0.959	1.46	0.657

The relative number of infections annually across the range of parameters considered:


```

In[ ]:= Table[
  If[  $\frac{\delta \kappa}{\delta - \text{incidence}(\delta + \kappa)} > 0$ ,  $\frac{\frac{365}{T} \left(1 - \frac{e^{-T \delta} \text{incidence} \beta - e^{-\text{incidence} T \beta} \delta}{\text{incidence} \beta - \delta}\right)}{365 \kappa \text{incidence}}$  ] /.
     $\beta \rightarrow \frac{\delta \kappa}{\delta - \text{incidence}(\delta + \kappa)}$  /. T  $\rightarrow 365 / 2$  /. incidence  $\rightarrow \text{incidenceTAB}[[i]]$  /.
     $\delta \rightarrow \delta \text{TAB}[[j]]$  /.  $\kappa \rightarrow \kappa \text{TAB}[[k]]$ , {i, 1, 3}, {j, 1, 3}, {k, 1, 3}] // Flatten
Out[ ]:= {0.601104, 0.590312, 0.543902, 0.606854, 0.58691, 0.58451, 0.638683, Null, 0.489813,
  0.504986, 0.524769, 0.490534, 0.559784, 0.570294, 0.551542, 0.421229, 0.459301,
  0.39604, Null, Null, 0.615533, 0.546921, Null, 0.619977, Null, Null, 0.657082}

Select[%, NumberQ[#] &]
Out[ ]:= {0.601104, 0.590312, 0.543902, 0.606854, 0.58691, 0.58451, 0.638683,
  0.489813, 0.504986, 0.524769, 0.490534, 0.559784, 0.570294, 0.551542,
  0.421229, 0.459301, 0.39604, 0.615533, 0.546921, 0.619977, 0.657082}

In[ ]:= {Min[%, Max[%, Mean[%]}]
Out[ ]:= {0.39604, 0.657082, 0.55048}

```

Next, we consider the SIR_n model. Note, however, that the endemic equilibrium number of infections is the same, $\hat{I} = \frac{\delta(\beta - \kappa)}{\beta(\delta + \kappa)}$, and so these general comments about NPI measures continue to hold.

Seroconversion & Vaccination: Finally, we consider both seroconversion and vaccination, allowing seroconversion following infection of q and following vaccination of q_v :

$$\begin{aligned} \text{eqns} = \{ & D[S[t], t] == \delta(1 - S[t] - I1[t]) - \beta S[t] \times I1[t] - q_v v + (1 - q) \kappa I1[t], \\ & D[I1[t], t] == \beta S[t] \times I1[t] - \kappa I1[t] \}; \end{aligned}$$

This system has two equilibria (disease absent and disease endemic):

```

In[ ]:= equilvs = Solve[{0 ==  $\delta(1 - S - I1) - \beta S I1 - q_v v + (1 - q) \kappa I1$ ,
  0 ==  $\beta S I1 - \kappa I1$ }, {S, I1}]

```

$$\text{Out[]} = \left\{ \left\{ S \rightarrow \frac{\delta - v q_v}{\delta}, I1 \rightarrow 0 \right\}, \left\{ S \rightarrow \frac{\kappa}{\beta}, I1 \rightarrow \frac{\beta \delta - \delta \kappa - v \beta q_v}{\beta(\delta + q \kappa)} \right\} \right\}$$

The endemic equilibrium can be written as:

$$\begin{aligned} \text{In[]} := \hat{I} &= \frac{\frac{q_v}{q} v}{\frac{\delta}{q} + \kappa}; \\ \% - I1 /. \text{equilvs}[[2]] /. \hat{I} &\rightarrow \frac{\frac{\delta}{q}(\beta - \kappa)}{\beta \left(\frac{\delta}{q} + \kappa\right)} // \text{Factor} \end{aligned}$$

```
Out[ ]:= 0
```

SIR_n model

Assume an SIR_n model with n recovered classes capturing the decline in neutralizing ability over time. Movement among the n classes and from R_n to S occurs at rate δ^*n so that the mean total time to move from R_1 to S is held constant at $1/\delta$.

Transmission at rate β (dependent on NPI measures) is then described by the differential equations:

```
In[ ]:= eqns = {D[S[t], t] ==  $\delta n R[n, t] - \beta S[t] \times I1[t]$ ,
               D[I1[t], t] ==  $\beta S[t] \times I1[t] - \kappa I1[t]$ ,
               D[R[1, t], t] ==  $\kappa I1[t] - \delta n R[1, t]$ ,
               D[R[j_, t], t] ==  $\delta n R[j - 1, t] - \delta n R[j, t]$ };
```

At equilibrium, the last equation indicates that $R[j, t] = R[j-1, t]$ for all $j > 1$. Furthermore, adding the first three equations indicates that $\delta n R[n, t] = \delta n R[1, t]$, so at equilibrium all R values are equal. Measuring the variables as a fraction of the full population ($S + I1 + n R == 1$), we then have:

```
equil = Solve[{0 ==  $\delta * n R - \beta S I1$ ,
               0 ==  $\beta S I1 - \kappa I1$ } /. R -> (1 - S - I1) / n, {S, I1}]
```

```
Out[ ]:= {{S -> 1, I1 -> 0}, {S ->  $\frac{\kappa}{\beta}$ , I1 ->  $\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}$ }}
```

This system has two equilibria (disease absent and disease endemic).

Below, we show that the eigenvalues for the disease-free equilibrium are always $\{-\delta n, \beta - \kappa\}$, while the stability properties (stable or unstable) of the endemic equilibrium may change as we increase the number of recovered classes. See Hethcote et al. (1981; SIAM J. APPL. MATH. 40:1 section 4) for more details about the stability properties of the SIR_n model.

Step 1: $n = 1$

```
tryn = 1;
eqns =  $\delta n R - \beta S I1$ ;
eqni =  $\beta S I1 - \kappa I1$ ;
eqnr =  $\kappa I1 - \delta n R$ ;

eqnset = {eqns, eqni} /. R -> 1 - S - I1;
varset = {S, I1};
stabmat = Table[D[eqnset[[i]], varset[[j]]], {i, 1, tryn + 1}, {j, 1, tryn + 1}];
% // MatrixForm
```

Out[]//MatrixForm=

$$\begin{pmatrix} -I1 \beta - n \delta & -S \beta - n \delta \\ I1 \beta & S \beta - \kappa \end{pmatrix}$$

```
In[ ]:= char = Det[λ IdentityMatrix[2] - stabmat] /.  
      {S →  $\frac{\kappa}{\beta}$ } (* Char poly with leading λn term*)
```

```
Out[ ]:= I1 n β δ + I1 β κ + I1 β λ + n δ λ + λ2
```

```
In[ ]:= Factor[% /. λ → 0]
```

```
Out[ ]:= I1 β (n δ + κ)
```

As shown by the trace and determinant condition (previous section), the endemic equilibrium is always stable with n=1.

Step 2: n = 2

```
In[ ]:= tryn = 2;  
eqns = δ n R[2] - β S I1;  
eqni = β S I1 - κ I1;  
eqnr1 = κ I1 - δ n R[1];  
eqnr2 = δ n R[1] - δ n R[2];  
  
eqnset = {eqns, eqni, eqnr1} /. R[tryn] → 1 - S - I1 - R[1];  
varset = {S, I1, R[1]};  
stabmat =  
  Table[D[eqnset[[i]], varset[[j]]], {i, 1, tryn + 1}, {j, 1, tryn + 1}] /. ii → i;  
% // MatrixForm
```

```
Out[ ]:= MatrixForm=
```

$$\begin{pmatrix} -I1 \beta - n \delta & -S \beta - n \delta & -n \delta \\ I1 \beta & S \beta - \kappa & 0 \\ 0 & \kappa & -n \delta \end{pmatrix}$$

```
In[ ]:= char = Det[λ IdentityMatrix[tryn + 1] - stabmat] /.  
      {S →  $\frac{\kappa}{\beta}$ } (* Char poly with leading λn term*)
```

```
Out[ ]:= I1 n β δ κ + (n δ + λ) (I1 n β δ + I1 β κ + I1 β λ + n δ λ + λ2)
```

All of the coefficients are positive, so stability is guaranteed if a1 a2-a3>0 from the Routh-Hurwitz conditions (Box 8.2 in Otto and Day):

```
In[ ]:= a1 = Coefficient[char, λ2];  
a2 = Coefficient[char, λ1];  
a3 = char /. λ → 0;
```

```
a1 a2 - a3 // Simplify
```

```
Out[ ]:= 4 I1 n2 β δ2 + 2 n3 δ3 + I12 β2 (2 n δ + κ)
```

As these terms are all positive, stability is guaranteed.

Step 3: n = 3

```

In[ ]:= Clear[eqnr, r, n]
tryn = 3;
eqns =  $\delta$  n R[3] -  $\beta$  S I1;
eqni =  $\beta$  S I1 -  $\kappa$  I1;
eqnR[1] =  $\kappa$  I1 -  $\delta$  n R[1];
Table[eqnR[nn_] :=  $\delta$  n R[nn - 1] -  $\delta$  n R[nn], {nn, 2, tryn}];

eqnset = Flatten[{eqns, eqni, Table[eqnR[nn], {nn, 1, tryn}]}] /.
  R[tryn]  $\rightarrow$  1 - S - I1 - Sum[R[jj], {jj, 1, tryn - 1}];
varset = Flatten[{S, I1, Table[R[nn], {nn, 1, tryn - 1}]}];
stabmat =
  Table[D[eqnset[[i]], varset[[j]]], {i, 1, tryn + 1}, {j, 1, tryn + 1}] /. ii  $\rightarrow$  i;
% // MatrixForm

```

Out[]:= MatrixForm=

$$\begin{pmatrix} -I1 \beta - n \delta & -S \beta - n \delta & -n \delta & -n \delta \\ I1 \beta & S \beta - \kappa & 0 & 0 \\ 0 & \kappa & -n \delta & 0 \\ 0 & 0 & n \delta & -n \delta \end{pmatrix}$$

```

In[ ]:= char = Det[ $\lambda$  IdentityMatrix[tryn + 1] - stabmat] /.
  {S  $\rightarrow$   $\frac{\kappa}{\beta}}$  (* Char poly with leading  $\lambda^n$  term*)

```

Out[]:= $I1 n^2 \beta \delta^2 \kappa + (n \delta + \lambda) (I1 n \beta \delta \kappa + (n \delta + \lambda) (I1 n \beta \delta + I1 \beta \kappa + I1 \beta \lambda + n \delta \lambda + \lambda^2))$

All of the coefficients are positive, so stability is guaranteed if $a_1 a_2 a_3 - a_3^2 - a_1^2 a_4 > 0$ from the Routh-Hurwitz conditions:

```

In[ ]:= a1 = Coefficient[char,  $\lambda^3$ ];
a2 = Coefficient[char,  $\lambda^2$ ];
a3 = Coefficient[char,  $\lambda^1$ ];
a4 = char /.  $\lambda \rightarrow 0$ ;

```

```

In[ ]:= a1 a2 a3 - a3^2 - a1^2 a4 /. n  $\rightarrow$  3 // Factor

```

Out[]:= $9 \delta (24 I1^3 \beta^3 \delta^2 + 216 I1^2 \beta^2 \delta^3 + 648 I1 \beta \delta^4 + 648 \delta^5 + 9 I1^3 \beta^3 \delta \kappa + 30 I1^2 \beta^2 \delta^2 \kappa - 27 I1 \beta \delta^3 \kappa + I1^3 \beta^3 \kappa^2)$

This is not clearly positive and can indeed be negative under a restricted range of parameters. Setting $\kappa=1$ (without loss of generality, setting the time unit to the average length of infection), we require $\delta < \frac{1}{324}$ (waning is >324 times slower than recovery):

In[]:= Reduce[$\left\{ \left(a_1 a_2 a_3 - a_3^2 - a_1^2 a_4 / . n \rightarrow 3 \right) < 0, I_1 == \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}, \beta > \kappa, \delta > 0, \kappa == 1 \right\}$]

Out[]:= $0 < \delta < \frac{1}{324} \&\&$
 $\text{Root}\left[-1 + 48 \delta + 276 \delta^2 + 891 \delta^3 + 1296 \delta^4 + 648 \delta^5 + (3 - 60 \delta + 174 \delta^2 + 837 \delta^3 + 648 \delta^4) \sqrt{1 + (-3 + 3 \delta + 174 \delta^2 + 216 \delta^3) \sqrt{1^2 + (1 + 9 \delta + 24 \delta^2) \sqrt{1^3 \&, 2}}} < \beta < \text{Root}\left[-1 + 48 \delta + 276 \delta^2 + 891 \delta^3 + 1296 \delta^4 + 648 \delta^5 + (3 - 60 \delta + 174 \delta^2 + 837 \delta^3 + 648 \delta^4) \sqrt{1 + (-3 + 3 \delta + 174 \delta^2 + 216 \delta^3) \sqrt{1^2 + (1 + 9 \delta + 24 \delta^2) \sqrt{1^3 \&, 3}}} \&\& \kappa == 1 \&\& I_1 == \frac{-\delta + \beta \delta}{\beta + \beta \delta}\right]$

e.g.,

In[]:= Reduce[$\left\{ \left(a_1 a_2 a_3 - a_3^2 - a_1^2 a_4 / . n \rightarrow 3 \right) < 0, I_1 == \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}, \beta > \kappa, \delta > 0, \kappa == 1, \delta == 1 / 400 \right\}$]

Out[]:= $\sqrt{1.08...} < \beta < \sqrt{1.16...} \&\& \kappa == 1 \&\& \delta == \frac{1}{400} \&\& I_1 == \frac{400 \left(-\frac{1}{400} + \frac{\beta}{400} \right)}{401 \beta}$

And the leading eigenvalue has become complex with a positive real root (unstable):

In[]:= Eigenvalues[
 $\text{stabmat} / . n \rightarrow \text{try} / . \left\{ S \rightarrow \frac{\kappa}{\beta}, I_1 \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} \right\} / . \kappa \rightarrow 1 / . \delta \rightarrow 1 / 400 / . \beta \rightarrow 1.1$]

Out[]:= $\{0.0000259256 + 0.0163337 i, 0.0000259256 - 0.0163337 i, -0.0114006 + 0.00530625 i, -0.0114006 - 0.00530625 i\}$

Even then, $\tilde{R}_0$ must be relatively small, with stability guaranteed as long as $\tilde{R}_0 = \frac{\beta}{\kappa} > 1.16$:

In[]:= Reduce[$\left\{ \left(a_1 a_2 a_3 - a_3^2 - a_1^2 a_4 / . n \rightarrow 3 \right) < 0, I_1 == \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}, \beta > \kappa, \delta > 0, \kappa == 1, \beta > 1.16 \right\}$]

... Reduce: Reduce was unable to solve the system with inexact coefficients. The answer was obtained by solving a corresponding exact system and numericizing the result.

Out[]:= False

This is consistent with Figure 3 of Hethcote et al. (1981) with $n=3$, where with κ arbitrarily set to one (their γ), instability of the endemic equilibrium requires that $\beta-1$ be in an intermediate zone (their $\sigma-1$) and δ be high enough (note that their $\alpha = \kappa/\epsilon = \kappa/(n \delta)$ so that δ has to be less than $1/300$ for α to be greater than 100, as in the figure).

We can use proof by induction based on the above changes as n increases to conclude that the characteristic polynomial will generally be:

$\text{Sum}\left[(n \delta + \lambda)^{x-1} (I_1 (n \delta)^{n-x} \beta \kappa), \{x, 1, n-1\}\right] + (n \delta + \lambda)^n (I_1 n \beta \delta + I_1 \beta \kappa + I_1 \beta \lambda + n \delta \lambda + \lambda^2)$

Again, all of the coefficients are positive (including at $\lambda=0$), and so there cannot be a real eigenvalue greater than 0 (the characteristic polynomial is positive at $\lambda=0$ and can only grow as λ rises above 0). But there can be imaginary eigenvalues whose real part is greater than 0 (Hethcote et al. 1981).

Evaluating the sum:

$$\text{Sum}[(n\delta + \lambda)^{x-1} (I1 (n\delta)^{n-x} \beta \kappa), \{x, 1, n-1\}] // \text{Factor}$$

$$\text{Out}[*]= - \frac{i \beta \kappa (n\delta (n\delta)^n + (n\delta)^n \lambda - n\delta (n\delta + \lambda)^n)}{\lambda (n\delta + \lambda)}$$

The characteristic polynomial can thus be written as:

$$\frac{I1 \beta \kappa (n\delta (n\delta + \lambda)^{n-1} - (n\delta)^n)}{\lambda} + (n\delta + \lambda)^{n-1} (I1 n \beta \delta + I1 \beta \kappa + I1 \beta \lambda + n\delta \lambda + \lambda^2)$$

Here we proceed with a series of rearrangements to obtain equation (4.5) in Hethcote et al. (1981):

$$- \frac{I1 \beta \kappa (n\delta)^n}{\lambda} + (n\delta + \lambda)^{n-1} \left(\frac{I1 \beta \kappa n\delta}{\lambda} + I1 n \beta \delta + I1 \beta \kappa + I1 \beta \lambda + n\delta \lambda + \lambda^2 \right)$$

which with $z = \lambda/(n\delta)$ and factoring out $(n\delta)^{n+1}$:

$$(n\delta)^{n+1} \left(- \frac{I1 \beta \kappa}{z (n\delta)^2} + (z + 1)^{n-1} \left(\frac{I1 \beta \kappa}{z (n\delta)^2} + \frac{I1 \beta \kappa}{(n\delta)^2} + \frac{I1 \beta (z+1)}{(n\delta)} + z + z^2 \right) \right)$$

then factoring out $(z + 1)^n$:

$$(n\delta)^{n+1} (z + 1)^n \left[- \frac{I1 \beta \kappa}{z (n\delta)^2} (z + 1)^{-n} + (z + 1)^{-1} \left(\frac{I1 \beta \kappa (z+1)}{z (n\delta)^2} + \frac{I1 \beta (z+1)}{(n\delta)} + z (z + 1) \right) \right]$$

$$(n\delta)^{n+1} (z + 1)^n \left[- \frac{I1 \beta \kappa}{z (n\delta)^2} (z + 1)^{-n} + \left(\frac{I1 \beta \kappa}{z (n\delta)^2} + \frac{I1 \beta}{(n\delta)} + z \right) \right]$$

$$(n\delta)^{n+1} (z + 1)^n \left[z - \frac{I1 \beta \kappa}{z (n\delta)^2} (z + 1)^{-n} + \left(\frac{I1 \beta \kappa}{z (n\delta)^2} + \frac{I1 \beta}{(n\delta)} \right) \right]$$

The term in square brackets matches (4.5):

$$\text{In}[*]:= \left(z - \frac{I1 \beta \kappa}{z (n\delta)^2} (z + 1)^{-n} + \left(\frac{I1 \beta \kappa}{z (n\delta)^2} + \frac{I1 \beta}{(n\delta)} \right) \right) - \left(z + \alpha \frac{\sigma - 1}{1 + n\alpha} \left(1 + \frac{\alpha}{z} (1 - (z + 1)^{-n}) \right) \right) /. \sigma \rightarrow$$

$$\beta / \kappa /. \alpha \rightarrow \kappa / (n\delta) /. z \rightarrow \lambda / (n\delta) /. I1 \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} // \text{PowerExpand} // \text{Simplify}$$

$$\text{Out}[*]= 0$$

As illustrated in Figure 3 of Hethcote et al., the equilibrium point is generally stable when $\tilde{R}_0$ is large (e.g., it is stable for $n \leq 6$ if $\tilde{R}_0 > 2$, which corresponds to $\sigma - 1 > 1$ in their Figure).

Thus, while we will not necessarily observe stability of the equilibrium point for n very large (e.g., fixed waning periods) and $\tilde{R}_0$ small enough, we focus on cases where the equilibrium is stable.

Accordingly, when $\tilde{R}_0 = \frac{\beta}{\kappa} > 1$, we expect case numbers to stabilize around $\hat{I} = \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}$. This endemic equilibrium can be rewritten in terms of $\tilde{R}_0$ as $\hat{I} = \frac{(\tilde{R}_0 - 1) \delta}{\tilde{R}_0 (\delta + \kappa)}$ and all of the calculations in the previous section apply.

Check: $n = 10$

```
In[ ]:= Clear[eqnr, R, n]
      tryn = 10;

      eqns =  $\delta$  n R[tryn] -  $\beta$  S I1;
      eqni =  $\beta$  S I1 -  $\kappa$  I1;
      eqnR[1] =  $\kappa$  I1 -  $\delta$  n R[1];
      Table[eqnR[nn_] :=  $\delta$  n R[nn - 1] -  $\delta$  n R[nn], {nn, 2, tryn}];

      eqnset = Flatten[{eqns, eqni, Table[eqnR[nn], {nn, 1, tryn}]}] /.
        R[tryn]  $\rightarrow$  1 - S - I1 - Sum[R[jj], {jj, 1, tryn - 1}];
      varset = Flatten[{S, I1, Table[R[nn], {nn, 1, tryn - 1}]}];
      stabmat =
        Table[D[eqnset[[i]], varset[[j]]], {i, 1, tryn + 1}, {j, 1, tryn + 1}] /. ii  $\rightarrow$  i;
      % // MatrixForm
```

Out[]//MatrixForm=

$$\begin{pmatrix} -I1 \beta - n \delta & -S \beta - n \delta & -n \delta & -n \delta & -n \delta & -n \delta & -n \delta & -n \delta & -n \delta & -n \delta & -n \delta \\ I1 \beta & S \beta - \kappa & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & \kappa & -n \delta & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & n \delta & -n \delta & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & n \delta & -n \delta & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & n \delta & -n \delta & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & n \delta & -n \delta & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & n \delta & -n \delta & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & n \delta & -n \delta & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & n \delta & -n \delta & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & n \delta & -n \delta \end{pmatrix}$$

```
In[ ]:= fullchar = Det[ $\lambda$  IdentityMatrix[tryn + 1] - stabmat] /.
      S  $\rightarrow$   $\frac{\kappa}{\beta}$  (* Char poly with leading  $\lambda^n$  term*)
```

```
Out[ ]:= I1 n^9  $\beta$   $\delta^9$   $\kappa$  +
      (n  $\delta$  +  $\lambda$ ) (I1 n^8  $\beta$   $\delta^8$   $\kappa$  + (n  $\delta$  +  $\lambda$ ) (I1 n^7  $\beta$   $\delta^7$   $\kappa$  + (n  $\delta$  +  $\lambda$ ) (I1 n^6  $\beta$   $\delta^6$   $\kappa$  + (n  $\delta$  +  $\lambda$ ) (I1 n^5  $\beta$   $\delta^5$   $\kappa$  +
      (n  $\delta$  +  $\lambda$ ) (I1 n^4  $\beta$   $\delta^4$   $\kappa$  + (n  $\delta$  +  $\lambda$ ) (I1 n^3  $\beta$   $\delta^3$   $\kappa$  + (n  $\delta$  +  $\lambda$ ) (I1 n^2  $\beta$   $\delta^2$   $\kappa$  + (n  $\delta$  +  $\lambda$ )
      (I1 n  $\beta$   $\delta$   $\kappa$  + (n  $\delta$  +  $\lambda$ ) (I1 n  $\beta$   $\delta$  + I1  $\beta$   $\kappa$  + I1  $\beta$   $\lambda$  + n  $\delta$   $\lambda$  +  $\lambda^2$ )))))))))
```

Compare to:

$$\text{In[]:= charpoly} = -\frac{I1 \beta \kappa (n \delta)^n}{\lambda} + (n \delta + \lambda)^{n-1} \left(\frac{I1 \beta \kappa n \delta}{\lambda} + I1 n \beta \delta + I1 \beta \kappa + I1 \beta \lambda + n \delta \lambda + \lambda^2 \right);$$

Checks out:

$$\text{In[]:= Factor}\left[\text{fullchar} / \text{charpoly} /. n \rightarrow \text{try}n /. \left\{S \rightarrow \frac{\kappa}{\beta}, I1 \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}\right\}\right]$$

Out[]:= 1

SIR_n model: Variants that are more immune evasive or transmissible

Here we allow the new variant to change the transmission rate (β) and/or the stage of waning at which infection is possible. Specifically, while there are n waning stages for the resident, we allow the mutant to infect at an earlier stage (the last m recovered stages). Specifically, we assume that for $k > n - m$, the new variant is able to infect recovered class $R[k]$ as well as those in the susceptible class

$$\begin{aligned} \text{In[]:= eqns} = \{ & D[S[t], t] == \delta n R[n, t] - \beta_1 S[t] \times I1[t] - \beta_2 S[t] \times I2[t], \\ & D[I1[t], t] == \beta_1 S[t] \times I1[t] - \kappa I1[t], \\ & D[I2[t], t] == \beta_2 S[t] \times I2[t] + \beta_2 \text{Sum}[R[k, t], \{k, 1 + n - m, n\}] \times I2[t] - \kappa I2[t], \\ & D[R[1, t], t] == \kappa I1[t] + \kappa I2[t] - \delta n R[1, t], \\ & D[R[j_, t], t] == \delta n R[j - 1, t] - \delta n R[j, t], (*For j \leq n - m *) \\ & D[R[k_, t], t] == \delta n R[k - 1, t] - \delta n R[k, t] - \beta_2 R[k, t] \times I2[t] \} (*For k > n - m *) \end{aligned}$$

Before the new variant is present ($I2=0$), the final equation is the same as the previous one. Setting these equations to zero (with $I2=0$), we have $R[j-1]=R[j]$ at equilibrium for the recovered classes besides the first recovered class. Furthermore, adding the first four equations (with $I2=0$) indicates that $\delta n R[n,t] = \delta n R[1,t]$, so at equilibrium all r values are equal.

Measuring the variables as a fraction of the full population ($S+I1+I2+n R == 1$), we then have at the endemic equilibrium ($I2=0$)

$$\text{In[]:= Solve}[S + I1 + n R == 1, R]$$

$$\text{Out[]:= } \left\{ \left\{ R \rightarrow \frac{1 - I1 - S}{n} \right\} \right\}$$


```

In[ ]:= equil = Solve[ {0 == δ n R - β1 S I1 ,
    0 == β1 S I1 - κ I1 ,
    0 == κ I1 - δ n R,
    0 == δ n R - δ n R} /. {R →  $\frac{1 - I1 - S}{n}$ },
    {S, I1}] // Simplify

Out[ ]:= { {S → 1, I1 → 0}, {S →  $\frac{\kappa}{\beta1}$ , I1 →  $\frac{\delta (\beta1 - \kappa)}{\beta1 (\delta + \kappa)}$ } }

In[ ]:= endemiceq = {S →  $\frac{\kappa}{\beta1}$ , I1 →  $\frac{\delta (\beta1 - \kappa)}{\beta1 (\delta + \kappa)}$ , R →  $\frac{(\beta1 - \kappa) \kappa}{n \beta1 (\delta + \kappa)}$ , I2 → 0};

```

By contrast, when the variant has fixed, the endemic equilibrium changes because there are then only effectively $n-m$ recovered classes:

```

In[ ]:= Solve[ {0 == δ n R - β2 S I2 ,
    0 == β2 S I2 - κ I2 ,
    0 == κ I2 - δ n R,
    0 == δ n R - δ n R} /. {R →  $\frac{1 - I2 - S}{n - m}$ },
    {S, I2}] // Simplify

Out[ ]:= { {S → 1, I2 → 0}, {S →  $\frac{\kappa}{\beta2}$ , I2 →  $\frac{n \delta (\beta2 - \kappa)}{\beta2 (-m \kappa + n (\delta + \kappa))}$ } }

```

which can be written as $I2 \rightarrow \frac{n \delta (\beta2 - \kappa)}{\beta2 (n \delta + (n-m) \kappa)}$. Immune evasiveness effectively reduces the return time to the susceptible state following infection, so that $\delta \rightarrow \delta + \Delta\delta$ where $\Delta\delta = \frac{m}{n-m} \delta$, causing the number of infected individuals at steady state to rise to:

```

In[ ]:=  $\frac{(\delta + \Delta\delta) (\beta1 + \Delta\beta - \kappa)}{(\beta1 + \Delta\beta) (\delta + \Delta\delta + \kappa)} /. \Delta\delta \rightarrow \frac{m}{n-m} \delta /. \Delta\beta \rightarrow \beta2 - \beta1;$ 

```

```
Factor[ (I2 /. %) [[2]] - %]
```

```
Out[ ]:= 0
```

We assume that the endemic equilibrium is stable and determine when it would be invaded by a new variant that changes the transmission rate and/or immune evasive properties of the population. Ordering the equations with the new variant infections last:

```

In[ ]:= {D[S[t], t] == δ n R[n, t] - β1 S[t] × I1[t] - β2 S[t] × I2[t],
    D[I1[t], t] == β1 S[t] × I1[t] - κ I1[t],
    D[R[1, t], t] == κ I1[t] + κ I2[t] - δ n R[1, t],
    D[R[j_, t], t] == δ n R[j - 1, t] - δ n R[j, t], (*For j ≤ n-m *)
    D[R[k_, t], t] == δ n R[k - 1, t] - δ n R[k, t] - β2 R[k, t] × I2[t], (*For k > n-m *)
    D[I2[t], t] == β2 S[t] × I2[t] + β2 Sum[R[k, t], {k, 1 + n - m, n}] × I2[t] - κ I2[t];

```

At the endemic equilibrium, the form of the Jacobian matrix is a block triangular matrix. With n recovered classes, there will be an $(n+2) \times (n+2)$ upper left matrix, which determines the stability of the endemic equilibrium. The bottom row consists of zeros except for the last element.

By considering only cases yielding a stable endemic equilibrium, stability to invasion by a new variant is governed by the derivative of the last equation with respect to the number of variant infections

$\left(\frac{d(dI_2/dt)}{dI_2}\right)$ evaluated at the endemic equilibrium:

```
In[ ]:= eqni2 =  $\beta_2 S I_2 + \beta_2 m R I_2 - \kappa I_2$ ;
eqnset = {eqni2};
varset = {I2};
stabmat = Table[D[eqnset[[i]], varset[[j]]], {i, 1, 1}, {j, 1, 1}]
```

```
Out[ ]:= { { m R  $\beta_2 + S \beta_2 - \kappa$  } }
```

At the endemic equilibrium, the number of susceptibles is $\hat{S} = \frac{\kappa}{\beta_1}$, so this eigenvalue corresponds to:

$$\begin{aligned} m R \beta_2 + S \beta_2 - \kappa \\ &= m R \beta_2 + \frac{\kappa}{\beta_1} \beta_2 - \kappa \\ &= m R \beta_2 + \frac{\kappa}{\beta_1} (\beta_2 - \beta_1) \\ &= m R \beta_2 + \kappa \frac{\Delta \beta}{\beta_1} \\ &= m R \beta_2 + \kappa \frac{\Delta \tilde{R}_0}{\tilde{R}_0} \end{aligned}$$

with the new lineage gaining a transmission advantage by infecting the last recovered classed (frequency $m R$) and/or increasing transmission. For a given proportional difference in β (or $\tilde{R}_0$), the higher the clearance rate, the higher the selective advantage of the new mutant.

Note that the eigenvalue is equal to the selection coefficient favouring the new variant. This can be shown as follows. By definition, selection s favouring a new type whose frequency is p is given by

$\frac{dp}{dt} \equiv s p q$, where $p = \frac{n_2}{n_1+n_2}$ when there are n_1 and n_2 infections by the resident and new variant. Because the resident variant is not growing at the endemic equilibrium ($\frac{dn_1}{dt} = 0$) and the new variant is growing at a per capita rate of λ ($\frac{dn_2}{dt} = \lambda n_2$), the selection coefficient is λ :

$$\frac{dp}{dt} \equiv s p q = \frac{d\left(\frac{n_2}{n_1+n_2}\right)}{dt} = \frac{\frac{dn_2}{dt}(n_1+n_2) - \frac{d(n_1+n_2)}{dt}n_2}{(n_1+n_2)^2} = \frac{\lambda n_2(n_1+n_2) - \lambda n_2^2}{(n_1+n_2)^2} = \lambda p q$$

Comment: The selective advantage of the new variant is coming not from shortening the waning period following infections by the new variant but by its ability to infect the currently recovered population (from past infections and vaccinations).

That is, a new variant that only reduces the waning period (increasing δ is effectively neutral). This is most easily seen in the original SIR model, with the resident and new variants having waning rates of δ_1 and δ_2 :

```

In[ ]:= eqns = {D[S[t], t] ==  $\delta_1 R_1[t] + \delta_2 R_2[t] - \beta S[t] \times I_1[t]$ ,
  D[I_1[t], t] ==  $\beta S[t] \times I_1[t] - \kappa I_1[t]$ ,
  D[R_1[t], t] ==  $\kappa I_1[t] - \delta_1 R_1[t]$ ,
  D[I_2[t], t] ==  $\beta S[t] \times I_2[t] - \kappa I_2[t]$ ,
  D[R_2[t], t] ==  $\kappa I_2[t] - \delta_2 R_2[t]$ };

In[ ]:= eqni2 =  $\beta S I_2 - \kappa I_2$ ;
eqnr2 =  $\kappa I_2 - \delta_2 R_2$ ;
eqnset = {eqni2, eqnr2};
varset = {I_2, R_2};
stabmat =
  Table[D[eqnset[[i]], varset[[j]]], {i, 1, 2}, {j, 1, 2}] /. {S ->  $\frac{\kappa}{\beta}$ , I_2 -> 0, R_2 -> 0}

Out[ ]:= {{0, 0}, { $\kappa$ ,  $-\delta_2$ }}

In[ ]:= Simplify[Max[Eigenvalues[%]], { $\delta_2 > 0$ }]

Out[ ]:= 0

```

LATENCY: ADDING A TRANSIENT INFECTED BUT NOT INFECTIOUS CLASS

COVID-19 infections are characterized by a short latent period, during which an individual is exposed but does not yet have detectable virus levels. The latent period for Omicron is estimated at 3.1 days (Xin et al. 2023; UKHSA). Including a latent class (E1) with exit rate $\epsilon = 1/3.1$:

```

In[ ]:= eqns = {D[S[t], t] ==  $\delta n R[n, t] - \beta S[t] \times I_1[t]$ ,
  D[E1[t], t] ==  $\beta S[t] \times I_1[t] - \epsilon E1[t]$ ,
  D[I_1[t], t] ==  $\epsilon E1[t] - \kappa I_1[t]$ ,
  D[R[1, t], t] ==  $\kappa I_1[t] - \delta n R[1, t]$ ,
  D[R[j_, t], t] ==  $\delta n R[j - 1, t] - \delta n R[j, t]$ };

Inclusion of a latent period leads to the equilibrium:

In[ ]:= Solve[{0 ==  $\delta * n R - \beta S I_1$ ,
  0 ==  $\beta S I_1 - \epsilon E1$ ,
  0 ==  $\epsilon E1 - \kappa I_1$ }] /. R -> (1 - S - E1 - I1) / n, {S, E1, I1}] // Simplify

Out[ ]:= {{S -> 1, E1 -> 0, I1 -> 0}, {S ->  $\frac{\kappa}{\beta}$ , E1 ->  $\frac{\delta (\beta - \kappa) \kappa}{\beta (\epsilon \kappa + \delta (\epsilon + \kappa))}$ , I1 ->  $\frac{\delta \epsilon (\beta - \kappa)}{\beta (\epsilon \kappa + \delta (\epsilon + \kappa))}$ }}

```

Because movement from the latent class is much faster than waning ($\epsilon \gg \delta$), including a latent period has little influence on the equilibrium: $\frac{\delta \epsilon (\beta - \kappa)}{\beta (\epsilon \kappa + \delta \kappa + \delta \epsilon)} \sim \frac{\delta \epsilon (\beta - \kappa)}{\beta (\epsilon \kappa + \delta \epsilon)} = \frac{\delta (\beta - \kappa)}{\beta (\kappa + \delta)}$.

Impact of a latent period on the rate of spread of a new variant:

```

In[ ]:= {D[S[t], t] ==  $\delta n R[n, t] - \beta_1 S[t] \times I_1[t] - \beta_2 S[t] \times I_2[t]$ ,
        D[E1[t], t] ==  $\beta S[t] \times I_1[t] - \epsilon E_1[t]$ ,
        D[I1[t], t] ==  $\epsilon E_1[t] - \kappa I_1[t]$ ,
        D[R[1, t], t] ==  $\kappa I_1[t] + \kappa I_2[t] - \delta n R[1, t]$ ,
        D[R[j_, t], t] ==  $\delta n R[j - 1, t] - \delta n R[j, t]$ , (*For j≤n-m *)
        D[R[k_, t], t] ==  $\delta n R[k - 1, t] - \delta n R[k, t] - \beta_2 R[k, t] \times I_2[t]$ , (*For k>n-m *)
        D[E2[t], t] ==  $\beta S[t] \times I_2[t] + \beta_2 \text{Sum}[R[k, t], \{k, 1 + n - m, n\}] \times I_2[t] - \epsilon E_2[t]$ ,
        D[I2[t], t] ==  $\epsilon E_2[t] - \kappa I_2[t]$ };

```

By considering only cases yielding a stable endemic equilibrium, stability to invasion by a new variant is governed by the derivative of the last two equations evaluated at the endemic equilibrium:

```

In[ ]:= eqne2 =  $\beta_2 S I_2 + \beta_2 m R I_2 - \epsilon E_2$ ;
eqni2 =  $\epsilon E_2 - \kappa I_2$ ;
eqnset = {eqne2, eqni2};
varset = {E2, I2};
stabmat = Table[D[eqnset[[i]], varset[[j]]], {i, 1, 2}, {j, 1, 2}]

```

```
Out[ ]:= {{- $\epsilon$ ,  $m R \beta_2 + S \beta_2$ }, { $\epsilon$ ,  $-\kappa$ }}
```

In the absence of a latent period, selection on the variant was $s \equiv m R \beta_2 + S \beta_2 - \kappa$. Compared to this selection coefficient, adding a latent period changes selection to this leading eigenvalue

```

In[ ]:= stabmat /.  $m R \beta_2 + S \beta_2 \rightarrow s + \kappa$  // Eigenvalues

```

```

Out[ ]:=  $\left\{ \frac{1}{2} \left( -\epsilon - \kappa - \sqrt{4 s \epsilon + (\epsilon + \kappa)^2} \right), \frac{1}{2} \left( -\epsilon - \kappa + \sqrt{4 s \epsilon + (\epsilon + \kappa)^2} \right) \right\}$ 

```

with the latent and infectious period short relative to the spread of the variant ($\epsilon, \kappa \gg s$), the rate of spread of a variant would be:

```

In[ ]:= Collect[Simplify[Normal[Series[%][[2]], {s, 0, 1}]], { $\epsilon > 0$ ,  $\kappa > 0$ ,  $s > 0$ }],  $\epsilon$ , Factor]

```

```

Out[ ]:=  $\frac{s \epsilon}{\epsilon + \kappa}$ 

```

which can be written as:

$$s \frac{1}{1 + \kappa / \epsilon}$$

For example, when $\epsilon=1/3$ and $\kappa=1/7$, the selection coefficient is 70% of s .

```

In[ ]:=  $\frac{1 / \kappa}{1 / \kappa + 1 / \epsilon}$  // Factor

```

```

Out[ ]:=  $\frac{\epsilon}{\epsilon + \kappa}$ 

```

SIR_n model: Variants that are more immune evasive or

transmissible (leaky)

Here we allow the new variant to change the transmission rate (β) and/or the stage of waning at which infection is possible. Specifically, while there are n waning stages for the resident, we allow the mutant to infect at an earlier stage (the last m recovered stages). Specifically, we assume that for $k > n - m$, the new variant is able to infect recovered class $R[k]$ as well as those in the susceptible class

$$\begin{aligned}
 \text{eqns} = \{ & D[S[t], t] = \delta n R[n, t] - \beta_1 S[t] \times I_1[t] - \beta_2 S[t] \times I_2[t], \\
 & D[I_1[t], t] = \\
 & \quad \beta_1 S[t] \times I_1[t] + \text{leak } \beta_1 \text{Sum}[R[k, t], \{k, 1, n\}] \times I_1[t] - \kappa I_2[t] - \kappa I_1[t], \\
 & D[I_2[t], t] = \beta_2 S[t] \times I_2[t] + \text{leak } \beta_2 \text{Sum}[R[k, t], \{k, 1, n\}] \times I_2[t] + \\
 & \quad \beta_2 \text{Sum}[R[k, t], \{k, 1 + n - m, n\}] \times I_2[t] - \kappa I_2[t], \\
 & D[R[1, t], t] = \kappa I_1[t] + \kappa I_2[t] - \delta n R[1, t] - \text{leak } (\beta_1 I_1[t] + \beta_2 I_2[t]) R[1, t], \\
 & D[R[j_, t], t] = \delta n R[j - 1, t] - \delta n R[j, t] - \text{leak } (\beta_1 I_1[t] + \beta_2 I_2[t]) R[j, t], \\
 & (*For j \leq n - m *) \\
 & D[R[k_, t], t] = \delta n R[k - 1, t] - \delta n R[k, t] - \\
 & \quad \text{leak } (\beta_1 I_1[t] + \beta_2 I_2[t]) R[k, t] - \beta_2 R[k, t] \times I_2[t] \} (*For k > n - m *);
 \end{aligned}$$

Before the new variant is present ($I_2=0$), setting these equations to zero (with $I_2=0$), we have

$R[j - 1] = R[j] \frac{\delta n + \text{leak } \beta_1 \hat{I}}{\delta n}$ at equilibrium for the recovered classes besides the first recovered class. These are not equal and are numerically calculated for a given value of n (for $n=5$, the resulting equation is a function of $\hat{I}^5$).

We assume that the endemic equilibrium is stable and determine when it would be invaded by a new variant that changes the transmission rate and/or immune evasive properties of the population.

Ordering the equations with the new variant infections last:

$$\begin{aligned}
 \{ & D[S[t], t] = \delta n R[n, t] - \beta_1 S[t] \times I_1[t] - \beta_2 S[t] \times I_2[t], \\
 & D[I_1[t], t] = \\
 & \quad \beta_1 S[t] \times I_1[t] + \text{leak } \beta_1 \text{Sum}[R[k, t], \{k, 1, n\}] \times I_1[t] - \kappa I_2[t] - \kappa I_1[t], \\
 & D[R[1, t], t] = \kappa I_1[t] + \kappa I_2[t] - \delta n R[1, t] - \text{leak } (\beta_1 I_1[t] + \beta_2 I_2[t]) R[1, t], \\
 & D[R[j_, t], t] = \delta n R[j - 1, t] - \delta n R[j, t] - \text{leak } (\beta_1 I_1[t] + \beta_2 I_2[t]) R[j, t], \\
 & (*For j \leq n - m *) \\
 & D[R[k_, t], t] = \delta n R[k - 1, t] - \delta n R[k, t] - \\
 & \quad \text{leak } (\beta_1 I_1[t] + \beta_2 I_2[t]) R[k, t] - \beta_2 R[k, t] \times I_2[t], (*For k > n - m *) \\
 & D[I_2[t], t] = \beta_2 S[t] \times I_2[t] + \text{leak } \beta_2 \text{Sum}[R[k, t], \{k, 1, n\}] \times I_2[t] + \\
 & \quad \beta_2 \text{Sum}[R[k, t], \{k, 1 + n - m, n\}] \times I_2[t] - \kappa I_2[t] \};
 \end{aligned}$$

At the endemic equilibrium, the form of the Jacobian matrix is a block triangular matrix. With n recovered classes, there will be an $(n+2) \times (n+2)$ upper left matrix, which determines the stability of the endemic equilibrium. The bottom row consists of zeros except for the last element.

By considering only cases yielding a stable endemic equilibrium, stability to invasion by a new variant is governed by the derivative of the last equation with respect to the number of variant infections

$\left(\frac{d(I_2/dt)}{dI_2}\right)$ evaluated at the endemic equilibrium:

```
In[ ]:= eqni2 =  $\beta_2 S I_2 + \text{leak } \beta_2 \text{ Sum}[R[k], \{k, 1, n\}] I_2 + \beta_2 \text{ Sum}[R[k], \{k, 1+n-m, n\}] I_2 - \kappa I_2$ ;
eqnset = {eqni2};
varset = {I2};
stabmat = Table[D[eqnset[[i]], varset[[j]]], {i, 1, 1}, {j, 1, 1}]
```

```
Out[ ]:=  $\left\{ \left\{ S \beta_2 - \kappa + \text{leak } \beta_2 \sum_{k=1}^n R[k] + \beta_2 \sum_{k=1+n-m}^n R[k] \right\} \right\}$ 
```

At the endemic equilibrium, setting $D[I_1[t], t]$ to zero gives $0 = \beta_1 S[t] + \text{leak } \beta_1 \text{ Sum}[R[k, t], \{k, 1, n\}] - \kappa$, or $\hat{S} + \text{Sum}[\hat{R}[k], \{k, 1, n\}] = \frac{\kappa}{\beta_1}$, so this eigenvalue corresponds to:

At the endemic equilibrium, the number of susceptibles is $\hat{S} = \frac{\kappa}{\beta_1}$, so this eigenvalue corresponds to:

$$\begin{aligned} & \beta_2 \sum_{k=1+n-m}^n R[k] + S \beta_2 + \text{leak } \beta_2 \sum_{k=1}^n R[k] - \kappa \\ &= \beta_2 \sum_{k=1+n-m}^n R[k] + \beta_2 \frac{\kappa}{\beta_1} - \kappa \\ &= \beta_2 \sum_{k=1+n-m}^n R[k] + \Delta \beta \frac{\kappa}{\beta_1} \end{aligned}$$

with the new lineage gaining a transmission advantage by infecting more of the recovered classes and/or increasing transmission (measured as in equation 1).

SIR_n model: Different NPI levels (no movement between NPI classes)

Assume an SIR_n model with waning at rate δ and transmission at rate β (dependent on NPI measures), as described by the differential equations:

```
In[ ]:= eqns = {D[S1[t], t] ==  $\delta n R1[n, t] - \beta S1[t] \times I1[t] - (1-p) \beta S1[t] \times I2[t]$ ,
D[I1[t], t] ==  $\beta S1[t] \times I1[t] + (1-p) \beta S1[t] \times I2[t] - \kappa I1[t]$ ,
D[R1[1, t], t] ==  $\kappa I1[t] - \delta n R1[1, t]$ ,
D[R1[j_, t], t] ==  $\delta n R1[j-1, t] - \delta n R1[j, t]$ ,

D[S2[t], t] ==  $\delta n R2[n, t] - (1-p) \beta S2[t] \times I1[t] - (1-p)^2 \beta S2[t] \times I2[t]$ ,
D[I2[t], t] ==  $(1-p) \beta S2[t] \times I1[t] + (1-p)^2 \beta S2[t] \times I2[t] - \kappa I2[t]$ ,
D[R2[1, t], t] ==  $\kappa I2[t] - \delta n R2[1, t]$ ,
D[R2[j_, t], t] ==  $\delta n R2[j-1, t] - \delta n R2[j, t]$ };
```

Here NPI measures protect by an amount p for those practicing the measures (reducing transmission by a factor $1-p$).

We measure the variables as a fraction of the full population and here assume a fixed fraction of individ-

uals engaged in the NPI measures (f), such that:

$$S1 + I1 + R1[1] + \dots R1[n] = 1 - f$$

$$S2 + I2 + R2[1] + \dots R2[n] = f$$

EQUILIBRIUM ANALYSIS

By the same logic as used with only one class of individuals, the last equation in each of the above two sets indicates that $R[j-1]=R[j]$ at equilibrium for both $R1$ and $R2$. Furthermore, summing the first three equations in each set indicates that $R[1]=R[j]$ for both $R1$ and $R2$ as well. We can thus focus on the first two equations in the above set to analyse the equilibrium, using the fact that $R1=(1-f-S1-I1)/n$ and $R2=(f-S2-I2)/n$.

This system has two equilibria (disease absent and disease endemic):

```

In[ ]:= equil = Solve[{0 == δ (1 - f - S1 - I1) - β S1 I1 - (1 - p) β S1 I2 ,
    0 == δ (f - S2 - I2) - (1 - p) β S2 I1 - (1 - p)2 β S2 I2 ,
    0 == β S1 I1 + (1 - p) β S1 I2 - κ I1 ,
    0 == (1 - p) β S2 I1 + (1 - p)2 β S2 I2 - κ I2 }, {S1, S2, I1, I2}] // Simplify

Out[ ]:= { {S1 → 1 - f, S2 → f, I1 → 0, I2 → 0}, {S1 → - $\frac{1}{2 p \beta} \left( \beta - p \beta - f p \beta + f p^2 \beta - p \kappa + \sqrt{(-1 + p)^2 (-1 + f p)^2 \beta^2 - 2 (1 + f (-2 + p)) (-1 + p) p \beta \kappa + p^2 \kappa^2} \right)$ , S2 →  $\frac{\beta - p \beta - f p \beta + f p^2 \beta + p \kappa + \sqrt{(-1 + p)^2 (-1 + f p)^2 \beta^2 - 2 (1 + f (-2 + p)) (-1 + p) p \beta \kappa + p^2 \kappa^2}}{2 (-1 + p)^2 p \beta}$ , I1 →  $\frac{1}{2 p \beta (\delta + \kappa)} \delta \left( \beta + p \beta - 3 f p \beta + f p^2 \beta - p \kappa + \sqrt{(-1 + p)^2 (-1 + f p)^2 \beta^2 - 2 (1 + f (-2 + p)) (-1 + p) p \beta \kappa + p^2 \kappa^2} \right)$ , I2 → - $\frac{1}{2 (-1 + p)^2 p \beta (\delta + \kappa)} \delta \left( -(-1 + p) (1 + f p (-3 + 2 p)) \beta + p \kappa + \sqrt{(-1 + p)^2 (-1 + f p)^2 \beta^2 - 2 (1 + f (-2 + p)) (-1 + p) p \beta \kappa + p^2 \kappa^2} \right)$  }, {S1 →  $\frac{1}{2 p \beta} \left( -\beta + p \beta + f p \beta - f p^2 \beta + p \kappa + \sqrt{(-1 + p)^2 (-1 + f p)^2 \beta^2 - 2 (1 + f (-2 + p)) (-1 + p) p \beta \kappa + p^2 \kappa^2} \right)$ , S2 →  $\frac{\beta - p \beta - f p \beta + f p^2 \beta + p \kappa - \sqrt{(-1 + p)^2 (-1 + f p)^2 \beta^2 - 2 (1 + f (-2 + p)) (-1 + p) p \beta \kappa + p^2 \kappa^2}}{2 (-1 + p)^2 p \beta}$ , I1 →  $\frac{1}{2 p \beta (\delta + \kappa)} \delta \left( \beta + p \beta - 3 f p \beta + f p^2 \beta - p \kappa - \sqrt{(-1 + p)^2 (-1 + f p)^2 \beta^2 - 2 (1 + f (-2 + p)) (-1 + p) p \beta \kappa + p^2 \kappa^2} \right)$ , I2 →  $\frac{1}{2 (-1 + p)^2 p \beta (\delta + \kappa)} \delta \left( (-1 + p) (1 + f p (-3 + 2 p)) \beta - p \kappa + \sqrt{(-1 + p)^2 (-1 + f p)^2 \beta^2 - 2 (1 + f (-2 + p)) (-1 + p) p \beta \kappa + p^2 \kappa^2} \right)$  } } }

```

Solving for the full equilibrium (as above) is less useful than relating the variables at equilibrium to one another:

```

In[ ]:= equilpart = Solve[{0 == δ (1 - f - S1 - I1) - β S1 I1 - (1 - p) β S1 I2,
    0 == β S1 I1 + (1 - p) β S1 I2 - κ I1 ,
    0 == (1 - p) β S2 I1 + (1 - p)2 β S2 I2 - κ I2}, {S2, I1, I2}] [[1]]

Out[ ]:= {S2 →  $\frac{-S1 \beta + \kappa}{(-1 + p)^2 \beta}$ , I1 →  $\frac{\delta - f \delta - S1 \delta}{\delta + \kappa}$ , I2 →  $-\frac{(-1 + f + S1) \delta (S1 \beta - \kappa)}{(-1 + p) S1 \beta (\delta + \kappa)}$  }

```

In the stability analysis, we'll also use:


```
In[ ]:= equilpartalt = Solve[{0 ==  $\beta$  S1 I1 + (1 - p)  $\beta$  S1 I2 -  $\kappa$  I1 ,
    0 == (1 - p)  $\beta$  S2 I1 + (1 - p)2  $\beta$  S2 I2 -  $\kappa$  I2}, {S2, I2}][[1]]
```

$$\text{Out[]} = \left\{ S2 \rightarrow \frac{-S1 \beta + \kappa}{(-1 + p)^2 \beta}, I2 \rightarrow \frac{I1 (S1 \beta - \kappa)}{(-1 + p) S1 \beta} \right\}$$

Solving for the remaining equation gives:

```
In[ ]:= equilpartsol = Collect[
    Numerator[Factor[ $\delta$  (f - S2 - I2) - (1 - p)  $\beta$  S2 I1 - (1 - p)2  $\beta$  S2 I2 /. equilpart]] /
    ( $\delta$  p  $\beta$ ), S1, Factor]
```

$$\text{Out[]} = S1^2 - \frac{(-1 + f) (-1 + p) \kappa}{p \beta} + \frac{S1 (\beta - p \beta - f p \beta + f p^2 \beta - p \kappa)}{p \beta}$$

```
In[ ]:= apart = 1;
```

$$\text{bpart} = \frac{\beta - p \beta - f p \beta + f p^2 \beta - p \kappa}{p \beta};$$

$$\text{cpart} = -\frac{(1 - f) (1 - p) \kappa}{p \beta};$$

$$\text{apart } S1^2 + \text{bpart } S1 + \text{cpart};$$

```
Factor[% - equilpartsol]
```

```
Out[ ]:= 0
```

Because $-4ac > 0$, $\text{Sqrt}[b^2 - 4ac]$ is larger in magnitude than b , so the relevant root is $-b + \text{Sqrt}[b^2 - 4ac]$ (the other root will always be negative).

$$\text{In[]:= } S1\text{root} = \frac{-\text{bpart} + \text{Sqrt}[\text{Simplify}[\text{bpart}^2 - 4 \text{cpart}]]}{2}$$

$$\text{Out[]} = \frac{1}{2} \left(-\frac{\beta - p \beta - f p \beta + f p^2 \beta - p \kappa}{p \beta} + \sqrt{\frac{4 (-1 + f) (-1 + p) p \beta \kappa + ((-1 + p) (-1 + f p) \beta - p \kappa)^2}{p^2 \beta^2}} \right)$$

Note that if $f = 0$, the root is $S1 = \frac{\kappa}{\beta}$, as seen in the case with no heterogeneity in NPI use:

```
In[ ]:= Solve[(equilpartsol /. f -> 0) == 0, S1]
```

$$\text{Out[]} = \left\{ \left\{ S1 \rightarrow \frac{-1 + p}{p} \right\}, \left\{ S1 \rightarrow \frac{\kappa}{\beta} \right\} \right\}$$

And if $p = 0$ (no protection), the root is $S1 = (1 - f) \frac{\kappa}{\beta}$

```
In[ ]:= Solve[(Numerator[Factor[equilpartsol]] /. p -> 0) == 0, S1]
```

$$\text{Out[]} = \left\{ \left\{ S1 \rightarrow \frac{\kappa - f \kappa}{\beta} \right\} \right\}$$

Since $S1 + I1 + r1 = 1 - f$, for this endemic equilibrium to be valid we require that $S1 < 1 - f$, which will be true when:

$$\frac{-bpart + \text{Sqrt}[bpart^2 - 4 cpart]}{2} < 1 - f$$

$$\text{Sqrt}[bpart^2 - 4 cpart] < 2(1 - f) + bpart$$

If the right hand-side is negative, this will never be satisfied and the equilibrium is invalid. The right-hand side can only be negative when the disease-free equilibrium is stable, which requires $((1 - f) + f(1 - p)^2) \beta < \kappa$ [see below].

```
In[ ]:= (2 (1 - f) + bpart) ;
```

$$\left((1 - f) + \frac{((1 - f) + f(1 - p)^2) \beta - \kappa + (1 - p) \kappa}{p \beta} \right) - \% // \text{Factor}$$

```
Out[ ]:= 0
```

Otherwise, if $2(1-f)+bpart$ is positive, the equilibrium will be valid only when:

$$bpart^2 - 4 cpart < (2(1 - f) + bpart)^2$$

which requires that the following be positive:

```
In[ ]:= (2 (1 - f) + bpart)^2 - (bpart^2 - 4 cpart) ;
```

$$(1 - f) \frac{4((1 - f) + f(1 - p)^2) \beta - \kappa}{p \beta} - \% // \text{Factor}$$

```
Out[ ]:= 0
```

This will never be positive when the disease-free equilibrium is stable $((1 - f) + f(1 - p)^2) \beta < \kappa$, so we do not have a valid endemic equilibrium if the disease cannot spread when rare.

In the simulations, we'll allow a fraction of seroconversion, q , with $(1-q)$ failing to seroconvert and returning to the susceptible class. With NPI heterogeneity, this leads to:

```
In[ ]:= equilpart2 = Solve[{0 == (1 - q) \kappa I1 + \delta (1 - f - S1 - I1) - \beta S1 I1 - (1 - p) \beta S1 I2,
```

$$0 = \beta S1 I1 + (1 - p) \beta S1 I2 - \kappa I1,$$

$$0 = (1 - p) \beta S2 I1 + (1 - p)^2 \beta S2 I2 - \kappa I2}, \{S2, I1, I2\}][[1]]$$

```
Out[ ]:= {S2 -> \frac{-S1 \beta + \kappa}{(-1 + p)^2 \beta}, I1 -> \frac{\delta - f \delta - S1 \delta}{\delta + q \kappa}, I2 -> -\frac{(-1 + f + S1) \delta (S1 \beta - \kappa)}{(-1 + p) S1 \beta (\delta + q \kappa)}}
```

This doesn't change equilpartsol though (so S1root is the same):

```
In[ ]:= Collect[
```

$$\text{Numerator}[\text{Factor}[(1 - q) \kappa I2 + \delta (f - S2 - I2) - (1 - p) \beta S2 I1 - (1 - p)^2 \beta S2 I2] / .$$

$$\text{equilpart2}]] / (\delta p \beta), S1, \text{Factor}];$$

```
% - equilpartsol
```

```
Out[ ]:= 0
```

In[]:= FullSimplify[I1 + I2 /. equilpart2 /. S1 → S1root, {0 < f < 1, 0 < p < 1, β > 0}]

$$\text{Out[]} = \frac{1}{2(-1+p)^2\beta(\delta+\kappa)}\delta\left((1+f(-2+p))(-1+p)p\beta - (2+(-2+p)p)\kappa + 2\sqrt{4(-1+f)(-1+p)p\beta\kappa + ((-1+p)(-1+fp)\beta - p\kappa)^2} - p\sqrt{4(-1+f)(-1+p)p\beta\kappa + ((-1+p)(-1+fp)\beta - p\kappa)^2}\right)$$

We'll also allow a fraction of susceptibles to vaccinate, moving into the first recovered class:

In[]:= equilpart3 = Solve[{0 == δ(1 - f - S1 - I1) - βS1I1 - (1 - p)βS1I2 - vS1,

$$0 = \beta S1 I1 + (1 - p)\beta S1 I2 - \kappa I1,$$

$$0 = (1 - p)\beta S2 I1 + (1 - p)^2\beta S2 I2 - \kappa I2], \{S2, I1, I2\}][[1]]$$

$$\text{Out[]} = \left\{ S2 \rightarrow \frac{-S1\beta + \kappa}{(-1+p)^2\beta}, I1 \rightarrow \frac{-S1v + \delta - f\delta - S1\delta}{\delta + \kappa}, I2 \rightarrow -\frac{(S1v - \delta + f\delta + S1\delta)(S1\beta - \kappa)}{(-1+p)S1\beta(\delta + \kappa)} \right\}$$

Solving for the remaining equation gives:

In[]:= equilpartsol3 =

$$\text{Collect[Numerator[Factor[\delta(f - S2 - I2) - (1 - p)\beta S2 I1 - (1 - p)^2\beta S2 I2 - vS2 /. equilpart3]] / ((v + \delta)p\beta), S1, Factor]$$

$$\text{Out[]} = S1^2 - \frac{(-1+f)(-1+p)\delta\kappa}{p\beta(v+\delta)} + \frac{S1(\beta\delta - p\beta\delta - fp\beta\delta + fp^2\beta\delta - pv\kappa - p\delta\kappa)}{p\beta(v+\delta)}$$

In[]:= apart = 1;

$$\text{bpart} = \frac{\beta\delta - p\beta\delta - fp\beta\delta + fp^2\beta\delta - p\kappa(v+\delta)}{p\beta(v+\delta)};$$

$$\text{cpart} = -\frac{(1-f)(1-p)\delta\kappa}{p\beta(v+\delta)};$$

$$\text{apart } S1^2 + \text{bpart } S1 + \text{cpart};$$

$$\text{Factor[\% - equilpartsol3]}$$

Out[]:= 0

Because $-4ac > 0$, $\text{Sqrt}[b^2 - 4ac]$ is larger in magnitude than b , so the relevant root is $-b + \text{Sqrt}[b^2 - 4ac]$ (the other root will always be negative).

$$\text{In[]:= S1root3} = \frac{-\text{bpart} + \text{Sqrt}[\text{Simplify}[\text{bpart}^2 - 4\text{cpart}]]}{2}$$

$$\text{Out[]} = \frac{1}{2} \left(-\frac{\beta\delta - p\beta\delta - fp\beta\delta + fp^2\beta\delta - p(v+\delta)\kappa}{p\beta(v+\delta)} + \sqrt{\frac{4(-1+f)(-1+p)p\beta\delta(v+\delta)\kappa + ((-1+p)(-1+fp)\beta\delta - p(v+\delta)\kappa)^2}{p^2\beta^2(v+\delta)^2}} \right)$$

```
In[ ]:= FullSimplify[I1 + I2 /. equilpart3 /. S1 → S1root3, {0 < f < 1, 0 < p < 1, β > 0}]
```

$$\text{Out[]} = \left(\left(-(-1+p) (-1+fp) \beta \delta + (v+\delta) \right. \right. \\ \left. \left((-2+p) \kappa + \sqrt{\frac{(-1+p)^2 (-1+fp)^2 \beta^2 \delta^2}{(v+\delta)^2} - \frac{2(1+f(-2+p))(-1+p)p\beta\delta\kappa}{v+\delta} + p^2 \kappa^2} \right) \right. \\ \left. \left(-(1+p+f(-3+p)p) \beta \delta + (v+\delta) \right. \right. \\ \left. \left. \left(p\kappa + \sqrt{\frac{(-1+p)^2 (-1+fp)^2 \beta^2 \delta^2}{(v+\delta)^2} - \frac{2(1+f(-2+p))(-1+p)p\beta\delta\kappa}{v+\delta} + p^2 \kappa^2} \right) \right) \right) / \\ \left(2(-1+p) \beta (\delta + \kappa) \left((-1+p) (-1+fp) \beta \delta - \right. \right. \\ \left. \left. (v+\delta) \left(p\kappa + \sqrt{\frac{(-1+p)^2 (-1+fp)^2 \beta^2 \delta^2}{(v+\delta)^2} - \frac{2(1+f(-2+p))(-1+p)p\beta\delta\kappa}{v+\delta} + p^2 \kappa^2} \right) \right) \right)$$

which reduces in the absence of NPI heterogeneity to:

```
In[ ]:= FullSimplify[% /. f → 0, {β > 0, κ > 0, p > 0, δ > 0, v > 0}]
```

$$\text{Out[]} = \begin{cases} \frac{\beta \delta - (v+\delta) \kappa}{\beta (\delta + \kappa)} & \beta \delta + p (v+\delta) \kappa \geq p \beta \delta \\ \frac{(-1+p) \beta \delta - (v+\delta) \kappa}{(-1+p)^2 \beta (\delta + \kappa)} & \text{True} \end{cases}$$

STABILITY ANALYSIS

* The disease-absent equilibrium is stable when $\left((1-f) + f(1-p)^2 \right) \beta < \kappa$.

* With one recovered class (n=1), the endemic equilibrium does not exist when the above holds but exists and is stable when it doesn't.

```
In[ ]:= eqnS1 =  $\delta (1 - f - S1 - I1) - \beta S1 I1 - (1-p) \beta S1 I2$  ;
eqnS2 =  $\delta (f - S2 - I2) - (1-p) \beta S2 I1 - (1-p)^2 \beta S2 I2$  ;
eqnI1 =  $\beta S1 I1 + (1-p) \beta S1 I2 - \kappa I1$  ;
eqnI2 =  $(1-p) \beta S2 I1 + (1-p)^2 \beta S2 I2 - \kappa I2$  ;

eqnset = {eqnS1, eqnI1, eqnS2, eqnI2};
varset = {S1, I1, S2, I2};

stabmat = Table[D[eqnset[[i]], varset[[j]]], {i, 1, 4}, {j, 1, 4}];
% // MatrixForm
```

```
Out[ ]:= //MatrixForm=
```

$$\begin{pmatrix} -I1 \beta - I2 (1-p) \beta - \delta & -S1 \beta - \delta & 0 & -(1-p) S1 \beta \\ I1 \beta + I2 (1-p) \beta & S1 \beta - \kappa & 0 & (1-p) S1 \beta \\ 0 & -(1-p) S2 \beta - I1 (1-p) \beta - I2 (1-p)^2 \beta - \delta & -(1-p)^2 S2 \beta - \delta & \\ 0 & (1-p) S2 \beta & I1 (1-p) \beta + I2 (1-p)^2 \beta & (1-p)^2 S2 \beta - \kappa \end{pmatrix}$$

The disease-absent equilibrium is stable when $\left((1-f) + f(1-p)^2 \right) \beta < \kappa$, so public health measures that are so strong that $\tilde{R}_0 = \left((1-f) + f(1-p)^2 \right) \frac{\beta}{\kappa} < 1$ would lead to the disappearance of COVID and no infections. We assume that this is not the case under current NPI measures:

```
In[ ]:= Collect[stabmat /. equil[[1]] // Eigenvalues, { $\beta$ }, Factor]
Out[ ]:=  $\{-\delta, -\delta, (1-2fp + fp^2) \beta - \kappa, -\kappa\}$ 
```

The disease-present equilibrium is stable (the real part of all eigenvalues are negative), if the Routh-Hurwitz conditions are satisfied (Box 8.2, Otto & Day).

Here, we only consider the case with one recovered class (n=1), noting that the endemic equilibrium could become unstable for $n > 1$ (Hethcote et al. 1981):

```
In[ ]:= Det[stabmat -  $\lambda$  IdentityMatrix[4]] // Factor;
charpoly = Collect[% / Coefficient[%,  $\lambda^4$ ],  $\lambda$ , Factor];
a1part = Coefficient[charpoly,  $\lambda^3$ ];
a2part = Coefficient[charpoly,  $\lambda^2$ ];
a3part = Coefficient[charpoly,  $\lambda$ ];
a4part = charpoly /.  $\lambda \rightarrow 0$ ; (*a4 equals the determinant*)
charpoly - ( $\lambda^4 + a1part \lambda^3 + a2part \lambda^2 + a3part \lambda + a4part$ ) // Factor
Out[ ]:= 0
```

This requires that the determinant be positive ($a4 > 0$):

In[]:= **a4part /. equilpart // Factor**

$$\text{Out[]:= } - \frac{(-1 + f + S1) \delta^2 \kappa (p S1^2 \beta + \kappa - f \kappa - p \kappa + f p \kappa)}{S1^2}$$

which can be written as the positive quantity given that the equilibrium is valid and

$$((1 - f) - S1) = I1 + R1 > 0:$$

$$\text{In[]:= } ((1 - f) - S1) \delta^2 \kappa \frac{(1 - f) (1 - p) \kappa + S1^2 \beta p}{S1^2};$$

%% / % // Factor

$$\text{Out[]:= } 1$$

and that the coefficient of λ^3 be positive ($a1 > 0$):

In[]:= **a1part /. equilpart // Factor**

$$\text{Out[]:= } \frac{2 S1 \delta^2 + 2 \delta \kappa - 2 f \delta \kappa - p \delta \kappa + f p \delta \kappa + S1 \delta \kappa + p S1 \delta \kappa + S1 \kappa^2}{S1 (\delta + \kappa)}$$

which can be written as the positive quantity:

$$\text{In[]:= } \frac{(1 - f) (2 - p) \delta \kappa + S1 (2 \delta^2 + \delta \kappa (1 + p) + \kappa^2)}{S1 (\delta + \kappa)};$$

%% / % // Factor

$$\text{Out[]:= } 1$$

and that the coefficient of λ be positive ($a3 > 0$):

In[]:= **whatami = (a3part /. equilpart) * S1^2 (\delta + \kappa) / (\delta \kappa) // Factor**

$$\text{Out[]:= } 2 p S1^2 \beta \delta - 2 f p S1^2 \beta \delta - 2 p S1^3 \beta \delta + 2 S1 \delta^2 - 2 f S1 \delta^2 - p S1 \delta^2 + f p S1 \delta^2 - S1^2 \delta^2 + p S1^2 \delta^2 + p S1^2 \beta \kappa - f p S1^2 \beta \kappa - p S1^3 \beta \kappa + 2 \delta \kappa - 4 f \delta \kappa + 2 f^2 \delta \kappa - 2 p \delta \kappa + 4 f p \delta \kappa - 2 f^2 p \delta \kappa + p S1 \delta \kappa - f p S1 \delta \kappa - S1^2 \delta \kappa + p S1^2 \delta \kappa + S1 \kappa^2 - f S1 \kappa^2 - p S1 \kappa^2 + f p S1 \kappa^2 - S1^2 \kappa^2 + p S1^2 \kappa^2$$

The above is somewhat harder to work with than the intermediate substitution equilpartalt, which writes the above in terms of I1 and S1:

In[]:= whatamia = Collect[S1² $\frac{a3part}{\kappa}$ /. equilpartalt, p, Factor]

$$\begin{aligned}
 Out[]:= & \frac{1}{\kappa} S1^2 \left(2 I1^2 \beta^2 \delta - 2 I1^2 p \beta^2 \delta - 2 I1 S1 \beta^2 \delta + 2 I1 p S1 \beta^2 \delta + 2 I1 \beta \delta^2 - I1 p \beta \delta^2 - S1 \beta \delta^2 - \right. \\
 & \frac{2 I1 \beta \delta (S1 \beta - \kappa)}{-1 + p} + \frac{4 I1 p \beta \delta (S1 \beta - \kappa)}{-1 + p} - \frac{2 I1 p^2 \beta \delta (S1 \beta - \kappa)}{-1 + p} + \frac{4 I1^2 \beta \delta (S1 \beta - \kappa)}{(-1 + p) S1} - \\
 & \frac{8 I1^2 p \beta \delta (S1 \beta - \kappa)}{(-1 + p) S1} + \frac{4 I1^2 p^2 \beta \delta (S1 \beta - \kappa)}{(-1 + p) S1} + \frac{2 I1 \delta^2 (S1 \beta - \kappa)}{(-1 + p) S1} - \frac{3 I1 p \delta^2 (S1 \beta - \kappa)}{(-1 + p) S1} + \\
 & \frac{I1 p^2 \delta^2 (S1 \beta - \kappa)}{(-1 + p) S1} + \frac{2 I1^2 \delta (S1 \beta - \kappa)^2}{(-1 + p)^2 S1^2} - \frac{6 I1^2 p \delta (S1 \beta - \kappa)^2}{(-1 + p)^2 S1^2} + \frac{6 I1^2 p^2 \delta (S1 \beta - \kappa)^2}{(-1 + p)^2 S1^2} - \\
 & \frac{2 I1^2 p^3 \delta (S1 \beta - \kappa)^2}{(-1 + p)^2 S1^2} + 2 I1^2 \beta^2 \kappa - 2 I1^2 p \beta^2 \kappa - I1 S1 \beta^2 \kappa + I1 p S1 \beta^2 \kappa + \\
 & 6 I1 \beta \delta \kappa - 3 I1 p \beta \delta \kappa - 2 S1 \beta \delta \kappa + 2 \delta^2 \kappa - \frac{I1 \beta (S1 \beta - \kappa) \kappa}{-1 + p} + \frac{2 I1 p \beta (S1 \beta - \kappa) \kappa}{-1 + p} - \\
 & \frac{I1 p^2 \beta (S1 \beta - \kappa) \kappa}{-1 + p} + \frac{4 I1^2 \beta (S1 \beta - \kappa) \kappa}{(-1 + p) S1} - \frac{8 I1^2 p \beta (S1 \beta - \kappa) \kappa}{(-1 + p) S1} + \frac{4 I1^2 p^2 \beta (S1 \beta - \kappa) \kappa}{(-1 + p) S1} + \\
 & \frac{6 I1 \delta (S1 \beta - \kappa) \kappa}{(-1 + p) S1} - \frac{9 I1 p \delta (S1 \beta - \kappa) \kappa}{(-1 + p) S1} + \frac{3 I1 p^2 \delta (S1 \beta - \kappa) \kappa}{(-1 + p) S1} + \frac{2 I1^2 (S1 \beta - \kappa)^2 \kappa}{(-1 + p)^2 S1^2} - \\
 & \frac{6 I1^2 p (S1 \beta - \kappa)^2 \kappa}{(-1 + p)^2 S1^2} + \frac{6 I1^2 p^2 (S1 \beta - \kappa)^2 \kappa}{(-1 + p)^2 S1^2} - \frac{2 I1^2 p^3 (S1 \beta - \kappa)^2 \kappa}{(-1 + p)^2 S1^2} + 2 I1 \beta \kappa^2 - I1 p \beta \kappa^2 + \\
 & 2 \delta \kappa^2 + \frac{2 I1 (S1 \beta - \kappa) \kappa^2}{(-1 + p) S1} - \frac{3 I1 p (S1 \beta - \kappa) \kappa^2}{(-1 + p) S1} + \frac{I1 p^2 (S1 \beta - \kappa) \kappa^2}{(-1 + p) S1} - \frac{2 I1 \beta \delta (-S1 \beta + \kappa)}{(-1 + p)^2} + \\
 & \frac{4 I1 p \beta \delta (-S1 \beta + \kappa)}{(-1 + p)^2} - \frac{2 I1 p^2 \beta \delta (-S1 \beta + \kappa)}{(-1 + p)^2} - \frac{\delta^2 (-S1 \beta + \kappa)}{(-1 + p)^2} + \frac{2 p \delta^2 (-S1 \beta + \kappa)}{(-1 + p)^2} - \\
 & \frac{p^2 \delta^2 (-S1 \beta + \kappa)}{(-1 + p)^2} - \frac{2 I1 \delta (S1 \beta - \kappa) (-S1 \beta + \kappa)}{(-1 + p)^3 S1} + \frac{6 I1 p \delta (S1 \beta - \kappa) (-S1 \beta + \kappa)}{(-1 + p)^3 S1} - \\
 & \frac{6 I1 p^2 \delta (S1 \beta - \kappa) (-S1 \beta + \kappa)}{(-1 + p)^3 S1} + \frac{2 I1 p^3 \delta (S1 \beta - \kappa) (-S1 \beta + \kappa)}{(-1 + p)^3 S1} - \frac{I1 \beta \kappa (-S1 \beta + \kappa)}{(-1 + p)^2} + \\
 & \frac{2 I1 p \beta \kappa (-S1 \beta + \kappa)}{(-1 + p)^2} - \frac{I1 p^2 \beta \kappa (-S1 \beta + \kappa)}{(-1 + p)^2} - \frac{2 \delta \kappa (-S1 \beta + \kappa)}{(-1 + p)^2} + \frac{4 p \delta \kappa (-S1 \beta + \kappa)}{(-1 + p)^2} - \\
 & \frac{2 p^2 \delta \kappa (-S1 \beta + \kappa)}{(-1 + p)^2} - \frac{I1 (S1 \beta - \kappa) \kappa (-S1 \beta + \kappa)}{(-1 + p)^3 S1} + \frac{3 I1 p (S1 \beta - \kappa) \kappa (-S1 \beta + \kappa)}{(-1 + p)^3 S1} - \\
 & \left. \frac{3 I1 p^2 (S1 \beta - \kappa) \kappa (-S1 \beta + \kappa)}{(-1 + p)^3 S1} + \frac{I1 p^3 (S1 \beta - \kappa) \kappa (-S1 \beta + \kappa)}{(-1 + p)^3 S1} \right)
 \end{aligned}$$

which can be written as the following positive quantity:

```
In[ ]:= S1^2 (2 I1 β δ p + δ^2 + I1 β κ p) +
        I1 S1 (δ^2 (2 - p) + δ κ + 3 (1 - p) δ κ + (1 - p) κ^2) + 2 I1^2 (1 - p) κ (δ + κ);
Factor[% - whatamia]
```

```
Out[ ]:= 0
```

and finally that the following be positive:

```
In[ ]:= whatamI2 =
        (a1part a2part a3part - (a3part^2 + a1part^2 a4part)) * S1^5 (δ + κ)^4 / (δ^2 κ) /. equilpart //
        Simplify
```

```
Out[ ]:= S1 (-1 + f + S1) (δ + κ)^2 (p S1^2 β + κ - f κ + (-1 + f) p κ)
        ((-1 + f) (-2 + p) δ κ + S1 (2 δ^2 + (1 + p) δ κ + κ^2))^2 +
        ((-1 + f) (-2 + p) δ κ + S1 (2 δ^2 + (1 + p) δ κ + κ^2)) ((-1 + f)^2 (-1 + p) δ κ^2 +
        p S1^3 β κ (δ + κ) - (-1 + f) S1 κ (2 (-2 + p) δ^2 + (-5 + 2 p) δ κ + (-3 + 2 p) κ^2) +
        S1^2 (-δ^3 - 2 p δ^2 κ + δ κ ((-1 + f) p β + κ - 3 p κ) + κ^2 ((-1 + f) p β + κ - 2 p κ)))
        (-2 (-1 + f)^2 δ κ + (-1 + f) S1 (2 δ^2 + κ^2) + S1^2 (δ^2 + δ κ + κ^2) +
        p (-1 + f + S1) (2 (-1 + f) δ κ + S1^2 β (2 δ + κ) - S1 (δ^2 + δ κ + κ^2))) -
        S1 κ (δ + κ)^2 (-2 (-1 + f)^2 δ κ + (-1 + f) S1 (2 δ^2 + κ^2) + S1^2 (δ^2 + δ κ + κ^2) +
        p (-1 + f + S1) (2 (-1 + f) δ κ + S1^2 β (2 δ + κ) - S1 (δ^2 + δ κ + κ^2)))^2
```

The above is somewhat harder to work with than the intermediate substitution `equilpartalt`, which writes the above in terms of `I1` and `S1`:

In[]:= whatamI2a =

Collect[(a1part a2part a3part - (a3part² + a1part² a4part)) S1⁵ / κ /. equilpartalt,
 δ , Factor] // Factor

Out[]:= 4 I1 S1⁴ δ^5 - 2 I1 p S1⁴ δ^5 + 2 S1⁵ δ^5 + 8 I1² p S1⁴ $\beta \delta^3 \kappa$ - 4 I1² p² S1⁴ $\beta \delta^3 \kappa$ +
 2 I1 p S1⁵ $\beta \delta^3 \kappa$ + 16 I1² S1³ $\delta^4 \kappa$ - 16 I1² p S1³ $\delta^4 \kappa$ + 4 I1² p² S1³ $\delta^4 \kappa$ + 20 I1 S1⁴ $\delta^4 \kappa$ -
 10 I1 p S1⁴ $\delta^4 \kappa$ + 4 S1⁵ $\delta^4 \kappa$ + 4 I1³ p² S1⁴ $\beta^2 \delta \kappa^2$ - 2 I1³ p³ S1⁴ $\beta^2 \delta \kappa^2$ + 16 I1³ p S1³ $\beta \delta^2 \kappa^2$ -
 16 I1³ p² S1³ $\beta \delta^2 \kappa^2$ + 4 I1³ p³ S1³ $\beta \delta^2 \kappa^2$ + 18 I1² p S1⁴ $\beta \delta^2 \kappa^2$ - 9 I1² p² S1⁴ $\beta \delta^2 \kappa^2$ +
 3 I1 p S1⁵ $\beta \delta^2 \kappa^2$ + 24 I1³ S1² $\delta^3 \kappa^2$ - 36 I1³ p S1² $\delta^3 \kappa^2$ + 16 I1³ p² S1² $\delta^3 \kappa^2$ -
 2 I1³ p³ S1² $\delta^3 \kappa^2$ + 52 I1² S1³ $\delta^3 \kappa^2$ - 56 I1² p S1³ $\delta^3 \kappa^2$ + 15 I1² p² S1³ $\delta^3 \kappa^2$ +
 24 I1 S1⁴ $\delta^3 \kappa^2$ - 13 I1 p S1⁴ $\delta^3 \kappa^2$ + 2 S1⁵ $\delta^3 \kappa^2$ + 2 I1³ p² S1⁴ $\beta^2 \kappa^3$ - I1³ p³ S1⁴ $\beta^2 \kappa^3$ +
 8 I1⁴ p S1² $\beta \delta \kappa^3$ - 12 I1⁴ p² S1² $\beta \delta \kappa^3$ + 4 I1⁴ p³ S1² $\beta \delta \kappa^3$ + 22 I1³ p S1³ $\beta \delta \kappa^3$ -
 26 I1³ p² S1³ $\beta \delta \kappa^3$ + 8 I1³ p³ S1³ $\beta \delta \kappa^3$ + 10 I1² p S1⁴ $\beta \delta \kappa^3$ - 5 I1² p² S1⁴ $\beta \delta \kappa^3$ +
 I1 p S1⁵ $\beta \delta \kappa^3$ + 16 I1⁴ S1 $\delta^2 \kappa^3$ - 32 I1⁴ p S1 $\delta^2 \kappa^3$ + 20 I1⁴ p² S1 $\delta^2 \kappa^3$ - 4 I1⁴ p³ S1 $\delta^2 \kappa^3$ +
 56 I1³ S1² $\delta^2 \kappa^3$ - 92 I1³ p S1² $\delta^2 \kappa^3$ + 46 I1³ p² S1² $\delta^2 \kappa^3$ - 7 I1³ p³ S1² $\delta^2 \kappa^3$ + 44 I1² S1³ $\delta^2 \kappa^3$ -
 53 I1² p S1³ $\delta^2 \kappa^3$ + 16 I1² p² S1³ $\delta^2 \kappa^3$ + 9 I1 S1⁴ $\delta^2 \kappa^3$ - 6 I1 p S1⁴ $\delta^2 \kappa^3$ + 6 I1⁴ p S1² $\beta \kappa^4$ -
 9 I1⁴ p² S1² $\beta \kappa^4$ + 3 I1⁴ p³ S1² $\beta \kappa^4$ + 7 I1³ p S1³ $\beta \kappa^4$ - 9 I1³ p² S1³ $\beta \kappa^4$ + 3 I1³ p³ S1³ $\beta \kappa^4$ +
 2 I1² p S1⁴ $\beta \kappa^4$ - I1² p² S1⁴ $\beta \kappa^4$ + 4 I1⁵ $\delta \kappa^4$ - 10 I1⁵ p $\delta \kappa^4$ + 8 I1⁵ p² $\delta \kappa^4$ - 2 I1⁵ p³ $\delta \kappa^4$ +
 26 I1⁴ S1 $\delta \kappa^4$ - 56 I1⁴ p S1 $\delta \kappa^4$ + 39 I1⁴ p² S1 $\delta \kappa^4$ - 9 I1⁴ p³ S1 $\delta \kappa^4$ + 32 I1³ S1² $\delta \kappa^4$ -
 59 I1³ p S1² $\delta \kappa^4$ + 35 I1³ p² S1² $\delta \kappa^4$ - 7 I1³ p³ S1² $\delta \kappa^4$ + 12 I1² S1³ $\delta \kappa^4$ - 17 I1² p S1³ $\delta \kappa^4$ +
 6 I1² p² S1³ $\delta \kappa^4$ + I1 S1⁴ $\delta \kappa^4$ - I1 p S1⁴ $\delta \kappa^4$ + 4 I1⁵ κ^5 - 10 I1⁵ p κ^5 + 8 I1⁵ p² κ^5 -
 2 I1⁵ p³ κ^5 + 8 I1⁴ S1 κ^5 - 19 I1⁴ p S1 κ^5 + 15 I1⁴ p² S1 κ^5 - 4 I1⁴ p³ S1 κ^5 + 5 I1³ S1² κ^5 -
 11 I1³ p S1² κ^5 + 8 I1³ p² S1² κ^5 - 2 I1³ p³ S1² κ^5 + I1² S1³ κ^5 - 2 I1² p S1³ κ^5 + I1² p² S1³ κ^5

Through a series of term eliminations, then factoring the rest, this can be written as the following strictly positive quantity (I'm sure there is something simpler, but I didn't bother):

In[]:= temp = S1² δ (I1 δ (2 - p) + S1 δ + I1 κ) (S1 δ + I1 κ + S1 κ) (2 S1 δ^2 + 2 I1 $\delta \kappa$ + 2 S1 $\delta \kappa$ + I1 κ^2) +
 I1² κ^3 (S1² β p (2 - p) + I1 (1 - p) κ + I1 (1 - p)² κ + (1 - p)² S1 κ)
 (I1 S1² β p + 2 I1² (1 - p) κ + I1 S1 κ + 2 I1 (1 - p) S1 κ + S1² κ) +
 2 I1 S1³ $\delta^3 \kappa$ (2 I1 S1 β p (2 - p) + S1² β p + 2 I1 (1 - p) δ + 2 I1 (1 - p)² δ + 3 (1 - p) S1 δ) +
 I1 S1³ $\beta \delta \kappa^2$ p² (2 I1² S1 β + 4 I1² δ + 9 I1 S1 δ + 3 S1² δ + 4 I1² κ + 5 I1 S1 κ + S1² κ) +
 (I1 $\kappa^2 \delta$ (1 - p)) (2 I1² p² S1⁴ β^2 + p S1³ (12 I1² + 4 I1² (1 - p) + 18 I1 S1 + 3 S1²) $\beta \delta$ +
 S1² (8 I1² + 10 I1² (1 - p) + 2 I1² (1 - p)² + 21 I1 S1 + 15 I1 (1 - p) S1 + 11 S1²) δ^2) +
 (I1 $\kappa^3 \delta$ (1 - p)) (p S1² (4 I1³ + 4 I1³ (1 - p) + 14 I1² S1 + 8 I1² (1 - p) S1 + 10 I1 S1² + S1³) β +
 S1 (4 I1³ + 8 I1³ (1 - p) + 4 I1³ (1 - p)² + 20 I1² S1 + 25 I1² (1 - p) S1 +
 7 I1² (1 - p)² S1 + 20 I1 S1² + 16 I1 (1 - p) S1² + 6 S1³) δ) +
 (I1 $\kappa^3 \delta$ (1 - p)) (2 I1⁴ (1 - p) (2 - p) + I1³ (5 + 12 (1 - p) + 9 (1 - p)²) S1 +
 I1² (10 + 14 (1 - p) + 7 (1 - p)²) S1² + I1 (5 + 6 (1 - p)) S1³ + S1⁴) κ ;
 (whatamI2a - temp) / (I1 $\kappa^3 \delta$ (1 - p)) // Factor

Out[]:= 0

Hence, the endemic equilibrium is stable when it exists when there is one recovered class (n=1), but it does not exist if the disease-absent equilibrium is stable.

INDIVIDUAL-LEVEL IMPLICATIONS

Accordingly, when $\tilde{R}_0 = ((1-f) + f(1-p)^2) \frac{\beta}{\kappa} > 1$, we expect case numbers to stabilize around $\hat{I}_1 + \hat{I}_2$.

If NPI measures are rare (f small), how does using those measures help those who do?

Here we calculate the relative risk of being infected among the f engaging in the NPI measures versus $1-f$ who don't:

$$\text{In}[\#] := \frac{I_2}{f} / \frac{I_1}{1-f} /. \text{equilpart} // \text{Factor}$$

$$\text{Out}[\#] := - \frac{(-1+f) (S_1 \beta - \kappa)}{f (-1+p) S_1 \beta}$$

$$\text{In}[\#] := \% /. \text{Solve}[\text{equilpartsol} == 0, \beta] [[1]] // \text{Factor}$$

$$\text{Out}[\#] := \frac{(-1+f) (-1+p)}{1-f-p+f p+p S_1}$$

which can be written as:

$$\text{In}[\#] := \frac{1}{1 + S_1 \frac{p}{(1-f)(1-p)}};$$

Factor [% / %%]

$$\text{Out}[\#] := 1$$

This is mathematically equivalent to the risk of becoming infected at any moment in time:

$$\text{In}[\#] := \frac{S_2 (1-p) (\beta I_1 + \beta (1-p) I_2)}{f} / \left(\frac{S_1 (\beta I_1 + \beta (1-p) I_2)}{1-f} \right) /. \text{equilpart} // \text{Factor}$$

$$\text{Out}[\#] := - \frac{(-1+f) (S_1 \beta - \kappa)}{f (-1+p) S_1 \beta}$$

$$\text{In}[\#] := \text{indivfactor} = \text{FullSimplify} \left[\right.$$

$$\left. \frac{1}{1 + S_1 \frac{p}{(1-f)(1-p)}} /. S_1 \rightarrow S_1 \text{root} /. \beta \rightarrow \frac{\kappa \tilde{R}_0}{(1-f+f(1-p)^2)}, \{0 < f < 1, 0 < p < 1, \tilde{R}_0 > 1\} \right]$$

$$\text{Out}[\#] := \left(2 (-1+f) (-1+p) \tilde{R}_0 \right) / \left(- (1+f (-2+p)) (-1+p) \tilde{R}_0 + (1+f (-2+p) p) \right.$$

$$\left. \left(p + \sqrt{p^2 + \frac{(-1+p) \tilde{R}_0 (-2 (1+f (-2+p)) p (1+f (-2+p) p) + (-1+p) (-1+f p)^2 \tilde{R}_0)}{(1+f (-2+p) p)^2}} \right) \right)$$

```
In[ ]:= {indivfactor /.  $\tilde{R}_0 \rightarrow 2$  /.  $p \rightarrow 1/4$  /.  $f \rightarrow 0$ ,
        Limit[indivfactor /.  $\tilde{R}_0 \rightarrow 2$  /.  $p \rightarrow 1/4$ ,  $f \rightarrow 1$ ]}
% //
N
```

```
Out[ ]:=  $\left\{ \frac{6}{7}, \frac{7}{8} \right\}$ 
```

```
Out[ ]:= {0.857143, 0.875}
```

```
In[ ]:= {indivfactor /.  $\tilde{R}_0 \rightarrow 2$  /.  $p \rightarrow 1/2$  /.  $f \rightarrow 0$ ,
        Limit[indivfactor /.  $\tilde{R}_0 \rightarrow 2$  /.  $p \rightarrow 1/2$ ,  $f \rightarrow 1$ ]}
% //
N
```

```
Out[ ]:=  $\left\{ \frac{2}{3}, \frac{3}{4} \right\}$ 
```

```
Out[ ]:= {0.666667, 0.75}
```

```
In[ ]:= {indivfactor /.  $\tilde{R}_0 \rightarrow 6$  /.  $p \rightarrow 1/4$  /.  $f \rightarrow 0$ ,
        Limit[indivfactor /.  $\tilde{R}_0 \rightarrow 6$  /.  $p \rightarrow 1/4$ ,  $f \rightarrow 1$ ]}
% //
N
```

```
Out[ ]:=  $\left\{ \frac{18}{19}, \frac{23}{24} \right\}$ 
```

```
Out[ ]:= {0.947368, 0.958333}
```

```
In[ ]:= {indivfactor /.  $\tilde{R}_0 \rightarrow 6$  /.  $p \rightarrow 1/2$  /.  $f \rightarrow 0$ ,
        Limit[indivfactor /.  $\tilde{R}_0 \rightarrow 6$  /.  $p \rightarrow 1/2$ ,  $f \rightarrow 1$ ]}
% //
N
```

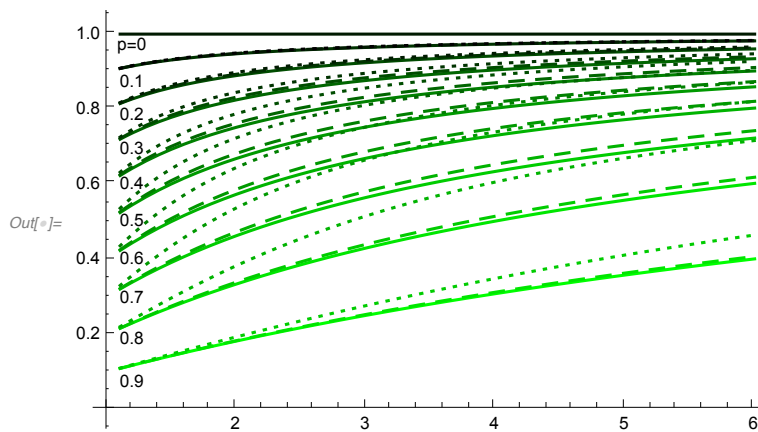
```
Out[ ]:=  $\left\{ \frac{6}{7}, \frac{11}{12} \right\}$ 
```

```
Out[ ]:= {0.857143, 0.916667}
```

```

In[ ]:= maxR0 = 6;
Show[
  Plot[
    Evaluate[indivfactor /. f -> 0.1 /. p -> Table[i, {i, 0, 0.9, 0.1}]], {R0, 1.1, maxR0},
    PlotStyle -> Table[RGBColor[0, i, 0], {i, 0.1, 1, 0.1}],
    Plot[Evaluate[indivfactor /. f -> 0.5 /. p -> Table[i, {i, 0.1, 0.9, 0.1}]], {R0, 1.1,
      maxR0}, PlotStyle -> Table[{Dashing[0.02], RGBColor[0, i, 0]}, {i, 0.1, 1, 0.1}],
    Plot[Evaluate[indivfactor /. f -> 0.9 /. p -> Table[i, {i, 0.1, 0.9, 0.1}]],
      {R0, 1.1, maxR0},
      PlotStyle -> Table[{Dashing[{0.002, 0.015}], RGBColor[0, i, 0]}, {i, 0, 0.9, 0.1}],
    Table[Graphics[Text[i, {1.2, indivfactor - 0.045 /. R0 -> 1.2 /. f -> 0.1 /. p -> i}]],
      {i, 0.1, 0.9, 0.1}],
    Graphics[Text["p=0", {1.2, indivfactor - 0.035 /. R0 -> 1.2 /. f -> 0.1 /. p -> 0}]],
    PlotRange -> {{1, maxR0}, {0, 1.0}}, AxesOrigin -> {1, 0}
  ]
]

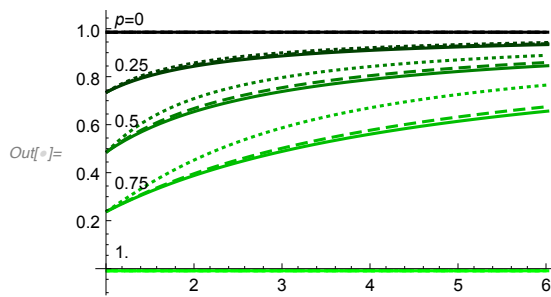
```



```

In[ ]:= maxR0 = 6;
Show[
  Plot[
    Evaluate[indivfactor /. f → 0.1 /. p → Table[i, {i, 0, 1, 0.25}]], {R̃₀, 1, maxR0},
    PlotStyle → Table[RGBColor[0, i, 0], {i, 0, 1, 0.25}]],
  Plot[Evaluate[indivfactor /. f → 0.5 /. p → Table[i, {i, 0, 1, 0.25}]], {R̃₀, 1,
    maxR0}, PlotStyle → Table[{Dashing[0.02], RGBColor[0, i, 0]}, {i, 0, 1, 0.25}]],
  Plot[Evaluate[indivfactor /. f → 0.9 /. p → Table[i, {i, 0, 1, 0.25}]], {R̃₀, 1, maxR0},
    PlotStyle → Table[{Dashing[{0.002, 0.015}], RGBColor[0, i, 0]}, {i, 0, 1, 0.25}]],
  Table[Graphics[Text[i, {1.1, indivfactor + 0.075 /. R̃₀ → 1.2 /. f → 0.1 /. p → i},
    {-1, 0}]], {i, 0.25, 1, 0.25}],
  Graphics[Text["p=0", {1.1, indivfactor + 0.04 /. R̃₀ → 1.2 /. f → 0.1 /. p → 0},
    {-1, 0}]],
  PlotRange → {{1, maxR0}, {-0.05, 1.02}}, AxesOrigin → {1, 0}, ImageSize → 250
]

```



```

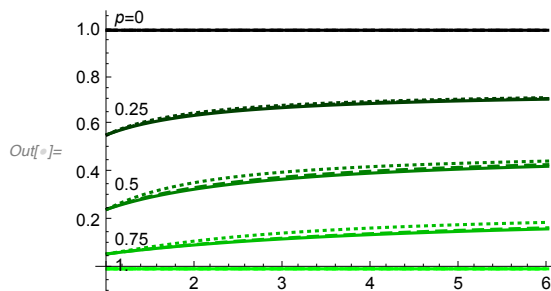
In[ ]:= commfactor = (1 - p) indivfactor;

```

```

In[ ]:= maxR0 = 6;
Show[
  Plot[Evaluate[commfactor /. f -> 0.1 /. p -> Table[i, {i, 0, 1, 0.25}]], {R0, 1, maxR0},
    PlotStyle -> Table[RGBColor[0, i, 0], {i, 0, 1, 0.25}]],
  Plot[Evaluate[commfactor /. f -> 0.5 /. p -> Table[i, {i, 0, 1, 0.25}]], {R0, 1, maxR0},
    PlotStyle -> Table[{Dashing[0.02], RGBColor[0, i, 0]}, {i, 0, 1, 0.25}]],
  Plot[Evaluate[commfactor /. f -> 0.9 /. p -> Table[i, {i, 0, 1, 0.25}]], {R0, 1, maxR0},
    PlotStyle -> Table[{Dashing[{0.002, 0.015}], RGBColor[0, i, 0]}, {i, 0, 1, 0.25}]],
  Table[Graphics[Text[i, {1.1, commfactor + 0.075 /. R0 -> 1.2 /. f -> 0.1 /. p -> i},
    {-1, 0}]], {i, 0.25, 0.5, 0.25}],
  Table[Graphics[Text[i, {1.1, commfactor + 0.05 /. R0 -> 1.2 /. f -> 0.1 /. p -> i},
    {-1, 0}]], {i, 0.75, 0.75, 0.25}],
  Table[Graphics[Text[i, {1.1, commfactor + 0.01 /. R0 -> 1.2 /. f -> 0.1 /. p -> i},
    {-1, 0}]], {i, 1, 1, 0.25}],
  Graphics[Text["p=0", {1.1, commfactor + 0.04 /. R0 -> 1.2 /. f -> 0.1 /. p -> 0},
    {-1, 0}]],
  PlotRange -> {{1, maxR0}, {-0.05, 1.02}}, AxesOrigin -> {1, 0}, ImageSize -> 250
]

```



Returning to the individual-level benefit, it may be easier to interpret as a benefit

$$\text{In[]:= } 1 - \frac{1}{1 + S1 \frac{p}{(1-f)(1-p)}};$$

$$\frac{1}{1 + \frac{(1-p)(1-f)}{p S1}} - \% // \text{Factor}$$

Out[]:= 0

In[]:= indivbenefit = 1 - FullSimplify[

$$\frac{1}{1 + S1 \frac{p}{(1-f)(1-p)}} /. S1 \rightarrow S1root /. \beta \rightarrow \frac{\kappa \tilde{R}_0}{(1 - f + f(1-p)^2)}, \{0 < f < 1, 0 < p < 1, \tilde{R}_0 > 1\}]$$

$$\text{Out[]} = 1 - \left(2(-1+f)(-1+p)\tilde{R}_0 \right) / \left(- (1+f(-2+p))(-1+p)\tilde{R}_0 + (1+f(-2+p)p) \right. \\ \left. \left(p + \sqrt{p^2 + \frac{(-1+p)\tilde{R}_0(-2(1+f(-2+p))p(1+f(-2+p)p) + (-1+p)(-1+fp)^2\tilde{R}_0)}{(1+f(-2+p)p)^2}} \right) \right)$$

In[]:= maxR0 = 6;

Show[

Plot[Evaluate[indivbenefit /. f → 0.1 /. p → Table[i, {i, 0, 0.9, 0.1}]],

{ $\tilde{R}_0$, 1.1, maxR0},

PlotStyle → Table[RGBColor[0, i, 0], {i, 0.1, 1, 0.1}]],

Plot[Evaluate[indivbenefit /. f → 0.5 /. p → Table[i, {i, 0.1, 0.9, 0.1}]], { $\tilde{R}_0$, 1.1, maxR0}, PlotStyle → Table[{Dashing[0.02], RGBColor[0, i, 0]}, {i, 0.1, 1, 0.1}]],

Plot[Evaluate[indivbenefit /. f → 0.9 /. p → Table[i, {i, 0.1, 0.9, 0.1}]],

{ $\tilde{R}_0$, 1.1, maxR0},

PlotStyle → Table[{Dashing[{0.002, 0.015}], RGBColor[0, i, 0]}, {i, 0.1, 1, 0.1}]],

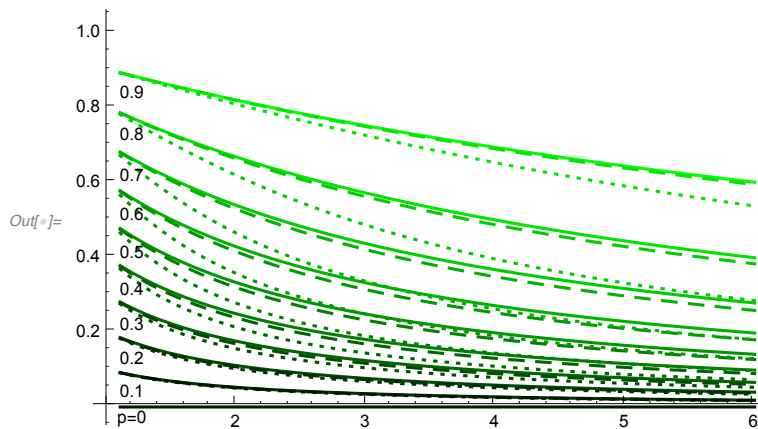
Table[Graphics[Text[i, {1.2, indivbenefit - 0.045 /. $\tilde{R}_0 \rightarrow 1.2$ /. f → 0.1 /. p → i}]],

{i, 0.1, 0.9, 0.1}],

Graphics[Text["p=0", {1.2, indivbenefit - 0.035 /. $\tilde{R}_0 \rightarrow 1.2$ /. f → 0.1 /. p → 0}]],

PlotRange → {{1, maxR0}, {0, 1.0}}, AxesOrigin → {1, 0}

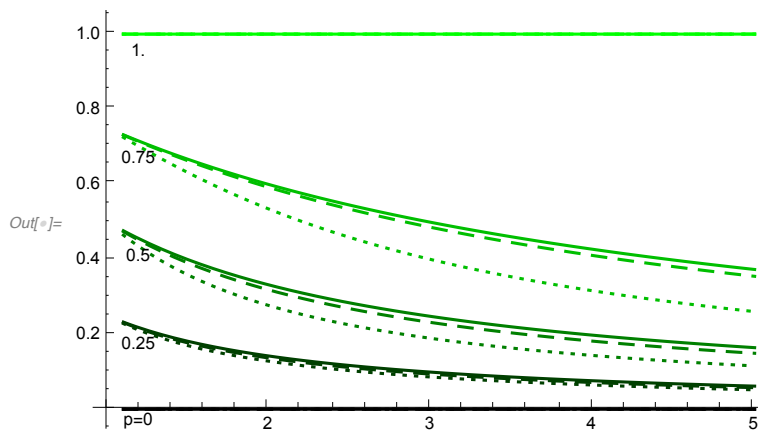
]



```

In[ ]:= maxR0 = 5;
Show[
  Plot[
    Evaluate[indivbenefit /. f -> 0.1 /. p -> Table[i, {i, 0, 1, 0.25}]], {R0, 1.1, maxR0},
    PlotStyle -> Table[RGBColor[0, i, 0], {i, 0, 1, 0.25}]],
  Plot[Evaluate[indivbenefit /. f -> 0.5 /. p -> Table[i, {i, 0, 1, 0.25}]], {R0, 1.1,
    maxR0}, PlotStyle -> Table[{Dashing[0.02], RGBColor[0, i, 0]}, {i, 0, 1, 0.25}]],
  Plot[Evaluate[indivbenefit /. f -> 0.9 /. p -> Table[i, {i, 0, 1, 0.25}]],
    {R0, 1.1, maxR0},
    PlotStyle -> Table[{Dashing[{0.002, 0.015}], RGBColor[0, i, 0]}, {i, 0, 1, 0.25}]],
  Table[Graphics[Text[i, {1.2, indivbenefit - 0.045 /. R0 -> 1.2 /. f -> 0.1 /. p -> i}]],
    {i, 0.25, 1, 0.25}],
  Graphics[Text["p=0", {1.2, indivbenefit - 0.035 /. R0 -> 1.2 /. f -> 0.1 /. p -> 0}]],
  PlotRange -> {{1, maxR0}, {0, 1.0}}, AxesOrigin -> {1, 0}
]

```



If f is small then $S1$ is approximately:

```

In[ ]:= Solve[Normal[Series[eqilpartsol /. S1 ->  $\frac{\kappa}{\beta} + f * oS1$ , {f, 0, 1}]]] == 0, oS1]

```

```

Out[ ]:= {{oS1 ->  $\frac{\kappa - 2 p \kappa + p^2 \kappa}{-\beta + p \beta - p \kappa}$ }}

```

```

In[ ]:= Normal[Series[ $\frac{I2}{f} / \frac{I1}{1-f}$  /. eqilpart /. S1 ->  $\frac{\kappa}{\beta} + f * \frac{\kappa - 2 p \kappa + p^2 \kappa}{-\beta + p \beta - p \kappa}$ , {f, 0, 0}]] // Factor

```

```

Out[ ]:=  $\frac{(-1 + p) \beta}{-\beta + p \beta - p \kappa}$ 

```

```

In[ ]:= Factor[% /.  $\beta \rightarrow \tilde{R}_0 \kappa$ ]

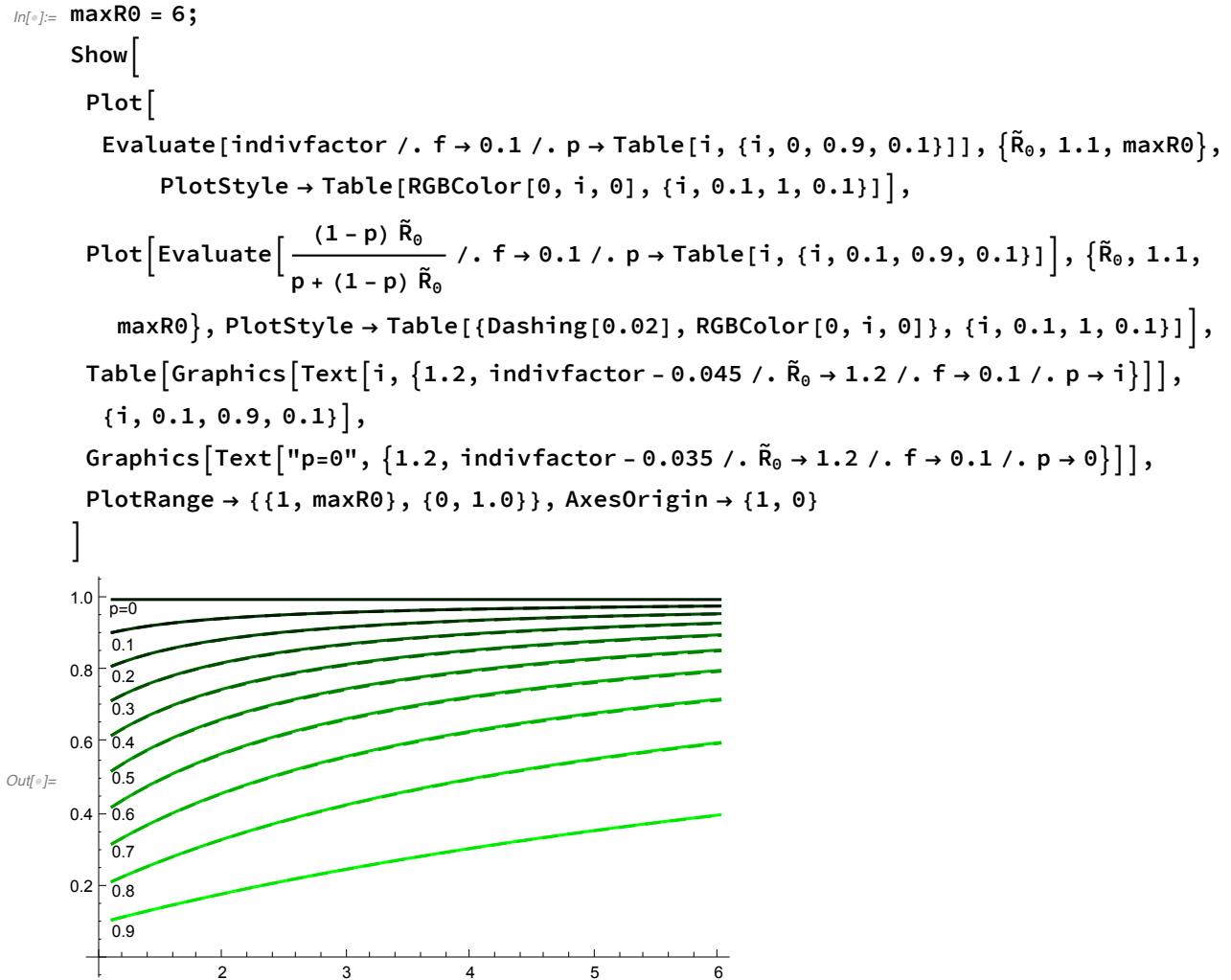
```

```

Out[ ]:=  $\frac{(-1 + p) \tilde{R}_0}{-p - \tilde{R}_0 + p \tilde{R}_0}$ 

```


which is very close to the $f=10\%$ curves explored above:



The dependence on $\tilde{R}_0$ emerges because people engaged in NPI measures are more likely to be susceptible and at risk of infection (not true if individuals who do or do not engage in NPIs rapidly change back and forth, see next section).

POPULATION-LEVEL IMPLICATIONS

We can also calculate the impact on the total number of infected individuals, $\hat{I}_1 + \hat{I}_2$, relative to that expected $\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}$ if nobody engaged in NPI measures:

```

In[ ]:= FullSimplify[Limit[I1 + I2 /. equilpart /. S1 -> S1root, f -> 0],
  {0 < f < 1, 0 < p < 1, beta > 0, kappa > 0, delta > 0}]

```

$$\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}$$

$$\text{In}[*]:= \frac{I1 + I2}{\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}} /. \text{equilpart} /. \beta \rightarrow \tilde{R}_0 \kappa // \text{Factor}$$

$$\text{Out}[*]= - \frac{(-1 + f + S1) (-1 + p S1 \tilde{R}_0)}{(-1 + p) S1 (-1 + \tilde{R}_0)}$$

which we can write as:

$$\text{In}[*]:= \frac{(1 - f - S1) (1 - p S1 \tilde{R}_0)}{(1 - p) S1 (\tilde{R}_0 - 1)};$$

or more simply as:

$$\text{In}[*]:= \frac{(1 - (S1 + S2)) \tilde{R}_0}{\tilde{R}_0 - 1};$$

$$\% - \frac{I1 + I2}{\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}} /. \tilde{R}_0 \rightarrow \beta / \kappa /. \text{equilpart} /. \text{Solve}[\text{equilpartsol} = 0, \beta][[1]] // \text{Factor}$$

$$\text{Out}[*]= 0$$

$$\text{In}[*]:= \frac{(1 - (S1 + S2)) \beta}{\beta - \kappa};$$

$$\% - \frac{I1 + I2}{\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}} /. \tilde{R}_0 \rightarrow \beta / \kappa /. \text{equilpart} /. \text{Solve}[\text{equilpartsol} = 0, \beta][[1]] // \text{Factor}$$

$$\text{Out}[*]= 0$$

Confirming that this equals one if there is no reduction in transmission (p=0):

$$\text{In}[*]:= \frac{I1 + I2}{\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}} /. \text{equilpart} /. \text{Solve}[\text{equilpartsol} = 0, \beta][[1]] /. p \rightarrow 0 // \text{Factor}$$

$$\text{Out}[*]= 1$$

$$\text{In}[*]:= \text{popfactor} =$$

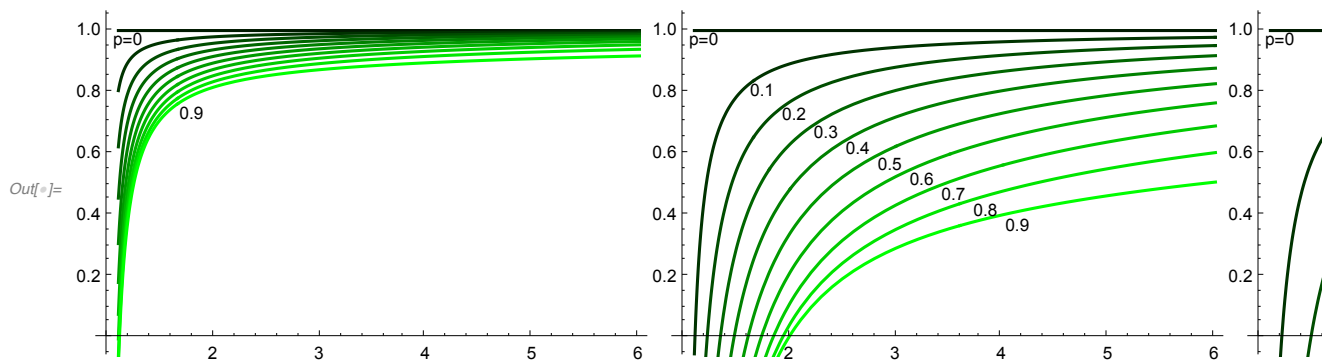
$$\text{FullSimplify}\left[\frac{I1 + I2}{\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}} /. \text{equilpart} /. S1 \rightarrow S1\text{root} /. \beta \rightarrow \tilde{R}_0 \kappa, \{0 < f < 1, 0 < p < 1, \tilde{R}_0 > 1\}\right]$$

$$\text{Out}[*]= \frac{1}{2 (-1 + p)^2 (-1 + \tilde{R}_0)} \left((1 + f (-2 + p)) (-1 + p) p \tilde{R}_0 + \right. \\ \left. 2 \left(-1 + \sqrt{p^2 + (-1 + p) \tilde{R}_0} (-2 (1 + f (-2 + p)) p + (-1 + p) (-1 + f p)^2 \tilde{R}_0) \right) - \right. \\ \left. p \left(-2 + p + \sqrt{p^2 + (-1 + p) \tilde{R}_0} (-2 (1 + f (-2 + p)) p + (-1 + p) (-1 + f p)^2 \tilde{R}_0) \right) \right)$$

```

In[ ]:= maxR0 = 6;
GraphicsGrid[{{
  Show[
    Plot[Evaluate[
      popfactor /. f → 0.1 /. p → Table[i, {i, 0, 0.9, 0.1}], {R̃₀, 1.1, maxR0},
      PlotStyle → Table[RGBColor[0, i, 0], {i, 0.1, 1, 0.1}], PlotRange → All],
    Table[
      Graphics[Text[i, {0.9 + i, popfactor - 0.045 /. R̃₀ → 0.8 + i /. f → 0.1 /. p → i}]],
      {i, 0.9, 0.9, 0.1}],
    Graphics[Text["p=0", {1.2, popfactor - 0.04 /. R̃₀ → 1.2 /. f → 0.5 /. p → 0}]],
    PlotRange → {{1, maxR0}, {0, 1.0}}, AxesOrigin → {1, 0}],
  Show[
    Plot[Evaluate[
      popfactor /. f → 0.5 /. p → Table[i, {i, 0, 0.9, 0.1}], {R̃₀, 1.1, maxR0},
      PlotStyle → Table[RGBColor[0, i, 0], {i, 0.1, 1, 0.1}], PlotRange → All],
    Table[Graphics[Text[i, {1.2 + i * 3 + 0.25, popfactor - 0.045 /. R̃₀ → 1.2 + i * 3 + 0.2 /.
      f → 0.5 /. p → i}]], {i, 0.1, 0.9, 0.1}],
    Graphics[Text["p=0", {1.2, popfactor - 0.04 /. R̃₀ → 1.2 /. f → 0.5 /. p → 0}]],
    PlotRange → {{1, maxR0}, {0, 1.0}}, AxesOrigin → {1, 0}],
  Show[
    Plot[Evaluate[
      popfactor /. f → 0.9 /. p → Table[i, {i, 0, 0.9, 0.1}], {R̃₀, 1.1, maxR0},
      PlotStyle → Table[RGBColor[0, i, 0], {i, 0.1, 1, 0.1}], PlotRange → All],
    Table[Graphics[Text[i, {1.5 + i * 6,
      popfactor - 0.045 /. R̃₀ → 1.4 + i * 6 /. f → 0.9 /. p → i}]], {i, 0.1, 0.9, 0.1}],
    Graphics[Text["p=0", {1.2, popfactor - 0.04 /. R̃₀ → 1.2 /. f → 0.9 /. p → 0}]],
    PlotRange → {{1, maxR0}, {0, 1.0}}, AxesOrigin → {1, 0}]
  ]}, Spacings → 0, ImageSize → 900]

```



```

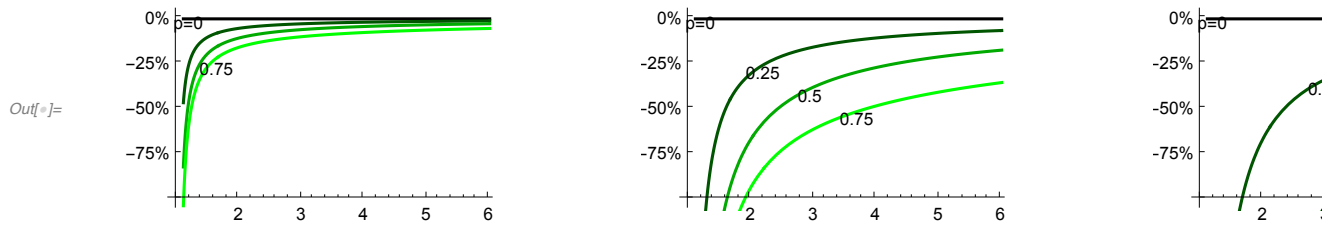
In[ ]:= ticks = {{0, "-100%"}, {0.25, "-75%"}, {0.5, "-50%"}, {0.75, "-25%"}, {1, "0%"};

```

```

In[ ]:= maxR0 = 6;
GraphicsGrid[{{
  Show[
    Plot[Evaluate[
      popfactor /. f → 0.1 /. p → Table[i, {i, 0, 0.75, 0.25}]], {R̃₀, 1.1, maxR0},
      PlotStyle → Table[RGBColor[0, i / 0.75, 0], {i, 0, 1, 0.25}], PlotRange → All],
    Table[
      Graphics[Text[i, {0.9 + i, popfactor - 0.045 /. R̃₀ → 0.8 + i /. f → 0.1 /. p → i}]],
      {i, 0.75, 0.75, 0.25}],
    Graphics[Text["p=0", {1.2, popfactor - 0.04 /. R̃₀ → 1.2 /. f → 0.5 /. p → 0}]],
    PlotRange → {{1, maxR0}, {0, 1.0}},
    AxesOrigin → {1, 0}, ImagePadding → 30, Ticks → {Automatic, ticks}],
  Show[
    Plot[Evaluate[
      popfactor /. f → 0.5 /. p → Table[i, {i, 0, 0.75, 0.25}]], {R̃₀, 1.1, maxR0},
      PlotStyle → Table[RGBColor[0, i / 0.75, 0], {i, 0, 1, 0.25}], PlotRange → All],
    Table[Graphics[Text[i, {1.2 + i * 3 + 0.25, popfactor - 0.045 /. R̃₀ → 1.2 + i * 3 + 0.2 /.
      f → 0.5 /. p → i}]], {i, 0.25, 0.75, 0.25}],
    Graphics[Text["p=0", {1.2, popfactor - 0.04 /. R̃₀ → 1.2 /. f → 0.5 /. p → 0}]],
    PlotRange → {{1, maxR0}, {0, 1.0}},
    AxesOrigin → {1, 0}, ImagePadding → 20, Ticks → {Automatic, ticks}],
  Show[
    Plot[Evaluate[
      popfactor /. f → 0.9 /. p → Table[i, {i, 0, 0.75, 0.25}]], {R̃₀, 1.1, maxR0},
      PlotStyle → Table[RGBColor[0, i / 0.75, 0], {i, 0, 1, 0.25}], PlotRange → All],
    Table[Graphics[
      Text[i, {1.5 + i * 6, popfactor - 0.045 /. R̃₀ → 1.4 + i * 6 /. f → 0.9 /. p → i}]], {i,
      0.25, 0.75, 0.25}],
    Graphics[Text["p=0", {1.2, popfactor - 0.04 /. R̃₀ → 1.2 /. f → 0.9 /. p → 0}]],
    PlotRange → {{1, maxR0}, {0, 1.0}},
    AxesOrigin → {1, 0}, ImagePadding → 20, Ticks → {Automatic, ticks}]
  }}, Spacings → 0, ImageSize → 800]

```



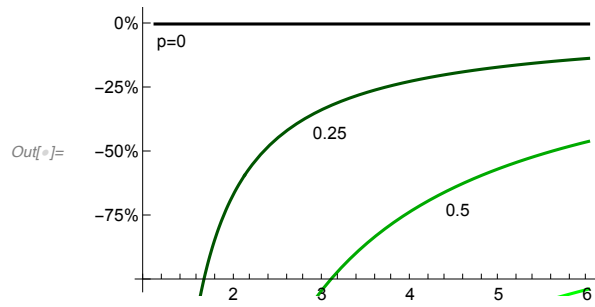
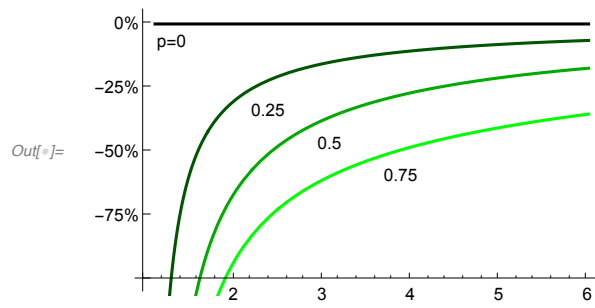
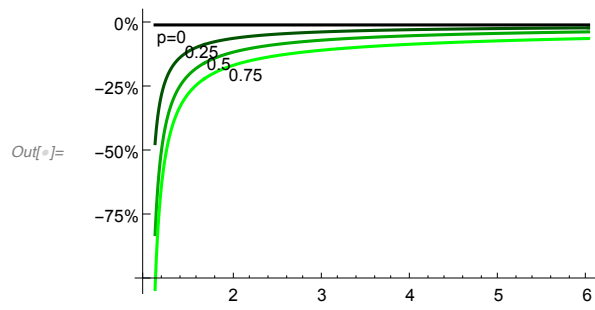
Padding issues so these were made separately:

```
In[ ]:= maxR0 = 6;
```

```
Show[
  Plot[
    Evaluate[popfactor /. f → 0.1 /. p → Table[i, {i, 0, 0.75, 0.25}]], {R̃₀, 1.1, maxR0},
    PlotStyle → Table[RGBColor[0, i / 0.75, 0], {i, 0, 1, 0.25}], PlotRange → All],
  Table[Graphics[
    Text[i, {1.2 + i, popfactor - 0.02 - 0.05 * i /. R̃₀ → 1.2 + i + 0.2 /. f → 0.1 /. p → i},
      {-1, 0}]], {i, 0.25, 0.75, 0.25}],
  (*Table[Graphics[Text[i, {0.9 + i, popfactor - 0.045 /. R̃₀ → 0.8 + i /. f → 0.1 /. p → i}]],
    {i, 0.25, 0.75, 0.25}], *)
  Graphics[Text["p=0", {1.3, popfactor - 0.06 /. R̃₀ → 1.2 /. f → 0.1 /. p → 0}]],
  PlotRange → {{1, maxR0}, {0, 1.0}}, AxesOrigin → {1, 0},
  ImagePadding → 30, Ticks → {Automatic, ticks}, ImageSize → 300]

Show[
  Plot[
    Evaluate[popfactor /. f → 0.5 /. p → Table[i, {i, 0, 0.75, 0.25}]], {R̃₀, 1.1, maxR0},
    PlotStyle → Table[RGBColor[0, i / 0.75, 0], {i, 0, 1, 0.25}], PlotRange → All],
  Table[Graphics[
    Text[i, {1.2 + i * 3 + 0.25, popfactor - 0.08 /. R̃₀ → 1.2 + i * 3 + 0.2 /. f → 0.5 /. p → i},
      {-1, 0}]], {i, 0.25, 0.75, 0.25}],
  Graphics[Text["p=0", {1.3, popfactor - 0.08 /. R̃₀ → 1.2 /. f → 0.5 /. p → 0}]],
  PlotRange → {{1, maxR0}, {0, 1.0}}, AxesOrigin → {1, 0},
  ImagePadding → 30, Ticks → {Automatic, ticks}, ImageSize → 300]

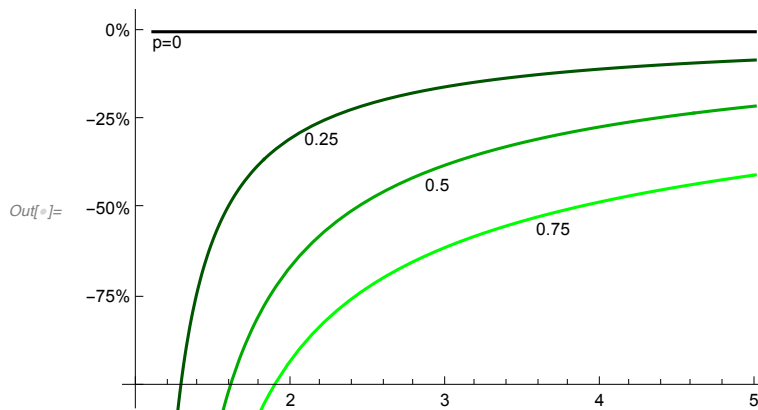
Show[
  Plot[
    Evaluate[popfactor /. f → 0.9 /. p → Table[i, {i, 0, 0.75, 0.25}]], {R̃₀, 1.1, maxR0},
    PlotStyle → Table[RGBColor[0, i / 0.75, 0], {i, 0, 1, 0.25}], PlotRange → All],
  Table[
    Graphics[Text[i, {1.4 + i * 6, popfactor - 0.08 /. R̃₀ → 1.4 + i * 6 /. f → 0.9 /. p → i},
      {-1, 0}]], {i, 0.25, 0.75, 0.25}],
  Graphics[Text["p=0", {1.3, popfactor - 0.08 /. R̃₀ → 1.2 /. f → 0.9 /. p → 0}]],
  PlotRange → {{1, maxR0}, {0, 1.0}}, AxesOrigin → {1, 0},
  ImagePadding → 30, Ticks → {Automatic, ticks}, ImageSize → 300]
```



```

In[ ]:= maxR0 = 5;
Show[
  Plot[
    Evaluate[popfactor /. f -> 0.5 /. p -> Table[i, {i, 0, 0.75, 0.25}]], {R0, 1.1, maxR0},
    PlotStyle -> Table[RGBColor[0, i / 0.75, 0], {i, 0, 1, 0.25}],
    Ticks -> {Automatic, ticks}],
  Table[Graphics[Text[i, {1.2 + i * 3 + 0.25, popfactor - 0.045 /. R0 -> 1.2 + i * 3 + 0.2 / .
    f -> 0.5 /. p -> i}]], {i, 0.25, 0.75, 0.25}],
  Graphics[Text["p=0", {1.2, popfactor - 0.04 /. R0 -> 1.2 /. f -> 0.5 /. p -> 0}]],
  PlotRange -> {{1, maxR0}, {-0.01, 1.0}}, AxesOrigin -> {1, 0}]

```



SIR_n model: Different NPI levels (rapid movement between NPI classes)

Alternatively, if individuals transition rapidly in whether or not they follow NPI measures, we have to allow movement between the first and second class. Here, we explore the opposite extreme, where movement is so rapid that the susceptible and recovered classes quickly approach an steady state number of followers and all that matters is the state of an individual (following with probability f or not following with probability $1-f$) at the time of infection.

The SIR_n model then becomes:

```

In[ ]:= eqns = {D[S[t], t] == δ n R[t] - β (1 - f) S[t] × I1[t] -
  β (1 - p) f S[t] × I1[t] - (1 - p) (1 - f) β S[t] × I2[t] - (1 - p)2 β f S[t] × I2[t],
  D[I1[t], t] == β (1 - f) S[t] × I1[t] + (1 - p) (1 - f) β S[t] × I2[t] - κ I1[t],
  D[I2[t], t] == β (1 - p) f S[t] × I1[t] + (1 - p)2 β f S[t] × I2[t] - κ I2[t],
  D[R[1, t], t] == κ I1[t] + κ I2[t] - δ n R[1, t],
  D[R[j_, t], t] == δ n R[j - 1, t] - δ n R[j, t]};

```

Here NPI measures protect by an amount p for those practicing the measures (reducing transmission by a factor $1-p$).

We measure the variables as a fraction of the full population:

$$S + I1 + I2 + R[1] + \dots R[n] = 1$$

EQUILIBRIUM ANALYSIS

By the same logic as used with only one class of individuals, the last equation in each of the above two sets indicates that $R[j-1]=R[j]$ at equilibrium. Furthermore, summing the first four equations indicates that $R[1]=R[j]$ as well. We can thus focus on the first three equations to analyse the equilibrium, using the fact that $R=(1-f-S-I1)/n$.

This system has two equilibria (disease absent and disease endemic):

$$\begin{aligned} \text{In[*]}:= & \text{equil} = \text{Solve} \left[\left\{ \begin{aligned} & 0 == \delta (1 - S - I1 - I2) - \\ & \beta (1 - f) S I1 - (1 - p) \beta f S I1 - (1 - p) \beta (1 - f) S I2 - (1 - p)^2 \beta f S I2, \\ & 0 == \beta (1 - f) S I1 + (1 - p) \beta (1 - f) S I2 - \kappa I1, \\ & 0 == (1 - p) \beta f S I1 + (1 - p)^2 \beta f S I2 - \kappa I2 \end{aligned} \right\}, \{S, I1, I2\} \right] // \text{Simplify} \\ \text{Out[*]}:= & \left\{ \left\{ S \rightarrow 1, I1 \rightarrow 0, I2 \rightarrow 0 \right\}, \left\{ S \rightarrow \frac{\kappa}{\beta + f(-2 + p)p\beta}, \right. \right. \\ & \left. \left. I1 \rightarrow \frac{(-1 + f)\delta(\beta + f(-2 + p)p\beta - \kappa)}{(-1 + fp)(1 + f(-2 + p)p)\beta(\delta + \kappa)}, I2 \rightarrow \frac{f(-1 + p)\delta(\beta + f(-2 + p)p\beta - \kappa)}{(-1 + fp)(1 + f(-2 + p)p)\beta(\delta + \kappa)} \right\} \right\} \end{aligned}$$

So either the disease is absent or it is at frequency:

$$\begin{aligned} \text{In[*]}:= & \text{equilsol} = \%[[2]]; \\ \text{In[*]}:= & I1 + I2 /. \text{equilsol} // \text{Factor} \\ \text{Out[*]}:= & \frac{\delta(\beta - 2fp\beta + fp^2\beta - \kappa)}{(1 - 2fp + fp^2)\beta(\delta + \kappa)} \\ \text{In[*]}:= & I1 / I2 /. \text{equilsol} // \text{Factor} \\ \text{Out[*]}:= & \frac{-1 + f}{f(-1 + p)} \end{aligned}$$

Note that $I1$ and $I2$ have the same sign and that $I1+I2$ is positive only if $\tilde{R}_0 = ((1-f) + f(1-p)^2) \frac{\beta}{\kappa} > 1$, which is when the disease can spread when rare (see stability analysis).

STABILITY ANALYSIS

* The disease-absent equilibrium is stable when $\left((1-f) + f(1-p)^2 \right) \beta < \kappa$.

* With one recovered class (n=1), the endemic equilibrium does not exist when the above holds but exists and is stable when it doesn't.

```
In[ ]:= eqns =  $\delta (1 - S - I1 - I2) - \beta (1 - f) S I1 -$   

 $\beta (1 - p) f S I1 - (1 - p) (1 - f) \beta S I2 - (1 - p)^2 \beta f S I2 ;$   

eqni1 =  $\beta (1 - f) S I1 + (1 - p) (1 - f) \beta S I2 - \kappa I1;$   

eqni2 =  $\beta (1 - p) f S I1 + (1 - p)^2 \beta f S I2 - \kappa I2;$ 
```

```
eqnset = {eqns, eqni1, eqni2};  
varset = {S, I1, I2};
```

```
In[ ]:= stabmat = Table[D[eqnset[[i]], varset[[j]]], {i, 1, 3}, {j, 1, 3}];  
% // MatrixForm
```

Out[]:= MatrixForm=

$$\begin{pmatrix} - (1-f) I1 \beta - f I1 (1-p) \beta - (1-f) I2 (1-p) \beta - f I2 (1-p)^2 \beta - \delta & - (1-f) S \beta - f (1-p) S \beta - \\ & (1-f) I1 \beta + (1-f) I2 (1-p) \beta & (1-f) S \beta - \kappa \\ & f I1 (1-p) \beta + f I2 (1-p)^2 \beta & f (1-p) S \beta \end{pmatrix}$$

As before, the disease-absent equilibrium is stable when $\left((1-f) + f(1-p)^2 \right) \beta < \kappa$, so public health measures that are so strong that $\tilde{R}_0 = \left((1-f) + f(1-p)^2 \right) \frac{\beta}{\kappa} < 1$ would lead to the disappearance of COVID and no infections. We assume that this is not the case under current NPI measures:

```
In[ ]:= Collect[stabmat /. equil[[1]] // Eigenvalues, { $\beta$ }, Factor]
```

Out[]:= $\{-\delta, (1-2fp + fp^2)\beta - \kappa, -\kappa\}$

The disease-present equilibrium is stable (the real part of all eigenvalues are negative), if the Routh-Hurwitz conditions are satisfied (Box 8.2, Otto & Day).

Here, we only consider the case with one recovered class (n=1), noting that the endemic equilibrium could become unstable for $n \gg 1$ (Hethcote et al. 1981):

```
In[ ]:= Det[stabmat -  $\lambda$  IdentityMatrix[3]] // Factor;  
charpoly = Collect[%/Coefficient[%,  $\lambda^3$ ],  $\lambda$ , Factor];  
a1part = Coefficient[charpoly,  $\lambda^2$ ];  
a2part = Coefficient[charpoly,  $\lambda$ ];  
a3part = charpoly /.  $\lambda \rightarrow 0$ ; (*a3 equals the determinant*)  
charpoly - ( $\lambda^3 + a1part \lambda^2 + a2part \lambda + a3part$ ) // Factor
```

Out[]:= 0

This requires that the determinant be positive ($a3 > 0$):

```
In[ ]:= a3part /. equilsol // Factor
```

```
Out[ ]:=  $-\delta \kappa \left( -\beta + 2 f p \beta - f p^2 \beta + \kappa \right)$ 
```

```
In[ ]:=  $\delta \kappa \left( \left( (1-f) + f (1-p)^2 \right) \beta - \kappa \right);$ 
```

```
%% - % // Factor
```

```
Out[ ]:= 0
```

which is positive as long as $\left((1-f) + f (1-p)^2 \right) \beta > \kappa$, i.e., the disease can spread when absent.

Stability also requires that the coefficient of λ^2 be positive ($a1>0$):

```
In[ ]:= a1part /. equilsol // Factor
```

```
Out[ ]:=  $\frac{\beta \delta - 2 f p \beta \delta + f p^2 \beta \delta + \delta^2 + \delta \kappa + \kappa^2}{\delta + \kappa}$ 
```

```
In[ ]:=  $\frac{\delta \left( \left( (1-f) + f (1-p)^2 \right) \beta - \kappa \right)}{\delta + \kappa} + (\delta + \kappa);$ 
```

```
%% - % // Factor
```

```
Out[ ]:= 0
```

which must also be positive when the disease can spread when rare.

Finally $a1$ $a2$ - $a3$ must be positive:

```
In[ ]:= whatami = (a1part a2part - a3part) /. equilsol // Factor
```

```
Out[ ]:=  $\frac{\delta \left( \beta - 2 f p \beta + f p^2 \beta + \delta \right) \left( \beta \delta^2 - 2 f p \beta \delta^2 + f p^2 \beta \delta^2 + 2 \beta \delta \kappa - 4 f p \beta \delta \kappa + 2 f p^2 \beta \delta \kappa + \kappa^3 \right)}{(\delta + \kappa)^2}$ 
```

```
In[ ]:=  $\frac{\delta \left( \left( (1-f) + f (1-p)^2 \right) \beta + \delta \right) \left( \kappa (\delta + \kappa)^2 + (\delta^2 + 2 \delta \kappa) \left( \left( (1-f) + f (1-p)^2 \right) \beta - \kappa \right) \right)}{(\delta + \kappa)^2};$ 
```

```
whatami - % // Factor
```

```
Out[ ]:= 0
```

which again must be positive as long as the disease can spread when rare.

Hence, the endemic equilibrium is stable when it exists when there is one recovered class ($n=1$), but it does not exist if the disease-absent equilibrium is stable.

INDIVIDUAL-LEVEL IMPLICATIONS

Accordingly, when $\tilde{R}_0 = \left((1-f) + f (1-p)^2 \right) \frac{\beta}{\kappa} > 1$, we expect case numbers to stabilize around $\hat{I}1 + \hat{I}2$.

How do NPI measures help those who are using them?

Here we calculate the relative risk of being infected among the f currently using NPI measures relative to the $1-f$ who are not:

```
In[ ]:=  $\frac{I2}{f} / \frac{I1}{1-f}$  /. equilsol // Factor
```

```
Out[ ]:= 1 - p
```

This is the same as calculating the risk of infection in any unit of time for a susceptible individual who does or does not use the NPI measures:

```
In[ ]:=  $\frac{\beta (1-p) I1 + \beta (1-p)^2 I2}{\beta I1 + \beta (1-p) I2}$  // Factor
```

```
Out[ ]:= 1 - p
```

```
In[ ]:= indivfactor = 1 - p;
```

```
In[ ]:= maxR0 = 6;
```

```
Show[
```

```
Plot[
```

```
  Evaluate[indivfactor /. f → 0.1 /. p → Table[i, {i, 0, 0.9, 0.1}]], { $\tilde{R}_0$ , 1.1, maxR0},
  PlotStyle → Table[RGBColor[0, i, 0], {i, 0.1, 1, 0.1}]],
```

```
Plot[Evaluate[indivfactor /. f → 0.5 /. p → Table[i, {i, 0.1, 0.9, 0.1}]], { $\tilde{R}_0$ , 1.1,
  maxR0}, PlotStyle → Table[{Dashing[0.02], RGBColor[0, i, 0]}, {i, 0.1, 1, 0.1}]],
```

```
Plot[Evaluate[indivfactor /. f → 0.9 /. p → Table[i, {i, 0.1, 0.9, 0.1}]],
  { $\tilde{R}_0$ , 1.1, maxR0},
```

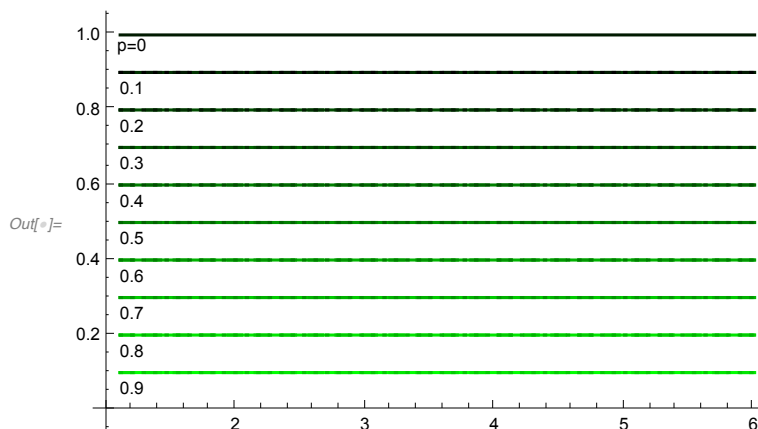
```
PlotStyle → Table[{Dashing[{0.002, 0.015}], RGBColor[0, i, 0]}, {i, 0, 0.9, 0.1}]],
```

```
Table[Graphics[Text[i, {1.2, indivfactor - 0.045 /.  $\tilde{R}_0$  → 1.2 /. f → 0.1 /. p → i}]],
  {i, 0.1, 0.9, 0.1}],
```

```
Graphics[Text["p=0", {1.2, indivfactor - 0.035 /.  $\tilde{R}_0$  → 1.2 /. f → 0.1 /. p → 0}]],
```

```
PlotRange → {{1, maxR0}, {0, 1.0}}, AxesOrigin → {1, 0}
```

```
]
```



When there is a fast rate of movement between classes then there's no longer a dependence on $\tilde{R}_0$. This is a bit counter-intuitive but occurs because individuals engaging in NPI measures stop soon, rather than build up a higher susceptible population.

POPULATION-LEVEL IMPLICATIONS

We can also calculate the impact on the total number of infected individuals, $\hat{I}_1 + \hat{I}_2$, relative to that expected $\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}$ if nobody engaged in NPI measures :

```
In[ ]:= FullSimplify[Limit[I1 + I2 /. equilsol, f -> 0], {0 < f < 1, 0 < p < 1, beta > 0, kappa > 0, delta > 0}]
```

```
Out[ ]:= 
$$\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}$$

```

```
In[ ]:= 
$$\frac{I1 + I2}{\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}} /. equilsol // Factor$$

```

```
Out[ ]:= 
$$\frac{\beta - 2 f p \beta + f p^2 \beta - \kappa}{(1 - 2 f p + f p^2) (\beta - \kappa)}$$

```

Confirming that this equals one if there is no reduction in transmission (p=0):

```
In[ ]:= % /. p -> 0 // Factor
```

```
Out[ ]:= 1
```

```
In[ ]:= popfactor = FullSimplify[
$$\frac{I1 + I2}{\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}} /. equilsol /. \beta \rightarrow \tilde{R}_0 \kappa, \{0 < f < 1, 0 < p < 1, R0 > 1\}$$
]
```

```
Out[ ]:= 
$$1 + \frac{f (-2 + p) p}{(1 + f (-2 + p) p) (-1 + \tilde{R}_0)}$$

```

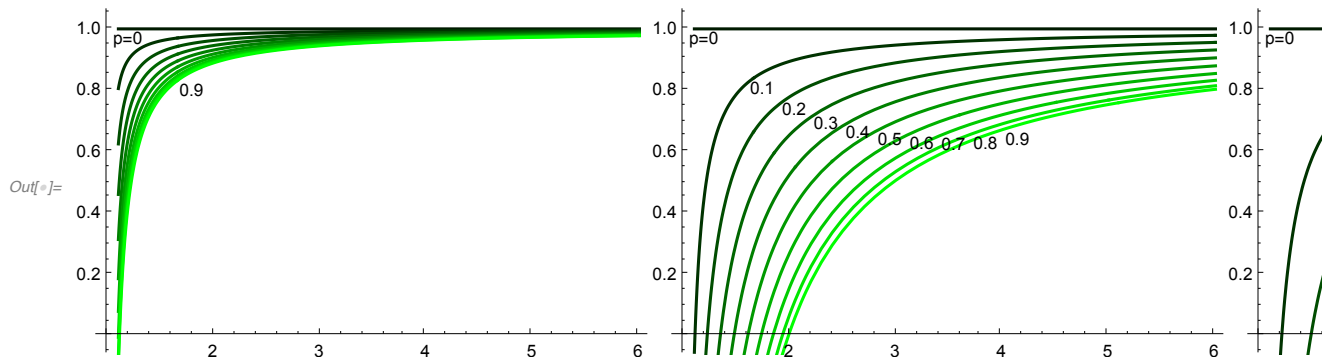
where we are measuring the benefit compared to a population without NPI measures, where

$$\tilde{R}_0 = \beta / \kappa.$$

```

In[ ]:= GraphicsGrid[{{
  Show[
    Plot[Evaluate[
      popfactor /. f -> 0.1 /. p -> Table[i, {i, 0, 0.9, 0.1}], {R0, 1.1, maxR0},
      PlotStyle -> Table[RGBColor[0, i, 0], {i, 0.1, 1, 0.1}], PlotRange -> All],
    Table[
      Graphics[Text[i, {0.9 + i, popfactor - 0.045 /. R0 -> 0.8 + i /. f -> 0.1 /. p -> i}]],
      {i, 0.9, 0.9, 0.1}],
    Graphics[Text["p=0", {1.2, popfactor - 0.04 /. R0 -> 1.2 /. f -> 0.5 /. p -> 0}]],
    PlotRange -> {{1, maxR0}, {0, 1.0}}, AxesOrigin -> {1, 0}],
  Show[
    Plot[Evaluate[
      popfactor /. f -> 0.5 /. p -> Table[i, {i, 0, 0.9, 0.1}], {R0, 1.1, maxR0},
      PlotStyle -> Table[RGBColor[0, i, 0], {i, 0.1, 1, 0.1}], PlotRange -> All],
    Table[Graphics[Text[i, {1.2 + i * 3 + 0.25, popfactor - 0.045 /. R0 -> 1.2 + i * 3 + 0.2 /
      f -> 0.5 /. p -> i}]], {i, 0.1, 0.9, 0.1}],
    Graphics[Text["p=0", {1.2, popfactor - 0.04 /. R0 -> 1.2 /. f -> 0.5 /. p -> 0}]],
    PlotRange -> {{1, maxR0}, {0, 1.0}}, AxesOrigin -> {1, 0}],
  Show[
    Plot[Evaluate[
      popfactor /. f -> 0.9 /. p -> Table[i, {i, 0, 0.9, 0.1}], {R0, 1.1, maxR0},
      PlotStyle -> Table[RGBColor[0, i, 0], {i, 0.1, 1, 0.1}], PlotRange -> All],
    Table[Graphics[Text[i, {1.5 + i * 6,
      popfactor - 0.045 /. R0 -> 1.4 + i * 6 /. f -> 0.9 /. p -> i}]], {i, 0.1, 0.9, 0.1}],
    Graphics[Text["p=0", {1.2, popfactor - 0.04 /. R0 -> 1.2 /. f -> 0.9 /. p -> 0}]],
    PlotRange -> {{1, maxR0}, {0, 1.0}}, AxesOrigin -> {1, 0}]
  }}, Spacings -> 0, ImageSize -> 900]

```



This is roughly similar to the population level benefit seen when NPI measures were fixed behaviours.

Impact on equilibrium

Changing transmission

Increasing β (or $\tilde{R}_0$) by $\Delta\beta$ (or $\Delta\tilde{R}_0$) changes the endemic equilibrium by the following proportional amount:

$$\begin{aligned} \text{In[*]} &:= \frac{\left(\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} \right) / . \beta \rightarrow \beta + \Delta\beta}{\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}} - 1 // \text{Factor} \\ \text{Out[*]} &:= \frac{\Delta\beta \kappa}{(\beta + \Delta\beta) (\beta - \kappa)} \end{aligned}$$

which can be rewritten as:

$$\begin{aligned} \text{In[*]} &:= \frac{\% * (\tilde{R}_0 - 1 / . \tilde{R}_0 \rightarrow \beta / \kappa)}{(\tilde{R}_0 - 1)} // \text{Factor} \\ \text{Out[*]} &:= \frac{\Delta\beta}{(\beta + \Delta\beta) (-1 + \tilde{R}_0)} \end{aligned}$$

or as:

$$\begin{aligned} \text{In[*]} &:= \frac{\left(\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} \right) / . \beta \rightarrow \beta + \Delta\beta}{\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}} - 1 / . \beta \rightarrow \tilde{R}_0 * \kappa / . \Delta\beta \rightarrow \Delta\tilde{R}_0 \kappa // \text{Factor} \\ \text{Out[*]} &:= \frac{\Delta\tilde{R}_0}{(-1 + \tilde{R}_0) (\tilde{R}_0 + \Delta\tilde{R}_0)} \end{aligned}$$

The impact is generally small when $\tilde{R}_0 \gg 1$ but can become high when $\tilde{R}_0$ is near 1 (i.e., when the susceptible pool is large). Nevertheless, the absolute increase is modest unless the variant increases $\tilde{R}_0$ substantially...

$$\begin{aligned} \text{In[*]} &:= \left\{ \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}, \left(\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} \right) / . \beta \rightarrow \beta + \Delta\beta \right\} / . \beta \rightarrow \tilde{R}_0 * \kappa / . \Delta\beta \rightarrow \Delta\tilde{R}_0 \kappa // \text{Factor} \\ \text{Out[*]} &:= \left\{ \frac{\delta (-1 + \tilde{R}_0)}{(\delta + \kappa) \tilde{R}_0}, \frac{\delta (-1 + \tilde{R}_0 + \Delta\tilde{R}_0)}{(\delta + \kappa) (\tilde{R}_0 + \Delta\tilde{R}_0)} \right\} \end{aligned}$$

Alternatively, consider increasing β (or $\tilde{R}_0$) by a factor c on the endemic equilibrium:

```
In[ ]:= 
$$\frac{\left( \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} \right) /. \beta \rightarrow \beta * (1 + c)}{\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}} - 1 /. \beta \rightarrow \tilde{R}_0 * \kappa // \text{Factor}$$

```

```
Out[ ]:= 
$$\frac{c}{(1 + c) (-1 + \tilde{R}_0)}$$

```

```
In[ ]:= % /. c → 1 /.  $\tilde{R}_0 \rightarrow \{1.1, 2, 3, 4\} // N$ 
```

```
Out[ ]:= {5., 0.5, 0.25, 0.166667}
```

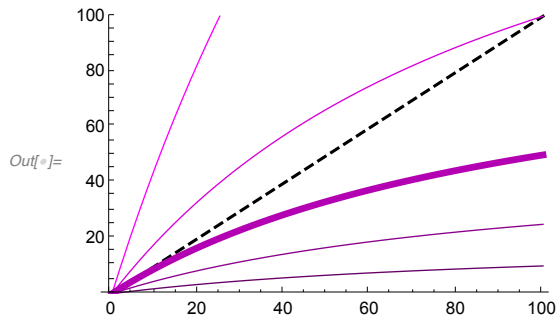
Because increasing transmission quickly depletes the susceptible pool, there may be little change in the endemic equilibrium (for example a doubling of transmission, $c=1$, only increases the endemic equilibrium by <25% if $\tilde{R}_0 > 3$. If $\tilde{R}_0$ is near 1, however, then a proportional change in transmission can have a large impact on the endemic equilibrium

```
In[ ]:= purpletab = Table[RGBColor[1 - i, 0, 1 - i], {i, 0, 0.65, 0.15}]
```

```
Out[ ]:= {■, ■, ■, ■, ■}
```

```
In[ ]:=
```

```
In[ ]:= Show[
  Plot[x, {x, 0, 100}, PlotRange → {Automatic, {0, 100}}, PlotStyle → {Black, Dashed}],
  Plot[Evaluate[ $100 * \frac{c}{(1 + c) (\tilde{R}_0 - 1)}$  /. c → x / 100 /.  $\tilde{R}_0 \rightarrow \{1.2, 1.5, 2, 3, 6\}$ ],
    {x, 0, 100}, PlotRange → {Automatic, {0, 100}},
    PlotStyle → Table[{Thickness[0.003], purpletab[[i]]}, {i, 1, 5}]],
  Plot[Evaluate[ $100 * \frac{c}{(1 + c) (\tilde{R}_0 - 1)}$  /. c → x / 100 /.  $\tilde{R}_0 \rightarrow 2$ ],
    {x, 0, 100}, PlotRange → {Automatic, {0, 100}},
    PlotStyle → {Thickness[0.015], purpletab[[3]]}],
  ImageSize → 250
]
```



For $\kappa=1/5$, this corresponds to the following values of β :


```

In[ ]:=  $\beta / . \beta \rightarrow R * \kappa / . \kappa \rightarrow 1 / 5 / . R \rightarrow \{1.2, 1.5, 2, 3, 4\} // N$ 
Out[ ]:= {0.24, 0.3, 0.4, 0.6, 0.8}

```

Changing waning rate

Increasing the long-term waning rate by $\Delta\delta$ changes the endemic equilibrium by the following proportional amount:

$$In[]:= \frac{\left(\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} / . \delta \rightarrow \delta + \Delta\delta \right)}{\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}} - 1 // \text{Factor}$$

$$Out[]:= \frac{\Delta\delta \kappa}{\delta (\delta + \Delta\delta + \kappa)}$$

When clearance is much faster than waning ($\kappa \gg \delta$), a rise in waning leads to a proportional increase in the equilibrium ($\frac{\Delta\delta}{\delta}$).

Alternatively, consider increasing δ by a factor c on the endemic equilibrium:

$$In[]:= \frac{\left(\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} / . \delta \rightarrow \delta * (1 + c) \right)}{\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}} - 1 // \text{Factor}$$

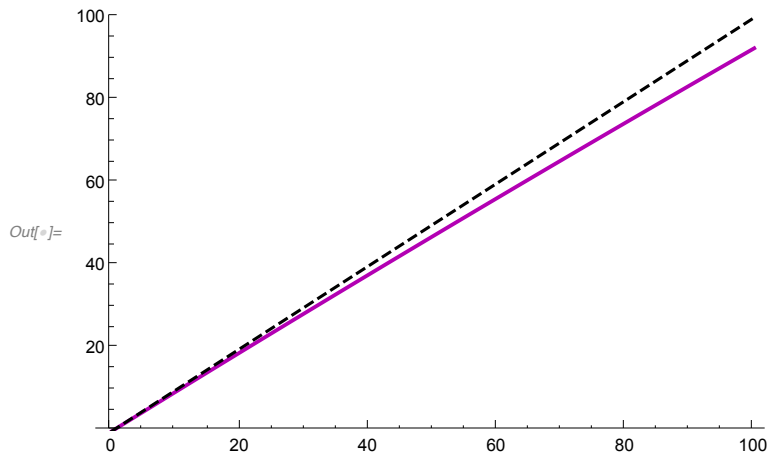
$$Out[]:= \frac{c \kappa}{\delta + c \delta + \kappa}$$

which is just c when $\kappa \gg \delta$. That is, a $X\%$ increase in the waning rate is expected to lead to a nearly $X\%$ increase in the equilibrium.

```

In[ ]:= Show[
  Plot[100 * (  $\frac{c \kappa}{\delta + c \delta + \kappa}$  ) /.  $\delta \rightarrow 1/125$  /.  $\kappa \rightarrow 1/5$  /.  $c \rightarrow x/100$ , {x, 0, 100},
    PlotRange -> {Automatic, {0, 100}}, PlotStyle -> {Thick, RGBColor[0.7, 0, 0.7]}],
  Plot[x, {x, 0, 100}, PlotRange -> {Automatic, {0, 100}}, PlotStyle -> {Black, Dashed}]
]

```

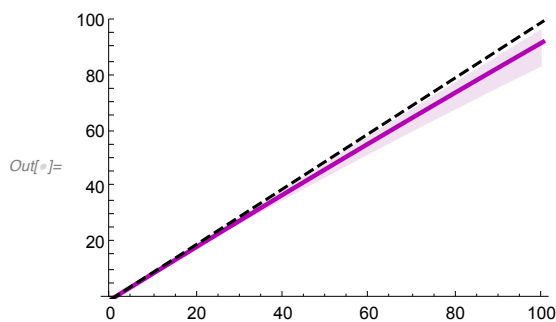


Over the range of parameters considered (see Appendix), the maximal value of $\frac{c \kappa}{\delta (1+c) + \kappa}$ will occur when δ is lowest (1/180) and κ highest (1/3), while the minimum value will occur when δ is highest (1/100) and κ lowest (1/10):

```

In[ ]:= Show[
  Plot[ $\left\{100 * \left(\frac{c \kappa}{\delta + c \delta + \kappa}\right) /. \delta \rightarrow 1 / 180 /. \kappa \rightarrow 1 / 3 /. c \rightarrow x / 100, \right.$ 
     $\left.100 * \left(\frac{c \kappa}{\delta + c \delta + \kappa}\right) /. \delta \rightarrow 1 / 100 /. \kappa \rightarrow 1 / 10 /. c \rightarrow x / 100\right\},$ 
    {x, 0, 100}, PlotRange -> {Automatic, {0, 100}}, PlotStyle -> None,
    Filling -> {1 -> {2}}, FillingStyle -> LightPurple],
  Plot[ $100 * \left(\frac{c \kappa}{\delta + c \delta + \kappa}\right) /. \delta \rightarrow 1 / 125 /. \kappa \rightarrow 1 / 5 /. c \rightarrow x / 100,$ 
    {x, 0, 100}, PlotRange -> {Automatic, {0, 100}},
    PlotStyle -> {Thickness[0.01], RGBColor[0.7, 0, 0.7]}],
  Plot[x, {x, 0, 100}, PlotRange -> {Automatic, {0, 100}},
    PlotStyle -> {Black, Dashed}],
  ImageSize -> 250
]

```

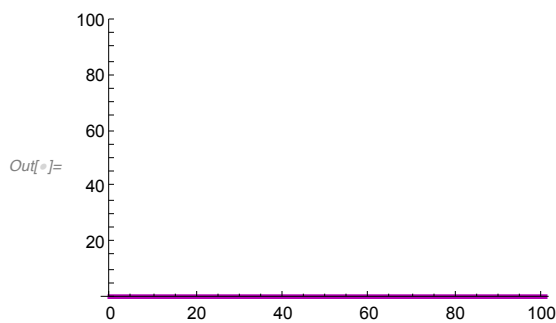


For transient immunity:

```

In[ ]:= Show[
  Plot[ $100 * 0 /. \delta \rightarrow 1 / 125 /. \kappa \rightarrow 1 / 5 /. c \rightarrow x / 100,$ 
    {x, 0, 100}, PlotRange -> {Automatic, {0, 100}},
    PlotStyle -> {Thickness[0.02], RGBColor[0.7, 0, 0.7]}],
  ImageSize -> 250
]

```



Changing vaccination rate

Impact on incidence of infectious individuals:

$$In[\#] := \frac{\beta \delta - \delta \kappa}{\beta (\delta + \kappa)} - \frac{\nu}{\delta + \kappa};$$

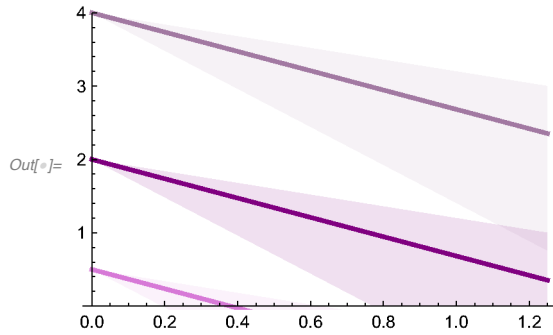
Over the range of parameters considered (see Appendix), the maximal value of $\frac{\nu}{\delta + \kappa}$ will occur when δ is lowest (1/180) and κ lowest (1/10), while the minimum value will occur when δ is highest (1/100) and κ highest (1/3):

$$In[\#] := \text{maxV} = 1.25;$$

```

In[ ]:= Show[
  Plot[
    {100 * (incidence -  $\frac{V}{\delta + \kappa}$ ) /. v -> V / 365 /.  $\delta \rightarrow 1 / 180$  /.  $\kappa \rightarrow 1 / 10$  /. incidence -> 0.02,
     100 * (incidence -  $\frac{V}{\delta + \kappa}$ ) /. v -> V / 365 /.  $\delta \rightarrow 1 / 100$  /.  $\kappa \rightarrow 1 / 3$  /. incidence -> 0.02},
    {V, 0, maxV}, PlotRange -> {Automatic, {0, 4}}, PlotStyle -> None,
    Filling -> {1 -> {2}}, FillingStyle -> LightPurple],
  Plot[100 * (incidence -  $\frac{V}{\delta + \kappa}$ ) /. v -> V / 365 /.  $\delta \rightarrow 1 / 125$  /.  $\kappa \rightarrow 1 / 5$  /. incidence -> 0.02,
    {V, 0, maxV}, PlotStyle -> {Thickness[0.01], Purple}],
  Plot[{100 * (incidence -  $\frac{V}{\delta + \kappa}$ ) /. v -> V / 365 /.  $\delta \rightarrow 1 / 180$  /.  $\kappa \rightarrow 1 / 10$  /.
    incidence -> 0.005,
    100 * (incidence -  $\frac{V}{\delta + \kappa}$ ) /. v -> V / 365 /.  $\delta \rightarrow 1 / 100$  /.  $\kappa \rightarrow 1 / 3$  /. incidence -> 0.005},
    {V, 0, maxV}, PlotStyle -> None, Filling -> {1 -> {2}},
    FillingStyle -> RGBColor[0.7, 0, 0.7, 0.05]},
  Plot[100 * (incidence -  $\frac{V}{\delta + \kappa}$ ) /. v -> V / 365 /.  $\delta \rightarrow 1 / 125$  /.  $\kappa \rightarrow 1 / 5$  /. incidence -> 0.005,
    {V, 0, maxV}, PlotStyle -> {Thickness[0.01], RGBColor[0.7, 0, 0.7, 0.5]}],
  Plot[{100 * (incidence -  $\frac{V}{\delta + \kappa}$ ) /. v -> V / 365 /.  $\delta \rightarrow 1 / 180$  /.  $\kappa \rightarrow 1 / 10$  /.
    incidence -> 0.04,
    100 * (incidence -  $\frac{V}{\delta + \kappa}$ ) /. v -> V / 365 /.  $\delta \rightarrow 1 / 100$  /.  $\kappa \rightarrow 1 / 3$  /. incidence -> 0.04},
    {V, 0, maxV}, PlotStyle -> None, Filling -> {1 -> {2}},
    FillingStyle -> RGBColor[0.3, 0, 0.3, 0.05]},
  Plot[100 * (incidence -  $\frac{V}{\delta + \kappa}$ ) /. v -> V / 365 /.  $\delta \rightarrow 1 / 125$  /.  $\kappa \rightarrow 1 / 5$  /. incidence -> 0.04,
    {V, 0, maxV}, PlotStyle -> {Thickness[0.01], RGBColor[0.3, 0, 0.3, 0.5]}],
  ImageSize -> 250
]

```



Parameter estimates

The Menegale et al. (2023) review of vaccine effectiveness studies estimates the waning rate from $A e^{-\delta t}$, where A is the vaccine effectiveness measured at 14 days (replacing their ω with δ). The half-life was defined as the time to reach half of the value of A :

$$A \text{Exp}[-\delta (t - 14)] = \frac{A}{2}$$

$$\text{Log}[2] = \delta (t - 14)$$

$$t = \frac{\text{Log}[2]}{\delta} + 14$$

as noted on page 3. Given half-lives of 87 and 111 days, this corresponds to waning rates of

$$\delta = \frac{\text{Log}[2]}{t-14}$$

$$\text{In[*]} := \frac{\text{Log}[2]}{t - 14} /. t \rightarrow \{87, 111\} // N$$

$$\text{Out[*]} = \{0.00949517, 0.00714585\}$$

These correspond to mean times to waning of 3-4 months:

$$\text{In[*]} := 1 / \%$$

$$\text{Out[*]} = \{105.317, 139.941\}$$

The implications for β and $\tilde{R}_0$ of the choice of parameters:

$$\text{In[*]} := \text{Solve}\left[\left(\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}\right) = \text{incidence}, \beta\right]$$

$$\text{Out[*]} = \left\{ \left\{ \beta \rightarrow -\frac{\delta \kappa}{-\delta + \text{incidence} \delta + \text{incidence} \kappa} \right\} \right\}$$

```
In[ ]:= Solve[ $\left(\frac{(\tilde{R}_0 - 1) \delta}{\tilde{R}_0 (\delta + \kappa)}\right) == \text{incidence}, \tilde{R}_0]$ 
```

```
Out[ ]:=  $\left\{ \left\{ \tilde{R}_0 \rightarrow -\frac{\delta}{-\delta + \text{incidence} \delta + \text{incidence} \kappa} \right\} \right\}$ 
```

Consider also the number of infections per year at the endemic equilibrium. The daily rate of infection is:

```
In[ ]:=  $\beta S I1 /. \text{equil}[[2]] /. \beta \rightarrow \tilde{R}_0 \kappa // \text{Factor}$ 
```

... **Part:** Part specification `equil[[2]]` is longer than depth of object.

... **ReplaceAll:** {`equil[[2]]`} is neither a list of replacement rules nor a valid dispatch table, and so cannot be used for replacing.

... **ReplaceAll:** {`equil[[2]]`} is neither a list of replacement rules nor a valid dispatch table, and so cannot be used for replacing.

```
Out[ ]:=  $I1 S \kappa \tilde{R}_0 /. \text{equil}[[2]]$ 
```

so the expected number of infections per year is:

```
In[ ]:= 365 * %
```

```
Out[ ]:= 365  $(I1 S \kappa \tilde{R}_0 /. \text{equil}[[2]])$ 
```

```
In[ ]:= % /.  $\tilde{R}_0 \rightarrow -\frac{\delta}{-\delta + \text{incidence} \delta + \text{incidence} \kappa} // \text{Simplify}$ 
```

... **ReplaceAll:** {`equil[[2]]`} is neither a list of replacement rules nor a valid dispatch table, and so cannot be used for replacing.

```
Out[ ]:= 365  $\left( \frac{I1 S \delta \kappa}{\delta - \text{incidence} \delta - \text{incidence} \kappa} /. \text{equil}[[2]] \right)$ 
```

Parameter range considered (nominal value of the parameter, minimum, and maximum):

```
In[ ]:= incidenceTAB = {0.02, 0.005, 0.04};
```

```
deltaTAB = {1 / 125, 1 / 100, 1 / 180};
```

```
kappaTAB = {1 / 5, 1 / 3, 1 / 10};
```

```

In[ ]:= Flatten[tabnov =
  Table[{incidence,  $\delta$ ,  $\kappa$ , If[ $\frac{\delta \kappa}{\delta - \text{incidence} (\delta + \kappa)} > 0$ ,  $\frac{\delta \kappa}{\delta - \text{incidence} (\delta + \kappa)}$ , "NA"],
    If[ $\frac{\delta}{\delta - \text{incidence} (\delta + \kappa)} > 0$ ,  $\frac{\delta}{\delta - \text{incidence} (\delta + \kappa)}$ , "NA"],
    If[ $\frac{\delta}{\delta - \text{incidence} (\delta + \kappa)} > 0$ ,  $1 / \frac{\delta}{\delta - \text{incidence} (\delta + \kappa)}$ , "NA"],
    If[ $\frac{\delta}{\delta - \text{incidence} (\delta + \kappa)} > 0$ ,  $365 \text{ incidence } \kappa$ , "NA"]}] /.
  incidence  $\rightarrow$  incidenceTAB[[i]] /.  $\delta \rightarrow \delta\text{TAB}[[j]]$  /.
   $\kappa \rightarrow \kappa\text{TAB}[[k]]$ , {i, 1, 3}, {j, 1, 3}, {k, 1, 3}], 2];
Join[{{"Incidence",  $\delta$ ,  $\kappa$ ,  $\beta$ ,  $\tilde{R}_0$ ,  $\hat{S}$ , "Annual rate"}}, (Round[1000  $\times$  %] / 1000.)] /.
(0.001` Round[1000 "NA"])  $\rightarrow$  "NA" // MatrixForm

```

Out[]//MatrixForm=

Incidence	δ	κ	β	$\tilde{R}_0$	$\hat{S}$	Annual rate
0.02	0.008	0.2	0.417	2.083	0.48	1.46
0.02	0.008	0.333	2.273	6.818	0.147	2.433
0.02	0.008	0.1	0.137	1.37	0.73	0.73
0.02	0.01	0.2	0.345	1.724	0.58	1.46
0.02	0.01	0.333	1.064	3.191	0.313	2.433
0.02	0.01	0.1	0.128	1.282	0.78	0.73
0.02	0.006	0.2	0.769	3.846	0.26	1.46
0.02	0.006	0.333	NA	NA	NA	NA
0.02	0.006	0.1	0.161	1.613	0.62	0.73
0.005	0.008	0.2	0.23	1.149	0.87	0.365
0.005	0.008	0.333	0.424	1.271	0.787	0.608
0.005	0.008	0.1	0.107	1.072	0.932	0.182
0.005	0.01	0.2	0.223	1.117	0.895	0.365
0.005	0.01	0.333	0.402	1.207	0.828	0.608
0.005	0.01	0.1	0.106	1.058	0.945	0.182
0.005	0.006	0.2	0.245	1.227	0.815	0.365
0.005	0.006	0.333	0.48	1.439	0.695	0.608
0.005	0.006	0.1	0.11	1.105	0.905	0.182
0.04	0.008	0.2	NA	NA	NA	NA
0.04	0.008	0.333	NA	NA	NA	NA
0.04	0.008	0.1	0.217	2.174	0.46	1.46
0.04	0.01	0.2	1.25	6.25	0.16	2.92
0.04	0.01	0.333	NA	NA	NA	NA
0.04	0.01	0.1	0.179	1.786	0.56	1.46
0.04	0.006	0.2	NA	NA	NA	NA
0.04	0.006	0.333	NA	NA	NA	NA
0.04	0.006	0.1	0.417	4.167	0.24	1.46

Range of β values:


```

In[ ]:= {Min[Table[If[ $\frac{\delta \kappa}{\delta - \text{incidence}(\delta + \kappa)} > 0$ ,  $\frac{\delta \kappa}{\delta - \text{incidence}(\delta + \kappa)}$ , Infinity] /.
incidence → incidenceTAB[[i]] /.  $\delta \rightarrow \delta\text{TAB}[[j]]$  /.
 $\kappa \rightarrow \kappa\text{TAB}[[k]]$ , {i, 1, 3}, {j, 1, 3}, {k, 1, 3}]],
Max[Table[If[ $\frac{\delta \kappa}{\delta - \text{incidence}(\delta + \kappa)} > 0$ ,  $\frac{\delta \kappa}{\delta - \text{incidence}(\delta + \kappa)}$ , 0] /.
incidence → incidenceTAB[[i]] /.  $\delta \rightarrow \delta\text{TAB}[[j]]$  /.
 $\kappa \rightarrow \kappa\text{TAB}[[k]]$ , {i, 1, 3}, {j, 1, 3}, {k, 1, 3}]]]}

Out[ ]:= {0.10582, 2.27273}

```

Range of $\tilde{R}_0$ values:

```

In[ ]:= {Min[Table[If[ $\frac{\delta}{\delta - \text{incidence}(\delta + \kappa)} > 0$ ,  $\frac{\delta}{\delta - \text{incidence}(\delta + \kappa)}$ , Infinity] /.
incidence → incidenceTAB[[i]] /.  $\delta \rightarrow \delta\text{TAB}[[j]]$  /.
 $\kappa \rightarrow \kappa\text{TAB}[[k]]$ , {i, 1, 3}, {j, 1, 3}, {k, 1, 3}]],
Max[Table[If[ $\frac{\delta}{\delta - \text{incidence}(\delta + \kappa)} > 0$ ,  $\frac{\delta}{\delta - \text{incidence}(\delta + \kappa)}$ , 0] /.
incidence → incidenceTAB[[i]] /.  $\delta \rightarrow \delta\text{TAB}[[j]]$  /.
 $\kappa \rightarrow \kappa\text{TAB}[[k]]$ , {i, 1, 3}, {j, 1, 3}, {k, 1, 3}]]]}

Out[ ]:= {1.0582, 6.81818}

```

The disease only persists when the denominators above are positive, which isn't possible if the disease incidence and clearance rates are too high relative to the waning rate (i.e.. $\kappa > 0.133333$ leads to the loss of the disease):

```

In[ ]:= Solve[( $\delta - \text{incidence}(\delta + \kappa)$  /. incidence → 0.04 /.  $\delta \rightarrow 1/180$ ) == 0,  $\kappa$ ]

Out[ ]:= {{ $\kappa \rightarrow 0.133333$ }}

```

Parameter estimates

(with different seroconversion rates)

The implications for β and $\tilde{R}_0$ of the choice of parameters:

```

In[ ]:= Solve[ $\left(\frac{\delta(\beta - \kappa)}{\beta(\delta + q\kappa)}\right) = \text{incidence}, \beta]$ 

Out[ ]:= {{ $\beta \rightarrow -\frac{\delta \kappa}{-\delta + \text{incidence} \delta + \text{incidence} q \kappa}$ }}}

```

$$\text{In}[*]:= \text{Solve}\left[\left(\frac{(\tilde{R}_0 - 1) \delta}{\tilde{R}_0 (\delta + q \kappa)}\right) == \text{incidence}, \tilde{R}_0\right]$$

$$\text{Out}[*]:= \left\{ \left\{ \tilde{R}_0 \rightarrow -\frac{\delta}{-\delta + \text{incidence} \delta + \text{incidence} q \kappa} \right\} \right\}$$

Consider also the number of infections per year at the endemic equilibrium. The daily rate of infection is:

$$\text{In}[*]:= \beta S I1 /. \left\{ S \rightarrow \frac{\kappa}{\beta}, I1 \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)} \right\} /. \beta \rightarrow \tilde{R}_0 \kappa // \text{Factor}$$

$$\text{Out}[*]:= \frac{\delta \kappa (-1 + \tilde{R}_0)}{(\delta + q \kappa) \tilde{R}_0}$$

so the expected number of infections per year is:

$$\text{In}[*]:= 365 * \%$$

$$\text{Out}[*]:= \frac{365 \delta \kappa (-1 + \tilde{R}_0)}{(\delta + q \kappa) \tilde{R}_0}$$

$$\text{In}[*]:= \% /. \tilde{R}_0 \rightarrow -\frac{\delta}{-\delta + \text{incidence} \delta + \text{incidence} q \kappa} // \text{Simplify}$$

$$\text{Out}[*]:= 365 \text{ incidence} \kappa$$

Parameter range considered (nominal value of the parameter, minimum, and maximum):

$$\text{In}[*]:= \text{incidenceTAB} = \{0.02, 0.005, 0.04\};$$

$$\delta \text{TAB} = \{1 / 125, 1 / 100, 1 / 180\};$$

$$\kappa \text{TAB} = \{1 / 5, 1 / 3, 1 / 10\};$$

$$q \text{TAB} = \{10 / 10, 8 / 10\};$$

$$\text{In}[*]:= \text{Flatten}\left[$$

$$\text{Table}\left[\left\{\text{incidence}, \delta, \kappa, q, \text{If}\left[\frac{\delta \kappa}{\delta - \text{incidence} (\delta + q \kappa)} > 0, \frac{\delta \kappa}{\delta - \text{incidence} (\delta + q \kappa)}, "NA"\right],\right.\right.$$

$$\left.\text{If}\left[\frac{\delta}{\delta - \text{incidence} (\delta + q \kappa)} > 0, \frac{\delta}{\delta - \text{incidence} (\delta + q \kappa)}, "NA"\right],\right.$$

$$\left.\text{If}\left[\frac{\delta}{\delta - \text{incidence} (\delta + q \kappa)} > 0, 1 / \frac{\delta}{\delta - \text{incidence} (\delta + q \kappa)}, "NA"\right],\right.$$

$$\left.\text{If}\left[\frac{\delta}{\delta - \text{incidence} (\delta + q \kappa)} > 0, 365 \text{ incidence} \kappa, "NA"\right]\right\} /.$$

$$\text{incidence} \rightarrow \text{incidenceTAB}[[i]] /. \delta \rightarrow \delta \text{TAB}[[j]] /. \kappa \rightarrow \kappa \text{TAB}[[k]] /.$$

$$q \rightarrow q \text{TAB}[[l]], \{i, 1, 3\}, \{j, 1, 3\}, \{k, 1, 3\}, \{l, 1, 2\}], 3];$$

$$\text{Join}\left[\left\{\left\{"Incidence", \delta, \kappa, q, \beta, \tilde{R}_0, \hat{S}, "Annual \text{ rate}"\right\}, (\text{Round}[1000 \times \%] / 1000.)\right\} /.$$

$$(0.001 \text{ Round}[1000 "NA"]) \rightarrow "NA" // \text{MatrixForm}$$

$$\text{Out}[*]//\text{MatrixForm} =$$

$$\begin{pmatrix} 0.02 & 0.005 & 0.04 \\ 0.001 & 0.001 & 0.001 \end{pmatrix}$$

$$\approx$$

$$\hat{=}$$

$$-$$

$$-$$

$$\backslash$$

Incidence	δ	κ	q	β	R_0	S	Annual rate
0.02	0.008	0.2	1.	0.417	2.083	0.48	1.46
0.02	0.008	0.2	0.8	0.345	1.724	0.58	1.46
0.02	0.008	0.333	1.	2.273	6.818	0.147	2.433
0.02	0.008	0.333	0.8	1.064	3.191	0.313	2.433
0.02	0.008	0.1	1.	0.137	1.37	0.73	0.73
0.02	0.008	0.1	0.8	0.128	1.282	0.78	0.73
0.02	0.01	0.2	1.	0.345	1.724	0.58	1.46
0.02	0.01	0.2	0.8	0.303	1.515	0.66	1.46
0.02	0.01	0.333	1.	1.064	3.191	0.313	2.433
0.02	0.01	0.333	0.8	0.746	2.239	0.447	2.433
0.02	0.01	0.1	1.	0.128	1.282	0.78	0.73
0.02	0.01	0.1	0.8	0.122	1.22	0.82	0.73
0.02	0.006	0.2	1.	0.769	3.846	0.26	1.46
0.02	0.006	0.2	0.8	0.495	2.475	0.404	1.46
0.02	0.006	0.333	1.	NA	NA	NA	NA
0.02	0.006	0.333	0.8	16.667	50.	0.02	2.433
0.02	0.006	0.1	1.	0.161	1.613	0.62	0.73
0.02	0.006	0.1	0.8	0.145	1.445	0.692	0.73
0.005	0.008	0.2	1.	0.23	1.149	0.87	0.365
0.005	0.008	0.2	0.8	0.223	1.117	0.895	0.365
0.005	0.008	0.333	1.	0.424	1.271	0.787	0.608
0.005	0.008	0.333	0.8	0.402	1.207	0.828	0.608
0.005	0.008	0.1	1.	0.107	1.072	0.932	0.182
0.005	0.008	0.1	0.8	0.106	1.058	0.945	0.182
0.005	0.01	0.2	1.	0.223	1.117	0.895	0.365
0.005	0.01	0.2	0.8	0.219	1.093	0.915	0.365
0.005	0.01	0.333	1.	0.402	1.207	0.828	0.608
0.005	0.01	0.333	0.8	0.387	1.161	0.862	0.608
0.005	0.01	0.1	1.	0.106	1.058	0.945	0.182
0.005	0.01	0.1	0.8	0.105	1.047	0.955	0.182
0.005	0.006	0.2	1.	0.245	1.227	0.815	0.365
0.005	0.006	0.2	0.8	0.235	1.175	0.851	0.365
0.005	0.006	0.333	1.	0.48	1.439	0.695	0.608
0.005	0.006	0.333	0.8	0.442	1.325	0.755	0.608
0.005	0.006	0.1	1.	0.11	1.105	0.905	0.182
0.005	0.006	0.1	0.8	0.108	1.083	0.923	0.182
0.04	0.008	0.2	1.	NA	NA	NA	NA
0.04	0.008	0.2	0.8	1.25	6.25	0.16	2.92
0.04	0.008	0.333	1.	NA	NA	NA	NA
0.04	0.008	0.333	0.8	NA	NA	NA	NA
0.04	0.008	0.1	1.	0.217	2.174	0.46	1.46
0.04	0.008	0.1	0.8	0.179	1.786	0.56	1.46
0.04	0.01	0.2	1.	1.25	6.25	0.16	2.92
0.04	0.01	0.2	0.8	0.625	3.125	0.32	2.92
0.04	0.01	0.333	1.	NA	NA	NA	NA
0.04	0.01	0.333	0.8	NA	NA	NA	NA
0.04	0.01	0.1	1.	0.179	1.786	0.56	1.46
0.04	0.01	0.1	0.8	0.156	1.562	0.64	1.46
0.04	0.006	0.2	1.	NA	NA	NA	NA
0.04	0.006	0.2	0.8	NA	NA	NA	NA

0.04	0.006	0.333	1.	NA	NA	NA	NA
0.04	0.006	0.333	0.8	NA	NA	NA	NA
0.04	0.006	0.1	1.	0.417	4.167	0.24	1.46
0.04	0.006	0.1	0.8	0.26	2.604	0.384	1.46

Range of β values:

```

In[ ]:= {Min[Table[If[ $\frac{\delta \kappa}{\delta - \text{incidence}(\delta + q \kappa)} > 0$ ,  $\frac{\delta \kappa}{\delta - \text{incidence}(\delta + q \kappa)}$ , Infinity] /.
    incidence  $\rightarrow$  incidenceTAB[[i]] /.  $\delta \rightarrow \delta\text{TAB}[[j]]$  /.  $\kappa \rightarrow \kappa\text{TAB}[[k]]$  /.
    q  $\rightarrow$  qTAB[[l]], {i, 1, 3}, {j, 1, 3}, {k, 1, 3}, {l, 1, 2}]],
    Max[Table[If[ $\frac{\delta \kappa}{\delta - \text{incidence}(\delta + q \kappa)} > 0$ ,  $\frac{\delta \kappa}{\delta - \text{incidence}(\delta + q \kappa)}$ , 0] /.
    incidence  $\rightarrow$  incidenceTAB[[i]] /.  $\delta \rightarrow \delta\text{TAB}[[j]]$  /.  $\kappa \rightarrow \kappa\text{TAB}[[k]]$  /.
    q  $\rightarrow$  qTAB[[l]], {i, 1, 3}, {j, 1, 3}, {k, 1, 3}, {l, 1, 2}]]]}

Out[ ]:= {0.104712, 16.6667}

```

Range of $\tilde{R}_0$ values:

```

In[ ]:= {Min[Table[If[ $\frac{\delta}{\delta - \text{incidence}(\delta + q \kappa)} > 0$ ,  $\frac{\delta}{\delta - \text{incidence}(\delta + q \kappa)}$ , Infinity] /.
    incidence  $\rightarrow$  incidenceTAB[[i]] /.  $\delta \rightarrow \delta\text{TAB}[[j]]$  /.  $\kappa \rightarrow \kappa\text{TAB}[[k]]$  /.
    q  $\rightarrow$  qTAB[[l]], {i, 1, 3}, {j, 1, 3}, {k, 1, 3}, {l, 1, 2}]],
    Max[Table[If[ $\frac{\delta}{\delta - \text{incidence}(\delta + \kappa)} > 0$ ,  $\frac{\delta}{\delta - \text{incidence}(\delta + \kappa)}$ , 0] /.
    incidence  $\rightarrow$  incidenceTAB[[i]] /.  $\delta \rightarrow \delta\text{TAB}[[j]]$  /.  $\kappa \rightarrow \kappa\text{TAB}[[k]]$  /.
    q  $\rightarrow$  qTAB[[l]], {i, 1, 3}, {j, 1, 3}, {k, 1, 3}, {l, 1, 2}]]]}

Out[ ]:= {1.04712, 6.81818}

```

The disease only persists when the denominators above are positive, which isn't possible if the disease incidence and clearance rates are too high relative to the waning rate (i.e.. $\kappa > 0.133333$ leads to the loss of the disease when there is full seroconversion):

```

In[ ]:= Solve[( $\delta - \text{incidence}(\delta + q \kappa)$ ) /. incidence  $\rightarrow$  0.04 /.  $\delta \rightarrow 1 / 180$  /. q  $\rightarrow$  1] == 0,  $\kappa$ ]

Out[ ]:= {{ $\kappa \rightarrow 0.133333$ }}

```

Parameter estimates

(with vaccination)

From Our World in Data: US vaccination rates {% per day and % per year} from Jan 1 - April 30, 2023

```

In[ ]:= 79 655.7167 / (331.9 * 106) * {100, 100 * 365}

Out[ ]:= {0.0239999, 8.75997}

```

France vaccination rates {% per day and % per year} from Jan 1 - April 30, 2023

$$\text{In}[\#] := 8744.758333 / (67.75 \times 10^6) * \{100, 100 * 365\}$$

$$\text{Out}[\#] = \{0.0129074, 4.7112\}$$

The implications for β and $\tilde{R}_0$ of the choice of parameters:

$$\text{In}[\#] := \text{Solve}\left[\left(\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} - \frac{v}{\delta + \kappa}\right) == \text{incidence}, \beta\right]$$

$$\text{Out}[\#] = \left\{\left\{\beta \rightarrow -\frac{\delta \kappa}{v - \delta + \text{incidence} \delta + \text{incidence} \kappa}\right\}\right\}$$

$$\text{In}[\#] := \text{Solve}\left[\left(\frac{(\tilde{R}_0 - 1) \delta}{\tilde{R}_0 (\delta + \kappa)} - \frac{v}{\delta + \kappa}\right) == \text{incidence}, \tilde{R}_0\right]$$

$$\text{Out}[\#] = \left\{\left\{\tilde{R}_0 \rightarrow -\frac{\delta}{v - \delta + \text{incidence} \delta + \text{incidence} \kappa}\right\}\right\}$$

Consider also the number of infections per year at the endemic equilibrium. The daily rate of infection is:

$$\text{In}[\#] := \beta S I1 /. \left\{S \rightarrow \frac{\kappa}{\beta}, I1 \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} - \frac{v}{\delta + \kappa}\right\} /. \beta \rightarrow \tilde{R}_0 \kappa // \text{Factor}$$

$$\text{Out}[\#] = -\frac{\kappa (\delta + v \tilde{R}_0 - \delta \tilde{R}_0)}{(\delta + \kappa) \tilde{R}_0}$$

so the expected number of infections per year is:

$$\text{In}[\#] := 365 * \%$$

$$\text{Out}[\#] = -\frac{365 \kappa (\delta + v \tilde{R}_0 - \delta \tilde{R}_0)}{(\delta + \kappa) \tilde{R}_0}$$

$$\text{In}[\#] := \% /. \tilde{R}_0 \rightarrow -\frac{\delta}{v - \delta + \text{incidence} \delta + \text{incidence} \kappa} // \text{Simplify}$$

$$\text{Out}[\#] = 365 \text{ incidence} \kappa$$

Parameter range considered (nominal value of the parameter, minimum, and maximum), with summer 2023 levels of vaccination from Canada [negligible effect]

$$\text{In}[\#] := \text{TRYv} = 0.00012;$$

$$\text{incidenceTAB} = \{0.02, 0.005, 0.04\};$$

$$\delta \text{TAB} = \{1 / 125, 1 / 100, 1 / 180\};$$

$$\kappa \text{TAB} = \{1 / 5, 1 / 3, 1 / 10\};$$

```

In[ ]:= Flatten[Table[
  {incidence,  $\delta$ ,  $\kappa$ , If[ $\frac{\delta \kappa}{\delta - \text{incidence} (\delta + \kappa) - \text{TRYv}} > 0$ ,  $\frac{\delta \kappa}{\delta - \text{incidence} (\delta + \kappa) - \text{TRYv}}$ ,
    "NA"], If[ $\frac{\delta}{\delta - \text{incidence} (\delta + \kappa) - \text{TRYv}} > 0$ ,  $\frac{\delta}{\delta - \text{incidence} (\delta + \kappa) - \text{TRYv}}$ , "NA"],
    If[ $\frac{\delta}{\delta - \text{incidence} (\delta + \kappa) - \text{TRYv}} > 0$ ,  $1 / \frac{\delta}{\delta - \text{incidence} (\delta + \kappa) - \text{TRYv}}$ , "NA"],
    If[ $\frac{\delta}{\delta - \text{incidence} (\delta + \kappa) - \text{TRYv}} > 0$ ,  $365 \text{ incidence } \kappa$ , "NA"]}] /.
  incidence  $\rightarrow$  incidenceTAB[[i]] /.  $\delta \rightarrow \delta\text{TAB}[[j]]$  /.
   $\kappa \rightarrow \kappa\text{TAB}[[k]]$ , {i, 1, 3}, {j, 1, 3}, {k, 1, 3}], 2];
Join[{{"Incidence",  $\delta$ ,  $\kappa$ ,  $\beta$ ,  $\tilde{R}_0$ ,  $\hat{S}$ , "Annual rate"}}, (Round[1000  $\times$  %] / 1000.)] /.
(0.001` Round[1000 "NA"])  $\rightarrow$  "NA" // MatrixForm

```

Out[]//MatrixForm=

Incidence	δ	κ	β	$\tilde{R}_0$	$\hat{S}$	Annual rate
0.02	0.008	0.2	0.43	2.151	0.465	1.46
0.02	0.008	0.333	2.532	7.595	0.132	2.433
0.02	0.008	0.1	0.14	1.399	0.715	0.73
0.02	0.01	0.2	0.352	1.761	0.568	1.46
0.02	0.01	0.333	1.106	3.319	0.301	2.433
0.02	0.01	0.1	0.13	1.302	0.768	0.73
0.02	0.006	0.2	0.839	4.195	0.238	1.46
0.02	0.006	0.333	NA	NA	NA	NA
0.02	0.006	0.1	0.167	1.671	0.598	0.73
0.005	0.008	0.2	0.234	1.17	0.855	0.365
0.005	0.008	0.333	0.432	1.296	0.772	0.608
0.005	0.008	0.1	0.109	1.09	0.917	0.182
0.005	0.01	0.2	0.227	1.133	0.883	0.365
0.005	0.01	0.333	0.408	1.225	0.816	0.608
0.005	0.01	0.1	0.107	1.072	0.933	0.182
0.005	0.006	0.2	0.252	1.26	0.793	0.365
0.005	0.006	0.333	0.495	1.485	0.673	0.608
0.005	0.006	0.1	0.113	1.132	0.883	0.182
0.04	0.008	0.2	NA	NA	NA	NA
0.04	0.008	0.333	NA	NA	NA	NA
0.04	0.008	0.1	0.225	2.247	0.445	1.46
0.04	0.01	0.2	1.351	6.757	0.148	2.92
0.04	0.01	0.333	NA	NA	NA	NA
0.04	0.01	0.1	0.182	1.825	0.548	1.46
0.04	0.006	0.2	NA	NA	NA	NA
0.04	0.006	0.333	NA	NA	NA	NA
0.04	0.006	0.1	0.458	4.579	0.218	1.46

```
In[ ]:= 100 - 100 tablowv / tabnov
```

```
Out[ ]:= { { { { 0., 0, 0, -3.22581, -3.22581, 3.125, 1.42109 × 10-14 },
               { 0., 0, 0, -11.3924, -11.3924, 10.2273, 0. },
               { 0., 0, 0, -2.0979, -2.0979, 2.05479, 1.42109 × 10-14 } },
            { { 0., 0, 0, -2.11268, -2.11268, 2.06897, 1.42109 × 10-14 },
               { 0., 0, 0, -3.9823, -3.9823, 3.82979, 0. },
               { 0., 0, 0, -1.5625, -1.5625, 1.53846, 1.42109 × 10-14 } },
            { { 0., 0, 0, -9.0604, -9.0604, 8.30769, 1.42109 × 10-14 }, { 0., 0, 0, 0, 0, 0, 0 },
               { 0., 0, 0, -3.60963, -3.60963, 3.48387, 1.42109 × 10-14 } } },
            { { { 0., 0, 0, -1.75439, -1.75439, 1.72414, 1.42109 × 10-14 },
                  { 0., 0, 0, -1.94384, -1.94384, 1.90678, 0. },
                  { 0., 0, 0, -1.63488, -1.63488, 1.60858, 1.42109 × 10-14 } },
               { { 0., 0, 0, -1.359, -1.359, 1.34078, 1.42109 × 10-14 },
                  { 0., 0, 0, -1.46999, -1.46999, 1.44869, 0. },
                  { 0., 0, 0, -1.28617, -1.28617, 1.26984, 1.42109 × 10-14 } },
               { { 0., 0, 0, -2.72246, -2.72246, 2.65031, 1.42109 × 10-14 },
                  { 0., 0, 0, -3.2076, -3.2076, 3.10791, 0. },
                  { 0., 0, 0, -2.4451, -2.4451, 2.38674, 1.42109 × 10-14 } } },
            { { { 0., 0, 0, 0, 0, 0, 0 }, { 0., 0, 0, 0, 0, 0, 0 },
                  { 0., 0, 0, -3.37079, -3.37079, 3.26087, 1.42109 × 10-14 } },
               { { 0., 0, 0, -8.10811, -8.10811, 7.5, 1.42109 × 10-14 }, { 0., 0, 0, 0, 0, 0, 0 },
                  { 0., 0, 0, -2.18978, -2.18978, 2.14286, 1.42109 × 10-14 } }, { { 0., 0, 0, 0, 0, 0, 0 },
                  { 0., 0, 0, 0, 0, 0, 0 }, { 0., 0, 0, -9.89011, -9.89011, 9., 1.42109 × 10-14 } } } }
```

```
In[ ]:= {Min[%], Max[%]}
```

```
Out[ ]:= {-11.3924, 10.2273}
```

With higher, fall 2022 levels of vaccination from Canada, the disease could become eradicated if transmission is low enough, while β and $\tilde{R}_0$ estimates rise while $\hat{S}$ declines:

```
In[ ]:= TRYv = 0.00174;
```

```
incidenceTAB = {0.02, 0.005, 0.04};
```

```
 $\delta$ TAB = {1 / 125, 1 / 100, 1 / 180};
```

```
 $\kappa$ TAB = {1 / 5, 1 / 3, 1 / 10};
```

```

In[ ]:= Flatten[tabhighv = Table[
  {incidence,  $\delta$ ,  $\kappa$ , If[ $\frac{\delta \kappa}{\delta - \text{incidence}(\delta + \kappa) - \text{TRYv}} > 0$ ,  $\frac{\delta \kappa}{\delta - \text{incidence}(\delta + \kappa) - \text{TRYv}}$ ,
    "NA"], If[ $\frac{\delta}{\delta - \text{incidence}(\delta + \kappa) - \text{TRYv}} > 0$ ,  $\frac{\delta}{\delta - \text{incidence}(\delta + \kappa) - \text{TRYv}}$ , "NA"]},
  If[ $\frac{\delta}{\delta - \text{incidence}(\delta + \kappa) - \text{TRYv}} > 0$ ,  $1 / \frac{\delta}{\delta - \text{incidence}(\delta + \kappa) - \text{TRYv}}$ , "NA"],
  If[ $\frac{\delta}{\delta - \text{incidence}(\delta + \kappa) - \text{TRYv}} > 0$ ,  $365 \text{ incidence } \kappa$ , "NA"]} /.
  incidence  $\rightarrow$  incidenceTAB[[i]] /.  $\delta \rightarrow \delta\text{TAB}[[j]]$  /.
   $\kappa \rightarrow \kappa\text{TAB}[[k]]$ , {i, 1, 3}, {j, 1, 3}, {k, 1, 3}], 2];
Join[{{"Incidence",  $\delta$ ,  $\kappa$ ,  $\beta$ ,  $\tilde{R}_0$ ,  $\hat{S}$ , "Annual rate"}}, (Round[1000  $\times$  %] / 1000.)] /.
(0.001` Round[1000 "NA"])  $\rightarrow$  "NA" // MatrixForm

```

Out[]//MatrixForm=

Incidence	δ	κ	β	$\tilde{R}_0$	$\hat{S}$	Annual rate
0.02	0.008	0.2	0.762	3.81	0.262	1.46
0.02	0.008	0.333	NA	NA	NA	NA
0.02	0.008	0.1	0.195	1.951	0.512	0.73
0.02	0.01	0.2	0.493	2.463	0.406	1.46
0.02	0.01	0.333	2.392	7.177	0.139	2.433
0.02	0.01	0.1	0.165	1.65	0.606	0.73
0.02	0.006	0.2	NA	NA	NA	NA
0.02	0.006	0.333	NA	NA	NA	NA
0.02	0.006	0.1	0.326	3.259	0.307	0.73
0.005	0.008	0.2	0.307	1.533	0.652	0.365
0.005	0.008	0.333	0.586	1.757	0.569	0.608
0.005	0.008	0.1	0.14	1.399	0.715	0.182
0.005	0.01	0.2	0.277	1.387	0.721	0.365
0.005	0.01	0.333	0.509	1.528	0.654	0.608
0.005	0.01	0.1	0.13	1.297	0.771	0.182
0.005	0.006	0.2	0.399	1.993	0.502	0.365
0.005	0.006	0.333	0.873	2.619	0.382	0.608
0.005	0.006	0.1	0.169	1.69	0.592	0.182
0.04	0.008	0.2	NA	NA	NA	NA
0.04	0.008	0.333	NA	NA	NA	NA
0.04	0.008	0.1	0.412	4.124	0.243	1.46
0.04	0.01	0.2	NA	NA	NA	NA
0.04	0.01	0.333	NA	NA	NA	NA
0.04	0.01	0.1	0.259	2.591	0.386	1.46
0.04	0.006	0.2	NA	NA	NA	NA
0.04	0.006	0.333	NA	NA	NA	NA
0.04	0.006	0.1	NA	NA	NA	NA


```
In[ ]:= 100 - 100 tabhighv / tabnov
```

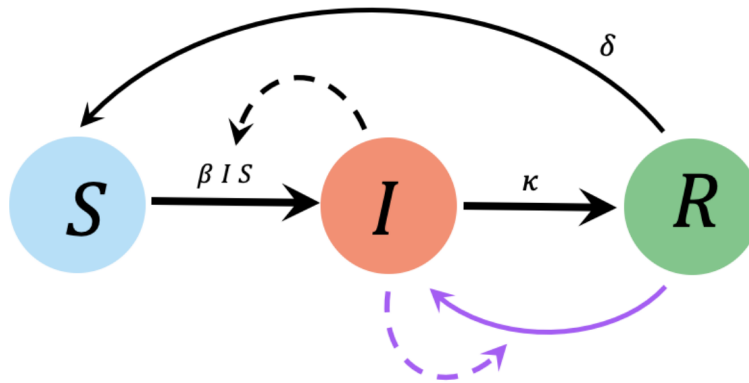
```
Out[ ]:= { { { { 0., 0, 0, -82.8571, -82.8571, 45.3125, 1.42109 × 10-14 },
               { 0., 0, 0, 100 - 44. NA, 100 - 14.6667 NA, 100 - 681.818 NA, 100 - 41.0959 NA },
               { 0., 0, 0, -42.439, -42.439, 29.7945, 1.42109 × 10-14 } },
           { { 0., 0, 0, -42.8571, -42.8571, 30., 1.42109 × 10-14 }, { 0., 0, 0, -124.88,
               -124.88, 55.5319, 0. }, { 0., 0, 0, -28.7129, -28.7129, 22.3077, 1.42109 × 10-14 } },
           { { 0., 0, 0, 100 - 130. NA, 100 - 26. NA, 100 - 384.615 NA, 100 - 68.4932 NA },
               { 0., 0, 0, 0, 0, 0, 0 }, { 0., 0, 0, -102.086, -102.086, 50.5161, 1.42109 × 10-14 } },
           { { { 0., 0, 0, -33.3333, -33.3333, 25., 1.42109 × 10-14 }, { 0., 0, 0, -38.2138,
               -38.2138, 27.6483, 0. }, { 0., 0, 0, -30.4196, -30.4196, 23.3244, 1.42109 × 10-14 } },
               { { 0., 0, 0, -24.1331, -24.1331, 19.4413, 1.42109 × 10-14 }, { 0., 0, 0, -26.592,
               -26.592, 21.006, 0. }, { 0., 0, 0, -22.5681, -22.5681, 18.4127, 1.42109 × 10-14 } },
               { { 0., 0, 0, -62.4153, -62.4153, 38.4294, 1.42109 × 10-14 },
               { 0., 0, 0, -82.0325, -82.0325, 45.0647, 0. },
               { 0., 0, 0, -52.9233, -52.9233, 34.6077, 1.42109 × 10-14 } } },
           { { { 0., 0, 0, 0, 0, 0, 0 }, { 0., 0, 0, 0, 0, 0, 0 },
               { 0., 0, 0, -89.6907, -89.6907, 47.2826, 1.42109 × 10-14 } },
               { { 0., 0, 0, 100 - 80. NA, 100 - 16. NA, 100 - 625. NA, 100 - 34.2466 NA },
               { 0., 0, 0, 0, 0, 0, 0 }, { 0., 0, 0, -45.0777, -45.0777, 31.0714, 1.42109 × 10-14 } },
               { { 0., 0, 0, 0, 0, 0, 0 }, { 0., 0, 0, 0, 0, 0, 0 },
               { 0., 0, 0, 100 - 240. NA, 100 - 24. NA, 100 - 416.667 NA, 100 - 68.4932 NA } } } }
```

```
In[ ]:= {Min[%], Max[%]}
```

```
Out[ ]:= {Min[-124.88, 100 - 681.818 NA, 100 - 625. NA, 100 - 416.667 NA, 100 - 384.615 NA,
           100 - 240. NA, 100 - 130. NA, 100 - 80. NA, 100 - 68.4932 NA, 100 - 44. NA, 100 - 41.0959 NA,
           100 - 34.2466 NA, 100 - 26. NA, 100 - 24. NA, 100 - 16. NA, 100 - 14.6667 NA],
          Max[55.5319, 100 - 681.818 NA, 100 - 625. NA, 100 - 416.667 NA, 100 - 384.615 NA,
           100 - 240. NA, 100 - 130. NA, 100 - 80. NA, 100 - 68.4932 NA, 100 - 44. NA, 100 - 41.0959 NA,
           100 - 34.2466 NA, 100 - 26. NA, 100 - 24. NA, 100 - 16. NA, 100 - 14.6667 NA]}
```

Alternative: SIR model (with leaky variants)

Now variant causes resistant class to be infectable (causing the recovered class to be leaky)



- Expected total waning time is $1/\delta$
- Recovery distribution is exponential

SIR model: Variants that are more immune evasive or transmissible

Here we allow the new variant to change the transmission rate (β) and/or the extent of leakiness of immunity (β_L):

$$\begin{aligned} \text{eqns} = \{ & D[S[t], t] == \delta R[t] - \beta_1 S[t] \times I_1[t] - \beta_2 S[t] \times I_2[t], \\ & D[I_1[t], t] == \beta_1 S[t] \times I_1[t] + \xi_1 \beta_1 R[t] \times I_1[t] - \kappa I_1[t], \\ & D[I_2[t], t] == \beta_2 S[t] \times I_2[t] + \xi_2 \beta_2 R[t] \times I_2[t] - \kappa I_2[t], \\ & D[R[t], t] == \kappa I_1[t] + \kappa I_2[t] - \delta R[t] - \xi_1 \beta_1 R[t] \times I_1[t] - \xi_2 \beta_2 R[t] \times I_2[t] \}; \end{aligned}$$

Before the new variant is present ($I_2=0$) and not leaky, the endemic equilibrium was found above (“Background: SIR model”) to be:

$$\text{In}[\#] := \text{endemic eq} = \left\{ S \rightarrow \frac{\kappa}{\beta_1}, I_1 \rightarrow \frac{\delta (\beta_1 - \kappa)}{\beta_1 (\delta + \kappa)}, R \rightarrow \frac{(\beta_1 - \kappa) \kappa}{\beta_1 (\delta + \kappa)}, I_2 \rightarrow 0 \right\};$$

$$\text{In}[\#] := S + I_1 + R /. \text{endemic eq} // \text{Factor}$$

$$\text{Out}[\#] = 1$$

The endemic equilibrium changes because of the leaky immunity and now solves a quadratic equilibrium equation:

$$\begin{aligned} \text{In}[\#] := \text{Simplify}[\text{Solve}[\{ & 0 == \delta R - \beta_1 S I_1, \\ & 0 == \beta_1 S I_1 + \xi_1 \beta_1 R I_1 - \kappa I_1 \}, \{ I_1, R \}], \{ \xi_1 > 0, \beta_1 > 0, \delta > 0, \kappa > 0 \}] \end{aligned}$$

$$\text{Out}[\#] = \left\{ \{ I_1 \rightarrow 0, R \rightarrow 0 \}, \left\{ I_1 \rightarrow \frac{\delta (-S \beta_1 + \kappa)}{S \beta_1^2 \xi_1}, R \rightarrow \frac{-S \beta_1 + \kappa}{\beta_1 \xi_1} \right\} \right\}$$

In[]:= S Numerator[S + I1 + R - 1 /. %[[2]]];

Collect[$\frac{\%}{\text{Coefficient}[\%, S^2]}$, S, Factor]

$$\text{Out[]} = S^2 + \frac{\delta \kappa}{\beta_1^2 (-1 + \xi_1)} - \frac{S (\delta - \kappa + \beta_1 \xi_1)}{\beta_1 (-1 + \xi_1)}$$

In[]:= newequil = Simplify[Solve[{0 == $\delta R - \beta_1 S I_1$,
 $0 == \beta_1 S I_1 + \xi_1 \beta_1 R I_1 - \kappa I_1$,
 $0 == \kappa I_1 - \delta R - \xi_1 \beta_1 R I_1$,
 $1 == S + I_1 + R$ }, {S, I1, R}], { $\beta_1 > 0$, $\xi_1 > 0$, $\delta > 0$, $\kappa > 0$ }]

$$\begin{aligned} \text{Out[]} = & \left\{ \left\{ S \rightarrow 1, I_1 \rightarrow 0, R \rightarrow 0 \right\}, \left\{ S \rightarrow \frac{\delta - \kappa + \beta_1 \xi_1 + \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 (-1 + \xi_1)}, \right. \right. \\ & I_1 \rightarrow -\frac{\delta + \kappa - \beta_1 \xi_1 + \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 \xi_1}, \\ & R \rightarrow -\frac{\delta + \kappa + \beta_1 \xi_1 - 2 \kappa \xi_1 + \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 (-1 + \xi_1) \xi_1} \left. \right\}, \\ & \left\{ S \rightarrow \frac{\delta - \kappa + \beta_1 \xi_1 - \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 (-1 + \xi_1)}, \right. \\ & I_1 \rightarrow \frac{-\delta - \kappa + \beta_1 \xi_1 + \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 \xi_1}, \\ & R \rightarrow -\frac{\delta + \kappa + \beta_1 \xi_1 - 2 \kappa \xi_1 - \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 (-1 + \xi_1) \xi_1} \left. \right\} \end{aligned}$$

where now the S and leakiness*R classes are identically susceptible, and these again sum to $\frac{\kappa}{\beta_1}$ at the new endemic equilibrium:

In[]:= Simplify[S + $\xi_1 R$ /. newequil[[3]], { $\beta_1 > 0$, $\xi_1 > 0$, $\delta > 0$, $\kappa > 0$ }]

$$\text{Out[]} = \frac{\kappa}{\beta_1}$$

If immunity isn't leaky for the resident ($\xi_1=0$) and if the variant causes only slight changes to leakiness and transmissibility, the equilibrium once the variant is fixed can be written as:

In[]:= I1 /. newequil[[3]] /. $\beta_1 \rightarrow \beta_2$ /. $\xi_1 \rightarrow \xi_2$;

Collect[
 Simplify[Normal[Series[% /. $\beta_2 \rightarrow \beta_1 + \Delta\beta \epsilon$ /. $\xi_2 \rightarrow \xi_1 + \Delta\xi \epsilon$ /. $\xi_1 \rightarrow 0$, { $\epsilon, 0, 1$ }]],
 { $\beta_1 > 0$, $\xi_1 > 0$, $\beta_2 > 0$, $\beta_{L2} > 0$, $\delta > 0$, $\kappa > 0$ }], $\Delta\xi$, Factor] /. $\epsilon \rightarrow 1$

$$\text{Out[]} = \frac{\delta (\beta_1 + \delta) \Delta\xi (\beta_1 - \kappa) \kappa}{\beta_1 (\delta + \kappa)^3} + \frac{\delta (\beta_1^2 - \beta_1 \kappa + \Delta\beta \kappa)}{\beta_1^2 (\delta + \kappa)}$$

which to leading order can be written as

```

In[ ]:=  $\left(1 - \frac{\kappa}{\beta_1 + \Delta\beta}\right) \frac{\delta + \Delta\delta}{\delta + \Delta\delta + \kappa} / \Delta\delta \rightarrow \frac{\Delta\xi (\beta_1 + \delta) \delta}{(\delta + \kappa)};$ 
Simplify[Normal[Series[Factor[%% - % / . Δβ → Δβ ∈ / . Δξ → Δξ ∈], {ε, 0, 0}]]] // Factor
Out[ ]:= 0

```

We next determine when the endemic equilibrium is stable would be invaded by a new variant that changes the transmission rate and/or immune evasive properties of the population. Ordering the equations with the new variant infections last:

```

{D[S[t], t] == δ R[t] - β1 S[t] × I1[t] - β2 S[t] × I2[t],
 D[I1[t], t] == β1 S[t] × I1[t] + ξ1 β1 R[t] × I1[t] - κ I1[t],
 D[R[t], t] == κ I1[t] + κ I2[t] - δ R[t] - ξ1 β1 R[t] × I1[t] - ξ2 β2 R[t] × I2[t],
 D[I2[t], t] == β2 S[t] × I2[t] + ξ2 β2 R[t] × I2[t] - κ I2[t]};

```

When $I_2[t]$ is rare and the system near the endemic equilibrium, the form of the Jacobian matrix is a block triangular matrix, with a 3x3 upper left matrix, which determines the stability of the endemic equilibrium (analysed in the previous section). The bottom row consists of zeros except for the last element $\left(\frac{d(I_2/dt)}{dI_2}\right)$, which determines stability when evaluated at the endemic equilibrium:

```

In[ ]:= eqni2 = β2 S I2 + ξ2 β2 R I2 - κ I2;
eqnset = {eqni2};
varset = {I2};
stabmat = Table[D[eqnset[[i]], varset[[j]]], {i, 1, 1}, {j, 1, 1}]
Out[ ]:= {{S β2 - κ + R β2 ξ2}}

```

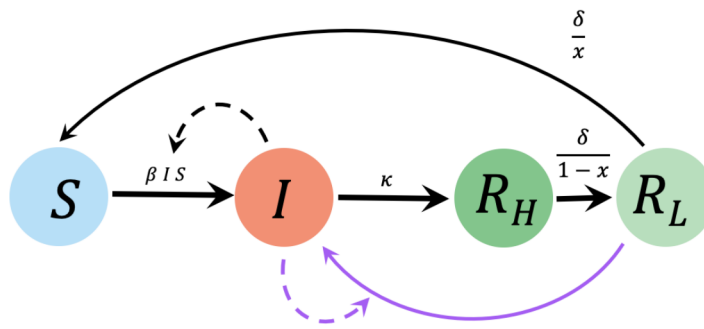
At the endemic equilibrium, the number of susceptibles is $\hat{S} + \xi_1 \hat{R} = \frac{\kappa}{\beta_1}$, so this eigenvalue corresponds to:

$$\begin{aligned}
 & \xi_2 \beta_2 \hat{R} + \hat{S} \beta_2 - \kappa \\
 &= \xi_2 \beta_2 \hat{R} + \left(\frac{\kappa}{\beta_1} - \xi_1 \hat{R}\right) \beta_2 - \kappa \\
 &= \Delta\xi \beta_2 \hat{R} + \kappa \frac{\Delta\beta}{\beta_1} \\
 &= \Delta\text{leakiness} \beta_2 \hat{R} + \hat{S} (\beta_2 - \beta_1)
 \end{aligned}$$

with the new lineage gaining a transmission advantage by infecting the recovered class ($\Delta\text{leakiness} \hat{R} \beta_2$) and/or increasing transmission to susceptible individuals.

Alternative: SIR_2 model

Model includes two waning classes, corresponding to high immunity early, decaying to a lower level of immunity that can be infected by a new variant.



- Considers only two compartments, R_H with higher immunity (not susceptible) and R_L with lower immunity (susceptible to variant)
- Expected total waning time is again $1/\delta$
- Biologically reasonable to consider the R compartments as antibody levels
- Causes a slightly humped distribution, but not very noticeable

We let the waning rate in the two classes be:

$$In[] := \left\{ \frac{\delta}{1-x}, \frac{\delta}{x} \right\};$$

so that the expected time to waning for the resident is:

$$In[] := 1 / \%[[1]] + 1 / \%[[2]] // \text{Factor}$$

$$Out[] := \frac{1}{\delta}$$

x determines the fraction of the waning period in which more immune evasive variants can infect.

SIR₂ model: Including high and low immunity classes

We consider an SIR₂ model with two recovered classes capturing the decline in neutralizing ability over time (with high and low antibody levels). Movement from R_H to R_L occurs at rate $\frac{\delta}{1-x}$ and from R_L to S occurs at rate $\frac{\delta}{x}$ so that the mean total time to move from R_H to S is held constant at $1/\delta$. When including a variant (next section), x determines the fraction of the expected waning period during which the variant (but not resident) can infect.

With waning rate in the two classes of:

$$In[] := \left\{ \frac{\delta}{1-x}, \frac{\delta}{x} \right\};$$

the expected total time to waning for the resident is:

```
In[ ]:= 1 / %[[1]] + 1 / %[[2]] // Factor
```

$$\text{Out[]} = \frac{1}{\delta}$$

The probability density function for the waning time is no longer exponential but has a hypoexponential distribution with probability density function given by:

```
In[ ]:= pdf[t_] = \frac{\lambda_1 \lambda_2}{\lambda_1 - \lambda_2} (\text{Exp}[-\lambda_2 t] - \text{Exp}[-\lambda_1 t]) /. \lambda_1 -> \frac{\delta}{1-x} /. \lambda_2 -> \frac{\delta}{x} // Simplify
```

$$\text{Out[]} = \frac{e^{\frac{t\delta}{(-1+x)x}} \left(e^{\frac{t\delta}{1-x}} - e^{\frac{t\delta}{x}} \right) \delta}{-1 + 2x}$$

which has a mean of $1/\delta$ (as expected)

```
In[ ]:= Simplify[Integrate[t \frac{\lambda_1 \lambda_2}{\lambda_1 - \lambda_2} (\text{Exp}[-\lambda_2 t] - \text{Exp}[-\lambda_1 t]), {t, 0, Infinity}],
  {\lambda_1 > 0, \lambda_2 > 0}] /. \lambda_1 -> \frac{\delta}{1-x} /. \lambda_2 -> \frac{\delta}{x} // Simplify
```

$$\text{Out[]} = \frac{1}{\delta}$$

and an $E[X^2]$ of:

```
In[ ]:= Simplify[Integrate[t^2 \frac{\lambda_1 \lambda_2}{\lambda_1 - \lambda_2} (\text{Exp}[-\lambda_2 t] - \text{Exp}[-\lambda_1 t]), {t, 0, Infinity}],
  {\lambda_1 > 0, \lambda_2 > 0}] /. \lambda_1 -> \frac{\delta}{1-x} /. \lambda_2 -> \frac{\delta}{x} // Simplify
```

$$\text{Out[]} = \frac{2(1-x+x^2)}{\delta^2}$$

so that the coefficient of variation squared is:

```
In[ ]:= \frac{\frac{2(1-x+x^2)}{\delta^2} - \left(\frac{1}{\delta}\right)^2}{\left(\frac{1}{\delta}\right)^2} // Simplify
```

$$\text{Out[]} = 1 - 2x + 2x^2$$

(i.e., a coefficient of variation of $\sqrt{(1-x)^2 + x^2}$). As expected, the coefficient of variation is one if x is either 0 or 1, but it is only $1/\sqrt{2}$ if $x = 1/2$ (equivalent to a gamma distribution with a CV of $1/\sqrt{2}$).

While this means that the resident and variant will have slightly different waning time distributions (CV of $\sqrt{(1-x)^2 + x^2}$ versus a CV of 1), the drop in vaccine effectiveness over time is similar enough that we neglect the difference.

Specifically, the probability of not having waned by time T (measured in time units of $1/\delta$) and so still

being immune is given by:

$$\text{In}[*]:= 1 - \text{Integrate}\left[\frac{\text{pdf}[y / \delta]}{\delta}, \{y, 0, T\}\right] // \text{FullSimplify}$$

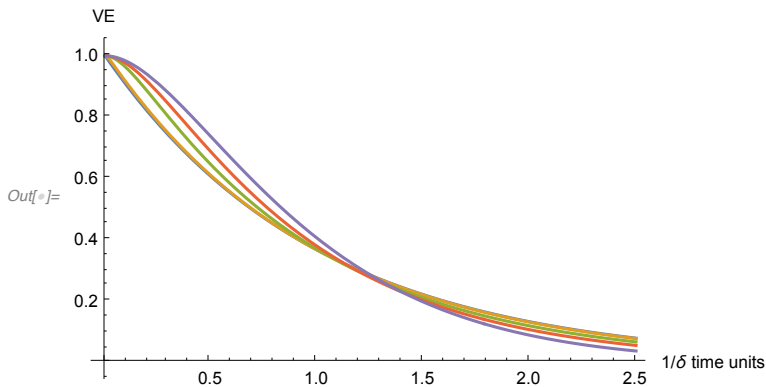
$$\text{Out}[*]= \frac{e^{-\frac{T}{x}} \left(e^T \left(\frac{1}{-1+x} + \frac{1}{x} \right) (-1+x) + x \right)}{-1+2x}$$

so that vaccine effectiveness over time varies slightly for different values of x but not by much:

```

In[*]:= Plot[{1 - CDF[ExponentialDistribution[1], T], % /. x -> 0.01,
             % /. x -> 0.1, % /. x -> 0.2, 1 - CDF[GammaDistribution[2, 1/2], T]},
            {T, 0, 2.5}, AxesLabel -> {"1/δ time units", "VE"}]

```



The disease model with transmission at rate β is then described by the differential equations:

$$\begin{aligned} \text{eqns} = \left\{ \begin{aligned} D[S[t], t] &= \frac{\delta}{x} RL[t] - \beta S[t] \times I1[t], \\ D[I1[t], t] &= \beta S[t] \times I1[t] - x I1[t], \\ D[RH[t], t] &= x I1[t] - \frac{\delta}{1-x} RH[t], \\ D[RL[t], t] &= \frac{\delta}{1-x} RH[t] - \frac{\delta}{x} RL[t] \end{aligned} \right\}; \end{aligned}$$

At equilibrium, the last equation indicates that $RL = \frac{x}{1-x} RH$. Measuring the variables as a fraction of the full population ($S+I1+RH+RL == 1$), this implies that RH will be $(1-x)(1-I1-S)$ and RL will be $x(1-I1-S)$ of the population at equilibrium:

$$\text{In}[*]:= \text{Solve}\left[\left(S + I1 + RH + RL /. RL \rightarrow \frac{x}{1-x} RH\right) == 1, RH\right]$$

$$\text{Out}[*]= \left\{ \left\{ RH \rightarrow (-1 + I1 + S) (-1 + x) \right\} \right\}$$

```

In[ ]:= equil = Solve[ { 0 ==  $\frac{\delta}{x}$  RL -  $\beta$  S I1,
                        0 ==  $\beta$  S I1 -  $\kappa$  I1,
                        0 ==  $\kappa$  I1 -  $\frac{\delta}{1-x}$  RH,
                        1 == S + I1 + RH + RL }, {S, I1, RH, RL}] // Simplify

Out[ ]:= { {S → 1, I1 → 0, RH → 0, RL → 0},
           { S →  $\frac{\kappa}{\beta}$ , I1 →  $\frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}$ , RH →  $-\frac{(-1 + x) (\beta - \kappa) \kappa}{\beta (\delta + \kappa)}$ , RL →  $\frac{x (\beta - \kappa) \kappa}{\beta (\delta + \kappa)}$  } }

```

This system has two equilibria (disease absent and disease endemic).

Below, we show that the eigenvalues for the disease-free equilibrium are always $\{-\delta, \beta - \kappa\}$, while the stability properties (stable or unstable) of the endemic equilibrium may change as we increase the number of recovered classes. See Hethcote et al. (1981; SIAM J. APPL. MATH. 40:1 section 4) for more details about the stability properties of the SIR_n model.

```

In[ ]:= eqns =  $\frac{\delta}{x}$  RL -  $\beta$  S I1;
eqni =  $\beta$  S I1 -  $\kappa$  I1;
eqnrH =  $\kappa$  I1 -  $\frac{\delta}{1-x}$  RH;
eqnrL =  $\frac{\delta}{1-x}$  RH -  $\frac{\delta}{x}$  RL;

eqnset = {eqns, eqni, eqnrH} /. RL → 1 - S - I1 - RH;
varset = {S, I1, RH};
stabmat = Table[D[eqnset[[i]], varset[[j]]], {i, 1, 3}, {j, 1, 3}] /. ii → i;
% // MatrixForm

```

Out[]//MatrixForm=

$$\begin{pmatrix} -I1 \beta - \frac{\delta}{x} & -S \beta - \frac{\delta}{x} & -\frac{\delta}{x} \\ I1 \beta & S \beta - \kappa & 0 \\ 0 & \kappa & -\frac{\delta}{1-x} \end{pmatrix}$$

```

In[ ]:= char = Det[ $\lambda$  IdentityMatrix[3] - stabmat] /.
           { S →  $\frac{\kappa}{\beta}$  } (* Char poly with leading  $\lambda^n$  term*)

```

$$Out[]:= \frac{I1 \beta \delta \kappa}{x} + \left(\frac{\delta}{1-x} + \lambda \right) \left(I1 \beta \left(\frac{\delta}{x} + \kappa \right) + \lambda \left(I1 \beta + \frac{\delta}{x} + \lambda \right) \right)$$

All of the coefficients are positive, so stability is guaranteed if $a_1 a_2 - a_3 > 0$ from the Routh-Hurwitz conditions (Box 8.2 in Otto and Day):


```
In[ ]:= a1 = Coefficient[char, λ2];
a2 = Coefficient[char, λ1];
a3 = char /. λ → 0;
```

```
a1 a2 - a3 // Simplify
```

$$\text{Out[]} = \frac{I1 \beta \delta^2 + \delta^3 - I1^2 (-1 + x) x \beta^2 (\delta - (-1 + x) x \kappa)}{(-1 + x)^2 x^2}$$

This can be written as $\frac{I1 \beta \delta^2 + \delta^3 + I1^2 (1-x) x \beta^2 (\delta + (1-x) x \kappa)}{(1-x)^2 x^2}$

As these terms are all positive, stability is guaranteed.

SIR₂ model: Variants that are more immune evasive or transmissible

Here we allow the new variant to change the transmission rate (β) and/or the stage of waning at which infection is possible. Specifically, we allow the mutant to infect the second recovered class with lower immunity (RL):

$$\begin{aligned} \text{eqns} = \left\{ \begin{aligned} D[S[t], t] &= \frac{\delta}{x} RL[t] - \beta_1 S[t] \times I1[t] - \beta_2 S[t] \times I2[t], \\ D[I1[t], t] &= \beta_1 S[t] \times I1[t] - \kappa I1[t], \\ D[I2[t], t] &= \beta_2 S[t] \times I2[t] + \beta_2 RL[t] \times I2[t] - \kappa I2[t], \\ D[RH[t], t] &= \kappa I1[t] + \kappa I2[t] - \frac{\delta}{1-x} RH[t], \\ D[RL[t], t] &= \frac{\delta}{1-x} RH[t] - \frac{\delta}{x} RL[t] - \beta_2 RL[t] \times I2[t] \end{aligned} \right\}; \end{aligned}$$

Before the new variant is present ($I2=0$), the endemic equilibrium was found above to equal:

$$\text{endemic eq} = \left\{ S \rightarrow \frac{\kappa}{\beta_1}, I1 \rightarrow \frac{\delta (\beta_1 - \kappa)}{\beta_1 (\delta + \kappa)}, RH \rightarrow (1-x) \frac{(\beta_1 - \kappa) \kappa}{\beta_1 (\delta + \kappa)}, RL \rightarrow x \frac{(\beta_1 - \kappa) \kappa}{\beta_1 (\delta + \kappa)}, I2 \rightarrow 0 \right\};$$

By contrast, when the variant has fixed, the endemic equilibrium changes because there are then only effectively $n-m$ recovered classes:

```

In[ ]:= newequil = Solve[ { 0 ==  $\frac{\delta}{x}$  RL -  $\beta_2$  S I2,
    0 ==  $\beta_2$  S I2 +  $\beta_2$  RL I2 -  $\kappa$  I2,
    0 ==  $\kappa$  I2 -  $\frac{\delta}{1-x}$  RH,
    1 == S + I2 + RH + RL }, {S, I2, RH, RL} ] // Simplify

Out[ ]:= { {S  $\rightarrow$  1, I2  $\rightarrow$  0, RH  $\rightarrow$  0, RL  $\rightarrow$  0}, {S  $\rightarrow$   $\frac{\kappa (\delta + \kappa - x \kappa)}{\beta_2 (\delta + x (\beta_2 - 2 \kappa) + \kappa)}$ ,
    I2  $\rightarrow$   $\frac{\delta (\beta_2 - \kappa)}{\beta_2 (\delta + \kappa - x \kappa)}$ , RH  $\rightarrow$   $-\frac{(-1+x) (\beta_2 - \kappa) \kappa}{\beta_2 (\delta + \kappa - x \kappa)}$ , RL  $\rightarrow$   $\frac{x (\beta_2 - \kappa) \kappa}{\beta_2 (\delta + x (\beta_2 - 2 \kappa) + \kappa)}$  } }

```

where now the S and RL classes are identically susceptible and sum to $\frac{\kappa}{\beta_2}$, as expected, at the new endemic equilibrium:

```

In[ ]:= S + RL /. newequil[[2]] // Factor

Out[ ]:=  $\frac{\kappa}{\beta_2}$ 

```

The number of infectious individuals becomes $I2 \rightarrow \frac{\frac{\delta}{1-x} (\beta_2 - \kappa)}{\beta_2 (\frac{\delta}{1-x} + \kappa)}$. Immune evasiveness effectively

reduces the return time to the susceptible state following infection, so that $\delta \rightarrow \delta + \Delta\delta$ where $\Delta\delta = \frac{x}{1-x} \delta$, causing the number of infected individuals at steady state to rise to:

```

In[ ]:=  $\frac{(\delta + \Delta\delta) (\beta_1 + \Delta\beta - \kappa)}{(\beta_1 + \Delta\beta) (\delta + \Delta\delta + \kappa)} / . \Delta\delta \rightarrow \frac{x}{1-x} \delta / . \Delta\beta \rightarrow \beta_2 - \beta_1;$ 

```

```

Factor[ (I2 /. newequil)[[2]] - %]

```

```

Out[ ]:= 0

```

We next determine when the endemic equilibrium is stable would be invaded by a new variant that changes the transmission rate and/or immune evasive properties of the population. Ordering the equations with the new variant infections last:

$$\begin{aligned}
 \{D[S[t], t] &= \frac{\delta}{1-x} RH[t] - \beta_1 S[t] \times I1[t] - \beta_2 S[t] \times I2[t], \\
 D[I1[t], t] &= \beta_1 S[t] \times I1[t] - \kappa I1[t], \\
 D[RH[t], t] &= \kappa I1[t] + \kappa I2[t] - \frac{\delta}{1-x} RH[t], \\
 D[RL[t], t] &= \frac{\delta}{1-x} RH[t] - \frac{\delta}{x} RL[t] - \beta_2 RL[t] \times I2[t], \\
 D[I2[t], t] &= \beta_2 S[t] \times I2[t] + \beta_2 RL[t] \times I2[t] - \kappa I2[t] \};
 \end{aligned}$$

When $I2[t]$ is rare and the system near the endemic equilibrium, the form of the Jacobian matrix is a block triangular matrix, with a 4x4 upper left matrix, which determines the stability of the endemic equilibrium (analysed in the previous section). The bottom row consists of zeros except for the last

element $\left(\frac{d(I_2/dt)}{dI_2}\right)$, which determines stability when evaluated at the endemic equilibrium:

```
In[ ]:= eqnI2 =  $\beta_2 S I_2 + \beta_2 R_L I_2 - \kappa I_2$ ;
eqnset = {eqnI2};
varset = {I2};
stabmat = Table[D[eqnset[[i]], varset[[j]]], {i, 1, 1}, {j, 1, 1}]

Out[ ]:= { {  $R_L \beta_2 + S \beta_2 - \kappa$  } }
```

At the endemic equilibrium, the number of susceptibles is $\hat{S} = \frac{\kappa}{\beta_1}$ and the total number of recovered individuals is $\hat{R} = R_H + R_L = \frac{(\beta_1 - \kappa) \kappa}{\beta_1 (\delta + \kappa)}$, so this eigenvalue corresponds to:

$$\begin{aligned} & \hat{R} L \beta_2 + \hat{S} \beta_2 - \kappa \\ &= x \hat{R} \beta_2 + \hat{S} \beta_2 - \hat{S} \beta_1 \\ &= x \hat{R} \beta_2 + \hat{S} (\beta_2 - \beta_1) \\ &= x \hat{R} \beta_2 + \kappa \frac{\Delta \beta}{\beta_1} \\ &= x \hat{R} \beta_2 + \kappa \frac{\Delta \tilde{R}_0}{\tilde{R}_0} \end{aligned}$$

with the new lineage gaining a transmission advantage by infecting the last recovered classed (frequency $x \hat{R}$) and/or increasing transmission to susceptible individuals. For a given proportional difference in β (or $\tilde{R}_0$), the higher the clearance rate, the higher the selective advantage of the new mutant.

LATENCY: ADDING A TRANSIENT INFECTED BUT NOT INFECTIOUS CLASS

COVID-19 infections are characterized by a short latent period, during which an individual is exposed but does not yet have detectable virus levels. The latent period for Omicron is estimated at 3.1 days (Xin et al. 2023; UKHSA). Including a latent class (E1) with exit rate $\epsilon = 1/3.1$:

$$\begin{aligned} \left\{ \begin{aligned} D[S[t], t] &= \frac{\delta}{x} R_L[t] - \beta_1 S[t] \times I_1[t] - \beta_2 S[t] \times I_2[t], \\ D[E1[t], t] &= \beta S[t] \times I_1[t] - \epsilon E1[t], \\ D[I_1[t], t] &= \epsilon E1[t] - \kappa I_1[t], \\ D[R_H[t], t] &= \kappa I_1[t] + \kappa I_2[t] - \frac{\delta}{1-x} R_H[t], \\ D[R_L[t], t] &= \frac{\delta}{1-x} R_H[t] - \frac{\delta}{x} R_L[t] - \beta_2 R_L[t] \times I_2[t], \\ D[E2[t], t] &= \beta S[t] \times I_2[t] + \beta_2 R_L[t] \times I_2[t] - \epsilon E2[t], \\ D[I_2[t], t] &= \epsilon E2[t] - \kappa I_2[t] \end{aligned} \right\}; \end{aligned}$$

Inclusion of a latent period changes the endemic equilibrium ($E_2=I_2=0$) to:

```

In[ ]:= equil = Solve[ { 0 ==  $\frac{\delta}{x}$  RL -  $\beta$  S I1,
                        0 ==  $\beta$  S I1 -  $\epsilon$  E1,
                        0 ==  $\epsilon$  E1 -  $\kappa$  I1,
                        0 ==  $\kappa$  I1 -  $\frac{\delta}{1-x}$  RH,
                        1 == S + E1 + I1 + RH + RL }, {S, E1, I1, RH, RL} ] // Simplify

Out[ ]:= { {S  $\rightarrow$  1, E1  $\rightarrow$  0, I1  $\rightarrow$  0, RH  $\rightarrow$  0, RL  $\rightarrow$  0}, {S  $\rightarrow$   $\frac{\kappa}{\beta}$ , E1  $\rightarrow$   $\frac{\delta (\beta - \kappa) \kappa}{\beta (\epsilon \kappa + \delta (\epsilon + \kappa))}$ ,
            I1  $\rightarrow$   $\frac{\delta \epsilon (\beta - \kappa)}{\beta (\epsilon \kappa + \delta (\epsilon + \kappa))}$ , RH  $\rightarrow$   $-\frac{(-1 + x) \epsilon (\beta - \kappa) \kappa}{\beta (\epsilon \kappa + \delta (\epsilon + \kappa))}$ , RL  $\rightarrow$   $\frac{x \epsilon (\beta - \kappa) \kappa}{\beta (\epsilon \kappa + \delta (\epsilon + \kappa))}$  } }

```

Because movement from the latent class is much faster than waning ($\epsilon \gg \delta$), including a latent period has little influence on the equilibrium: $\frac{\delta \epsilon (\beta - \kappa)}{\beta (\epsilon \kappa + \delta \kappa + \delta \epsilon)} \sim \frac{\delta \epsilon (\beta - \kappa)}{\beta (\epsilon \kappa + \delta \epsilon)} = \frac{\delta (\beta - \kappa)}{\beta (\kappa + \delta)}$.

Impact of a latent period on the rate of spread of a new variant is determined by the leading eigenvalue of the following stability matrix:

```

In[ ]:= eqne2 =  $\beta$ 2 S I2 +  $\beta$ 2 RL I2 -  $\epsilon$  E2;
eqni2 =  $\epsilon$  E2 -  $\kappa$  I2;
eqnset = {eqne2, eqni2};
varset = {E2, I2};
stabmat = Table[D[eqnset[[i]], varset[[j]]], {i, 1, 2}, {j, 1, 2}]

Out[ ]:= { {- $\epsilon$ , RL  $\beta$ 2 + S  $\beta$ 2}, { $\epsilon$ , - $\kappa$ }}

```

In the absence of a latent period, selection on the variant was $s \equiv \text{RL } \beta 2 + S \beta 2 - \kappa$. Compared to this selection coefficient, adding a latent period changes selection to this leading eigenvalue

```

In[ ]:= stabmat /. RL  $\beta$ 2 + S  $\beta$ 2  $\rightarrow$  s +  $\kappa$  // Eigenvalues

Out[ ]:= {  $\frac{1}{2} (-\epsilon - \kappa - \sqrt{4 s \epsilon + (\epsilon + \kappa)^2})$ ,  $\frac{1}{2} (-\epsilon - \kappa + \sqrt{4 s \epsilon + (\epsilon + \kappa)^2})$  }

```

with the latent and infectious period short relative to the spread of the variant ($\epsilon, \kappa \gg s$), the rate of spread of a variant would be:

```

In[ ]:= Collect[Simplify[Normal[Series[%[[2]], {s, 0, 1}]], { $\epsilon > 0$ ,  $\kappa > 0$ ,  $s > 0$ }],  $\epsilon$ , Factor]

Out[ ]:=  $\frac{s \epsilon}{\epsilon + \kappa}$ 

```

which can be written as:

$$s \frac{1}{1 + \kappa / \epsilon}$$

For example, when $\epsilon=1/3$ and $\kappa=1/7$, the selection coefficient is 70% of s .

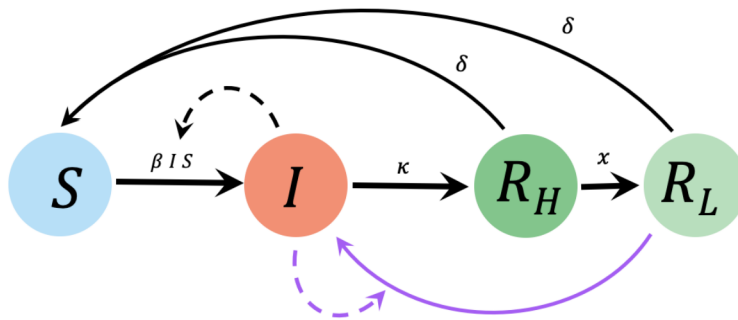
$$In[] := \frac{1 / \kappa}{1 / \kappa + 1 / \epsilon} \text{ // Factor}$$

$$Out[] := \frac{\epsilon}{\epsilon + \kappa}$$

For the parameters considered typical of Omicron (next section), selection would only be ~70 % as strong with a latent period. We ignore this correction to simplify the model presentation.

Second alternative: SIR₂ model

Model includes two waning classes, where both wane to susceptibility at the same rate (δ), but the second class can be infected by the variant:



- Considers only two compartments, RH (not susceptible) and RL (susceptible to variant), where the expected total waning time is $1/\delta$
 - Not biologically clear what these compartments are, given that all return to the susceptible class at the same rate.
 - Waning time distribution is always exponential
- x determines the fraction of the waning period in which more immune evasive variants can infect.

SIR₂ model: Including high and low immunity classes

The disease model with transmission at rate β is then described by the differential equations:

$$\begin{aligned} \text{eqns} = \{ & D[S[t], t] = \delta RL[t] + \delta RH[t] - \beta S[t] \times I1[t], \\ & D[I1[t], t] = \beta S[t] \times I1[t] - \kappa I1[t], \\ & D[RH[t], t] = \kappa I1[t] - \delta (1+x) RH[t], \\ & D[RL[t], t] = x \delta RH[t] - \delta RL[t] \}; \end{aligned}$$

At equilibrium, the last equation indicates that $RL = x RH$ (no longer equal in frequency). Measuring the variables as a fraction of the full population ($S+I1+RH+RL == 1$), this implies that RH will be $\frac{(1-I1-S)}{1+x}$ and RL will be $x (1-I1-S)$ of the population at equilibrium:

```
In[ ]:= Solve[(S + I1 + RH + RL /. RL -> x RH) == 1, RH]
```

```
Out[ ]:= {{RH -> \frac{1 - I1 - S}{1 + x}}}
```

```
In[ ]:= equil = Solve[{0 == \delta RL + \delta RH - \beta S I1,
  0 == \beta S I1 - \kappa I1,
  0 == \kappa I1 - \delta (1 + x) RH,
  1 == S + I1 + RH + RL}, {S, I1, RH, RL}] // Simplify
```

```
Out[ ]:= {{S -> 1, I1 -> 0, RH -> 0, RL -> 0},
  {S -> \frac{\kappa}{\beta}, I1 -> \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}, RH -> \frac{(\beta - \kappa) \kappa}{(1 + x) \beta (\delta + \kappa)}, RL -> \frac{x (\beta - \kappa) \kappa}{(1 + x) \beta (\delta + \kappa)}}}
```

This system has two equilibria (disease absent and disease endemic).

Below, we show that the eigenvalues for the disease-free equilibrium are always $\{-\delta n, \beta - \kappa\}$, while the stability properties (stable or unstable) of the endemic equilibrium may change as we increase the number of recovered classes. See Hethcote et al. (1981; SIAM J. APPL. MATH. 40:1 section 4) for more details about the stability properties of the SIR_n model.

```
In[ ]:= eqns = \frac{\delta}{x} RL - \beta S I1;
```

```
eqni = \beta S I1 - \kappa I1;
```

```
eqnrH = \kappa I1 - \frac{\delta}{1 - x} RH;
```

```
eqnrL = \frac{\delta}{1 - x} RH - \frac{\delta}{x} RL;
```

```
eqnset = {eqns, eqni, eqnrH} /. RL -> 1 - S - I1 - RH;
```

```
varset = {S, I1, RH};
```

```
stabmat = Table[D[eqnset[[i]], varset[[j]]], {i, 1, 3}, {j, 1, 3}] /. ii -> i;
```

```
% // MatrixForm
```

```
Out[ ]//MatrixForm=
```

$$\begin{pmatrix} -I1 \beta - \frac{\delta}{x} & -S \beta - \frac{\delta}{x} & -\frac{\delta}{x} \\ I1 \beta & S \beta - \kappa & 0 \\ 0 & \kappa & -\frac{\delta}{1-x} \end{pmatrix}$$

```
In[ ]:= char = Det[\lambda IdentityMatrix[3] - stabmat] /.
```

```
{S -> \frac{\kappa}{\beta}} (* Char poly with leading \lambda^n term*)
```

```
Out[ ]:= \frac{I1 \beta \delta \kappa}{x} + \left( \frac{\delta}{1-x} + \lambda \right) \left( I1 \beta \left( \frac{\delta}{x} + \kappa \right) + \lambda \left( I1 \beta + \frac{\delta}{x} + \lambda \right) \right)
```

All of the coefficients are positive, so stability is guaranteed if $a_1 a_2 - a_3 > 0$ from the Routh-Hurwitz conditions (Box 8.2 in Otto and Day):

```
In[ ]:= a1 = Coefficient[char, λ2];
a2 = Coefficient[char, λ1];
a3 = char /. λ → 0;
```

```
a1 a2 - a3 // Simplify
```

$$\text{Out[]} = \frac{I1 \beta \delta^2 + \delta^3 - I1^2 (-1+x) \times \beta^2 (\delta - (-1+x) \times \kappa)}{(-1+x)^2 x^2}$$

This can be written as $\frac{I1 \beta \delta^2 + \delta^3 + I1^2 (1-x) \times \beta^2 (\delta + (1-x) \times \kappa)}{(1-x)^2 x^2}$

As these terms are all positive, stability is guaranteed.

SIR₂ model: Variants that are more immune evasive or transmissible

Here we allow the new variant to change the transmission rate (β) and/or the stage of waning at which infection is possible. Specifically, we allow the mutant to infect the second recovered class with lower immunity (RL):

```
eqns = {D[S[t], t] == δ RH[t] + δ RL[t] - β1 S[t] × I1[t] - β2 S[t] × I2[t],
D[I1[t], t] == β1 S[t] × I1[t] - κ I1[t],
D[I2[t], t] == β2 S[t] × I2[t] + β2 RL[t] × I2[t] - κ I2[t],
D[RH[t], t] == κ I1[t] + κ I2[t] - δ (1+x) RH[t],
D[RL[t], t] == x δ RH[t] - δ RL[t] - β2 RL[t] × I2[t]};
```

Before the new variant is present (I2=0), the endemic equilibrium was found above to equal:

$$\text{In[]} := \text{endemic eq} = \left\{ S \rightarrow \frac{\kappa}{\beta1}, I1 \rightarrow \frac{\delta (\beta1 - \kappa)}{\beta1 (\delta + \kappa)}, RH \rightarrow \frac{(\beta - \kappa) \kappa}{(1+x) \beta (\delta + \kappa)}, RL \rightarrow \frac{x (\beta - \kappa) \kappa}{(1+x) \beta (\delta + \kappa)}, I2 \rightarrow 0 \right\};$$

$$\text{In[]} := \frac{RL}{RL + RH} /. \text{endemic eq} // \text{Factor}$$

$$\text{Out[]} = \frac{x}{1+x}$$

By contrast, when the variant has fixed, the endemic equilibrium changes because there are then only effectively n-m recovered classes:

```
In[ ]:= newequil = Solve[{0 == δ RH + δ RL - β2 S I2,
  0 == β2 S I2 + β2 RL I2 - κ I2,
  0 == κ I2 - δ (1 + x) RH,
  1 == S + I2 + RH + RL}, {S, I2, RH, RL}] // Factor
```

$$\text{Out[]} = \left\{ \left\{ S \rightarrow 1, I2 \rightarrow 0, RH \rightarrow 0, RL \rightarrow 0 \right\}, \left\{ S \rightarrow \frac{(\beta 2 + \delta + x \delta) \kappa}{\beta 2 (\beta 2 + x \beta 2 + \delta + x \delta - x \kappa)}, \right. \right. \\ \left. \left. I2 \rightarrow \frac{(1 + x) \delta (\beta 2 - \kappa)}{\beta 2 (\delta + x \delta + \kappa)}, RH \rightarrow \frac{(\beta 2 - \kappa) \kappa}{\beta 2 (\delta + x \delta + \kappa)}, RL \rightarrow \frac{x (\beta 2 - \kappa) \kappa}{\beta 2 (\beta 2 + x \beta 2 + \delta + x \delta - x \kappa)} \right\} \right\}$$

where now the S and RL classes are identically susceptible and sum to $\frac{\kappa}{\beta 2}$, as expected, at the new endemic equilibrium:

```
In[ ]:= S + RL /. newequil[[2]] // Factor
```

$$\text{Out[]} = \frac{\kappa}{\beta 2}$$

The number of infectious individuals becomes $I2 \rightarrow \frac{(1+x) \delta (\beta 2 - \kappa)}{\beta 2 ((1+x) \delta + \kappa)}$. Immune evasiveness effectively reduces the return time to the susceptible state following infection, so that $\delta \rightarrow \delta + \Delta\delta$ where $\Delta\delta = x \delta$, causing the number of infected individuals at steady state to rise to:

$$\text{In[]} := \frac{(\delta + \Delta\delta) (\beta 1 + \Delta\beta - \kappa)}{(\beta 1 + \Delta\beta) (\delta + \Delta\delta + \kappa)} /. \Delta\delta \rightarrow x \delta /. \Delta\beta \rightarrow \beta 2 - \beta 1;$$

```
Factor[(I2 /. newequil)[[2]] - %]
```

$$\text{Out[]} = 0$$

We next determine when the endemic equilibrium is stable would be invaded by a new variant that changes the transmission rate and/or immune evasive properties of the population. Ordering the equations with the new variant infections last:

$$\begin{aligned} D[S[t], t] &= \delta RH[t] + \delta RL[t] - \beta 1 S[t] \times I1[t] - \beta 2 S[t] \times I2[t], \\ D[I1[t], t] &= \beta 1 S[t] \times I1[t] - \kappa I1[t], \\ D[RH[t], t] &= \kappa I1[t] + \kappa I2[t] - (1 + x) \delta RH[t], \\ D[RL[t], t] &= x \delta RH[t] - \delta RL[t] - \beta 2 RL[t] \times I2[t], \\ D[I2[t], t] &= \beta 2 S[t] \times I2[t] + \beta 2 RL[t] \times I2[t] - \kappa I2[t]; \end{aligned}$$

When $I2[t]$ is rare and the system near the endemic equilibrium, the form of the Jacobian matrix is a block triangular matrix, with a 4x4 upper left matrix, which determines the stability of the endemic equilibrium (analysed in the previous section). The bottom row consists of zeros except for the last element $\left(\frac{d(I2/dt)}{dI2}\right)$, which determines stability when evaluated at the endemic equilibrium:


```

In[ ]:= eqni2 =  $\beta_2 S I_2 + \beta_2 RL I_2 - \kappa I_2$ ;
eqnset = {eqni2};
varset = {I2};
stabmat = Table[D[eqnset[[i]], varset[[j]]], {i, 1, 1}, {j, 1, 1}]

```

```
Out[ ]:= { {RL  $\beta_2 + S \beta_2 - \kappa$  } }
```

At the endemic equilibrium, the number of susceptibles is $\hat{S} = \frac{\kappa}{\beta_1}$ and the total number of recovered individuals is $\hat{R} = RH + RL = \frac{(\beta_1 - \kappa) \kappa}{\beta_1 (\delta + \kappa)}$, so this eigenvalue corresponds to:

$$\begin{aligned}
 & \hat{R}L \beta_2 + \hat{S} \beta_2 - \kappa \\
 &= \frac{\kappa}{1+\kappa} \hat{R} \beta_2 + \hat{S} \beta_2 - \hat{S} \beta_1 \\
 &= \frac{\kappa}{1+\kappa} \hat{R} \beta_2 + \hat{S} (\beta_2 - \beta_1) \\
 &= \frac{\kappa}{1+\kappa} \hat{R} \beta_2 + \kappa \frac{\Delta \beta}{\beta_1} \\
 &= \frac{\kappa}{1+\kappa} \hat{R} \beta_2 + \kappa \frac{\Delta \tilde{R}_0}{\tilde{R}_0}
 \end{aligned}$$

with the new lineage gaining a transmission advantage by infecting the last recovered classed (frequency $\frac{\kappa}{1+\kappa} \hat{R}$) and/or increasing transmission to susceptible individuals. For a given proportional difference in β (or $\tilde{R}_0$), the higher the clearance rate, the higher the selective advantage of the new mutant.