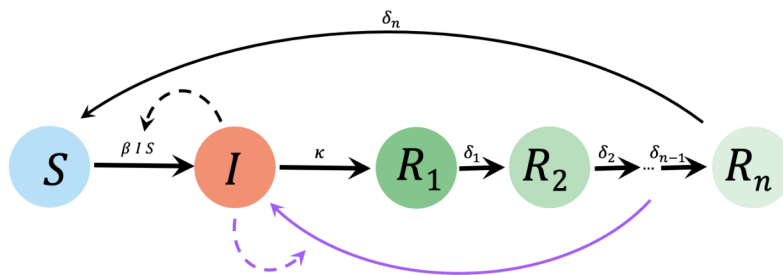


Exploring transients around steady state: SIR_n model

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



Variant evolution

Figure 2B: persistently immune evasive ($n=5$) (increases mean waning rate by 67%)

Can infect last two classes ($m=2$)

```
ln[0]:= maxtime = 500;
maxy = 8;

Parameters:

ln[0]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
TRYf = 99 / 100; (*Starting fraction of resident*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)

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

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

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

$In[] := \text{TRYinf} = 1 / 50; (*\text{Assumed initial endemic frequency of infected individuals}*)$

$$\text{TRY}\beta = \frac{\text{TRY}\delta \text{TRY}\kappa}{\text{TRY}\delta - \text{TRYinf} \text{TRY}\delta - \text{TRYconvert} \text{TRYinf} \text{TRY}\kappa};$$

$$\frac{\text{TRY}\beta}{\text{TRY}\kappa} // N$$

$Out[] := 2.08333$

Variant has the same transmissibility:

$In[] := \text{TRY}\beta V = \text{TRY}\beta;$

but infects earlier during waning. Specifically, we assume five waning classes and the variant infects two earlier.

$In[] := \text{TRY}n = 5;$

$\text{TRY}m = 2;$

Thus, the mean waning rate (once fixed) increases by 67%:

$$In[] := \frac{\text{TRY}\delta + \Delta\delta}{\text{TRY}\delta} /. \Delta\delta \rightarrow \frac{\text{TRY}m}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta // N$$

$Out[] := 1.66667$

while the mean waiting time decreases by 40%:

$In[] := 1 / \%$

$Out[] := 0.6$

Starting equilibrium would be (r_0 includes all of the n resistance classes):

$$\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)} \right\}$$

$$In[] := \text{start} = \left\{ s_0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i_0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, \right. \\ \left. r_0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right\}$$

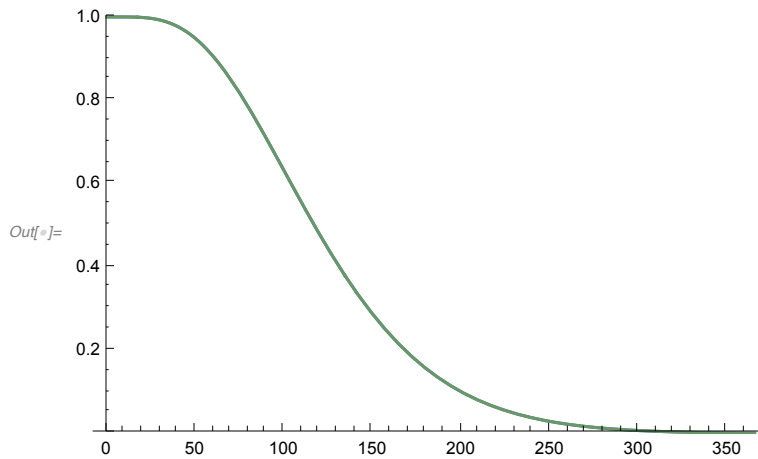
$$Out[] := \left\{ s_0 \rightarrow \frac{12}{25}, i_0 \rightarrow \frac{1}{50}, r_0 \rightarrow \frac{1}{2} \right\}$$

Waning distribution for a population of younger and older individuals:

```

In[ ]:= Show[
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ TRYn)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.4, 0.8]],
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ0 TRYn)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]

```



Now the susceptible and resistant classes depend only on age (not whether they carried a variant before):

[NOTE: For the ease of colouring, the first stage class is the variant.]

```

In[ ]:= {ages = 2, stages = 2, n = TRYn};

```

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta O$ _,  $\kappa$ _, q_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta O$ ,  $\kappa$ , q}, start] =
    Block[{ages = 2, stages = 2, n = TRYn},
      dsdt[j_, t_] =
        (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] + n *  $\delta$ [j] * r[n, j, t] -
        Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] *
        Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
        Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 1] * i[j, 1, t];
      didt[j_, 2, t_] = Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] -
         $\kappa$ [j, 2] * i[j, 2, t];
      drdt[1, j_, t_] = q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] - n *  $\delta$ [j] * r[1, j, t];
      For[nn = 2, nn ≤ n - TRYm, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      For[nn = n + 1 - TRYm, nn ≤ n, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] -
          Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      pars = { $\beta$ [j_, 1] →  $\beta V$ ,  $\beta$ [j_, 2] →  $\beta$ ,  $\delta$ [1] →  $\delta Y$ ,  $\delta$ [2] →  $\delta O$ ,  $\kappa$ [j_, jj_] →  $\kappa$ };
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[{s[j, t], Table[i[j, jj, t], {jj, 1, stages}],
        Table[r[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      r[n, ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[Table[{D[s[j, t], t] == dsdt[j, t],
        Table[D[i[j, jj, t], t] == didt[j, jj, t], {jj, 1, stages}],
        Table[D[r[nn, j, t], t] == drdt[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0, Table[r[nn, j, 0] ==
          (frac[j, 1] + frac[j, 2])  $\frac{r0}{n}$ , {nn, 1, n}]}], {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};

```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

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

```
In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1, colours[[i]]}}, {i, 2, Length[all]}]];
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

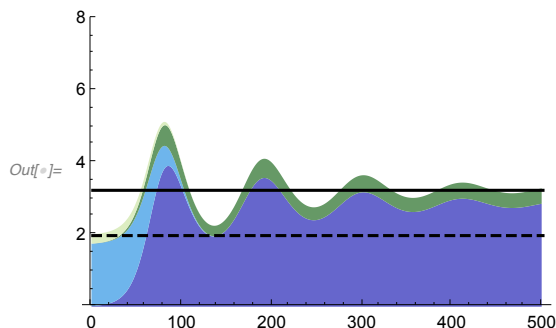
```
( <70,Res <70,Mutant
  70+,Res 70+,Mutant )
```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};
```

```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```
In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[ Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> None, Filling -> {{1 -> {0, }}, {2 -> {{1, }},
    {3 -> {{2, }}, {4 -> {{3, }}}}},
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
    PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
    {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]
```



Mutant fraction change between t=0 and t=50:

$$\text{In}[*]:= \frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]} /. \text{solution}[\text{partemp}, \text{start}] /. t \rightarrow 50$$

$$\text{Out}[*]= \{0.384091\}$$

$$\text{In}[*]:= \text{Solve}\left[\text{Exp}[s \, 50] == \left(\frac{p50 / (1 - p50)}{p0 / (1 - p0)}\right) /. p50 \rightarrow \% /. p0 \rightarrow 1 - \text{TRYf}\right], s][[1]]$$

 **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

$$\text{Out}[*]= \{s \rightarrow 0.082458\}$$

This is consistent with the predicted selection coefficient:

$$\text{In}[*]:= \frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \frac{\text{TRY}m}{\text{TRY}n} \left(\frac{\text{TRY}\kappa \text{TRYconvert} (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right) \text{TRY}\beta V // N$$

$$\text{Out}[*]= 0.0833333$$

New equilibrium:

$$\text{In}[*]:= \left(\frac{(\text{TRY}\delta + \Delta\delta) (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V (\text{TRY}\delta + \Delta\delta) + \text{TRY}\kappa \text{TRYconvert}} \right) /. \Delta\delta \rightarrow \frac{\text{TRY}m}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta // N$$

$$\text{Out}[*]= 0.0325$$

% rise in the endemic equilibrium:

$$\text{In}[*]:= 100 * \frac{(\% - \text{TRYinf})}{\text{TRYinf}}$$

$$\text{Out}[*]= 62.5$$

The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

$$\text{In}[*]:= \text{partemp} = \left\{ \text{TRY}p, \text{TRY}f, \text{TRY}older, \text{TRY}\beta, \text{TRY}\beta V, \frac{8}{10} \text{TRY}\delta, \frac{8}{10} \text{TRY}\delta 0, \text{TRY}\kappa, \frac{8}{10} \right\};$$

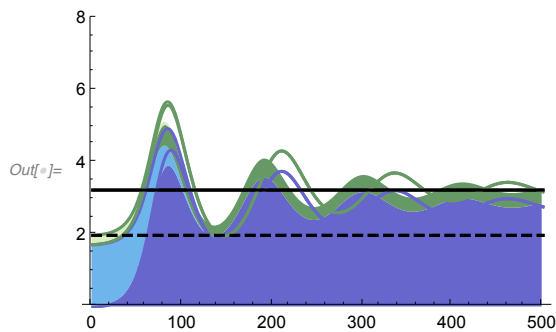
$$\text{In}[*]:= \text{solution}[\text{partemp}, \text{start}];$$

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Seroconversion affects the dynamics (curves compared to the previous shaded plot) but not the initial speed of spread of the variant (described by the selection coefficient) or the equilibrium.

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```

Figure 2A: transiently immune evasive (n=5) (increases mean waning rate by 67%)

Can infect last two classes (m=2)

```

In[ ]:= maxtime = 500;
maxy = 8;
Parameters:

```

```

In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
TRYf = 99 / 100; (*Starting fraction of resident*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)

```

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

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

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

```

In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
TRYβ =  $\frac{\text{TRY} \delta \text{ TRY} \kappa}{\text{TRY} \delta - \text{TRYinf } \text{TRY} \delta - \text{TRYconvert } \text{TRYinf } \text{TRY} \kappa}$ ;

```

$$\frac{\text{TRY} \beta}{\text{TRY} \kappa} // \text{N}$$

```
Out[ ]:= 2.08333
```

Variant has the same transmissibility:

```
In[ ]:= TRYβV = TRYβ;
```

but infects earlier during waning. Specifically, we assume five waning classes and the variant infects two earlier (40% reduction in mean waning time):

```

In[ ]:= TRYn = 5;
TRYm = 2;

```

Starting equilibrium would be (r0 includes all of the n resistance classes):

$$\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)} \right\}$$

$$\text{In[]:= start} = \left\{ s0 \rightarrow \frac{\text{TRY} \kappa}{\text{TRY} \beta}, i0 \rightarrow \frac{\text{TRY} \delta (\text{TRY} \beta - \text{TRY} \kappa)}{\text{TRY} \beta (\text{TRY} \delta + \text{TRY} \kappa \text{ TRYconvert})}, \right. \\ \left. r0 \rightarrow 1 - \frac{\text{TRY} \kappa}{\text{TRY} \beta} - \frac{\text{TRY} \delta (\text{TRY} \beta - \text{TRY} \kappa)}{\text{TRY} \beta (\text{TRY} \delta + \text{TRY} \kappa \text{ TRYconvert})} \right\}$$

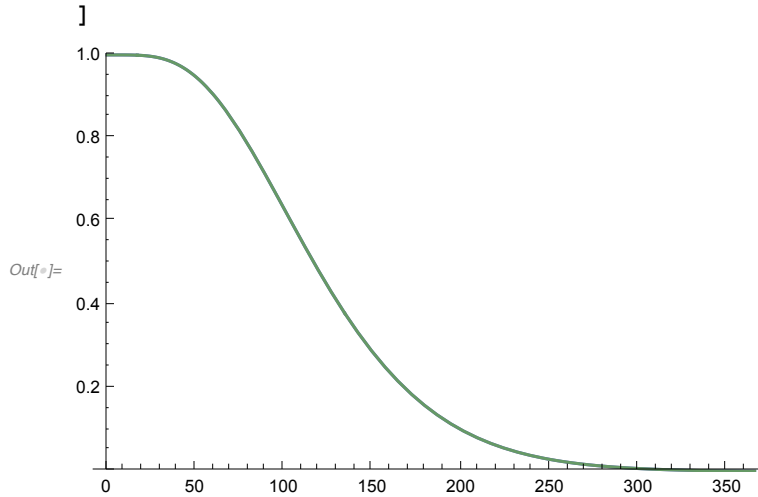
$$\text{Out[]:= } \left\{ s0 \rightarrow \frac{12}{25}, i0 \rightarrow \frac{1}{50}, r0 \rightarrow \frac{1}{2} \right\}$$

Waning distribution for a population of younger and older individuals:

```

In[ ]:= Show[
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ TRYn)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.4, 0.8]],
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ0 TRYn)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]

```



Now the susceptible and resistant classes depend only on age (not whether they carried a variant before):

[NOTE: For the ease of colouring, the first stage class is the variant.]

```

In[ ]:= {ages = 2, stages = 2, exposures = 2, n = TRYn};

```

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_, β_, βV_, δY_, δ0_, κ_, q_}, start] :=
  solution[{p, f, older, β, βV, δY, δ0, κ, q}, start] =
    Block[{ages = 2, stages = 2, exposures = 2, n = TRYn},
      dsdt[j_, zz_, t_] = (1 - q) * Sum[κ[j, jj] * i[j, jj, zz, t], {jj, 1, stages}] +
        n * δ[j] * r[n, j, zz, t] - Sum[β[k, kk] * i[k, kk, kkk, t],
          {k, 1, ages}, {kk, 1, stages}, {kkk, 1, exposures}] * s[j, zz, t];
      (*For the susceptible and recovered classes,
      we introduce zz to measure whether individuals have ever
      been exposed to the new variant (zz=1) or not (zz=2),
      this allows us to model transient immunity. We assume that those who
      do not seroconvert, with probability 1-c, remain in their zz class.*)
      didt[j_, 1, 1, t_] = Sum[β[k, 1] * i[k, 1, kkk, t], {k, 1, ages}, {kkk, 1, exposures}] *
        Sum[r[nn, j, 2, t], {nn, n + 1 - TRYm, n}] + Sum[β[k, 1] * i[k, 1, kkk, t],
          {k, 1, ages}, {kkk, 1, exposures}] * s[j, 1, t] - κ[j, 1] * i[j, 1, 1, t];
      (*This is the variant [stage 1], but it can only infect the
      recovering individuals who have never been exposed to a variant
      infection [stage 2]. Once infected by the variant these will move into the
      first type of recovering individual [zz=1] and are no longer available*)
      didt[j_, 1, 2, t_] = Sum[β[k, 1] * i[k, 1, kkk, t], {k, 1, ages}, {kkk, 1, exposures}] *

```

```

s[j, 2, t] - κ[j, 1] * i[j, 1, 2, t];
(*Although no infection with the variant lacks exposure to the variant,
we allow this in case some fail to seroconvert, with probability 1-c.*)
diddt[j_, 2, zz_, t_] = Sum[β[k, 2] * i[k, 2, kkk, t], {k, 1, ages},
{kkk, 1, exposures}] * s[j, zz, t] - κ[j, 2] * i[j, 2, zz, t];
drdt[1, j_, 1, t_] = q * (κ[j, 1] * i[j, 1, 1, t] + κ[j, 1] * i[j, 1, 2, t] +
κ[j, 2] * i[j, 2, 1, t]) - n * δ[j] * r[1, j, 1, t];
(*All infections with the variant move into this first resistance class only,
as do those exposed in prior infections (i[j,2,1,t]).*)
drdt[1, j_, 2, t_] = q * (κ[j, 2] * i[j, 2, 2, t]) - n * δ[j] * r[1, j, 2, t];
For[nn = 2, nn ≤ n - TRYm, nn++,
drdt[nn, j_, zz_, t_] = n * δ[j] * r[nn - 1, j, zz, t] - n * δ[j] * r[nn, j, zz, t];
];
For[nn = n + 1 - TRYm, nn ≤ n, nn++,
drdt[nn, j_, 1, t_] = n * δ[j] * r[nn - 1, j, 1, t] - n * δ[j] * r[nn, j, 1, t];
drdt[nn, j_, 2, t_] = n * δ[j] * r[nn - 1, j, 2, t] - Sum[β[k, 1] * i[k, 1, kkk, t],
{k, 1, ages}, {kkk, 1, exposures}] * r[nn, j, 2, t] - n * δ[j] * r[nn, j, 2, t];
(*Only those that have not been infected before by the new variant [stage 2]
can become infected earlier by the new variant [stage 1]*);
pars = {β[j_, 1] → βV, β[j_, 2] → β, δ[1] → δY, δ[2] → δO, κ[j_, jj_] → κ};
frac[1, 1] = (1 - older) (1 - f);
frac[2, 1] = older (1 - f);
frac[1, 2] = (1 - older) f;
frac[2, 2] = older f;
nvars = Drop[Flatten[Table[{Table[s[j, zz, t], {zz, 1, exposures}],
Table[i[j, jj, zz, t], {jj, 1, stages}, {zz, 1, exposures}],
Table[r[nn, j, zz, t], {nn, 1, n}, {zz, 1, exposures}]}], {j, 1, ages}]], -1];
r[n, ages, exposures, t_] = 1 - Total[nvars];
neqns = Drop[
Flatten[Table[{Table[D[s[j, zz, t], t] == dsdt[j, zz, t], {zz, 1, exposures}],
Table[D[i[j, jj, zz, t], t] == didt[j, jj, zz, t], {jj, 1, stages},
{zz, 1, exposures}], Table[D[r[nn, j, zz, t], t] == drdt[nn, j, zz, t],
{nn, 1, n}, {zz, 1, exposures}]}], {j, 1, ages}]], -1];
nstart = Drop[Flatten[Table[{
Table[i[j, jj, 1, 0] == 0, {jj, 1, stages}],
Table[i[j, jj, 2, 0] == frac[j, jj] i0, {jj, 1, stages}],
s[j, 1, 0] == 0, (*Nobody starts exposed to the variant*)
s[j, 2, 0] == (frac[j, 1] + frac[j, 2]) * s0,
Table[r[nn, j, 1, 0] == 0, {nn, 1, n}],
Table[r[nn, j, 2, 0] == (frac[j, 1] + frac[j, 2])  $\frac{r0}{n}$ , {nn, 1, n}]}],
{j, 1, ages}]] /. start, -1];
(*All susceptible and resistant individuals initially

```

```

      susceptible to the new variant [in stage 2] *)
NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
]

```

```
In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
```

```
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}
```

```
In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};
```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

```
Out[ ]:= {
```

```
In[ ]:= coltab = Join[{{1 -> {0, colours[[1]]}}},
  Table[{i -> {i - 1, colours[[i]]}}, {i, 2, Length[all]}]];
Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

Out[]//MatrixForm=

```

(
  <70,Res    
  <70,Mutant 
  70+,Res    
  70+,Mutant 
)

```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};
```

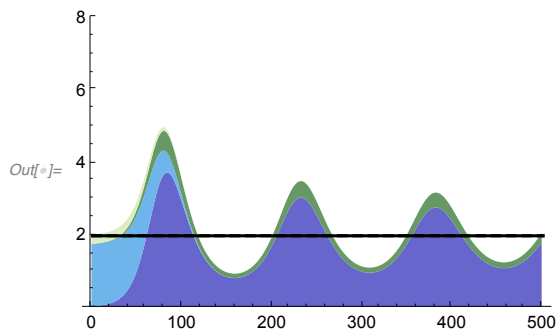
```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```

In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[
    Sum[100 i[all[[c, 1]], all[[c, 2]], 1, t] + 100 i[all[[c, 1]], all[[c, 2]], 2, t] /.
      solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
    {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
    PlotStyle -> None, Filling -> {{1 -> {0, Blue}}, {2 -> {1, Blue}},
      {3 -> {2, Green}}, {4 -> {3, Green}}}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
    PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n-0} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n-0} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
    {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Mutant fraction change between t=0 and t=50:

```

In[ ]:= 
$$\frac{\text{Sum}[i[j, 1, zz, t], \{j, 1, \text{ages}\}, \{zz, 1, \text{exposures}\}]}{\text{Sum}[i[j, jj, zz, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}, \{zz, 1, \text{exposures}\}]} /. \text{solution}[partemp, start] /. t \rightarrow 50$$

Out[ ]:= {0.383419}

```

```

In[ ]:= Solve[Exp[s 50] ==  $\left( \frac{p50 / (1 - p50)}{p0 / (1 - p0)} \right) /. p50 \rightarrow \% /. p0 \rightarrow 1 - \text{TRY}f$ ], s][[1]]

```

Solve: Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```

Out[ ]:= {s -> 0.0824012}

```

This is consistent with the predicted selection coefficient:

$$In[] := \frac{TRY\beta V - TRY\beta}{TRY\beta} TRY\kappa + \frac{TRYm}{TRYn} \left(\frac{TRY\kappa TRYconvert (TRY\beta - TRY\kappa)}{TRY\beta (TRY\delta + TRY\kappa TRYconvert)} \right) TRY\beta V // N$$

Out[] = 0.0833333

New equilibrium:

$$In[] := \left(\frac{(TRY\delta + \Delta\delta) (TRY\beta V - TRY\kappa)}{TRY\beta V ((TRY\delta + \Delta\delta) + TRY\kappa TRYconvert)} \right) /. \Delta\delta \rightarrow \frac{0}{TRYn - 0} TRY\delta // N$$

Out[] = 0.02

% rise in the endemic equilibrium:

$$In[] := 100 * \frac{(\% - TRYinf)}{TRYinf}$$

Out[] = 0.

The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

$$In[] := partemp = \left\{ TRYp, TRYf, TRYolder, TRY\beta, TRY\beta V, \frac{8}{10} TRY\delta, \frac{8}{10} TRY\delta 0, TRY\kappa, \frac{8}{10} \right\};$$

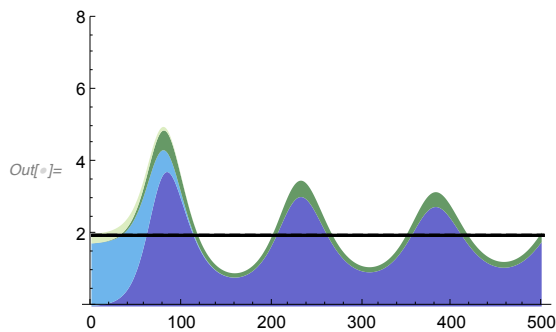
In[] := solution[partemp, start];

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[ Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n-\theta} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n-\theta} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Seroconversion affects the dynamics (curves compared to the previous shaded plot) but not the initial speed of spread of the variant (described by the selection coefficient) or the equilibrium.

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```

Figure 3 & S2B: more transmissible (n=5)

```

In[ ]:= maxtime = 500;
maxy = 8;
Parameters:

```

```
In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
TRYf = 99 / 100; (*Starting fraction of resident*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
i →  $\frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)}$ 
```

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

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

```
In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
TRYβ =  $\frac{\text{TRY}\delta \text{TRY}\kappa}{\text{TRY}\delta - \text{TRYinf} \text{TRY}\delta - \text{TRYconvert} \text{TRYinf} \text{TRY}\kappa}$ ;
```

```
 $\frac{\text{TRY}\beta}{\text{TRY}\kappa} // N$ 
```

```
Out[ ]:= 2.08333
```

Variant has a higher transmissibility (set to have the same selection coefficient as for the immune evasive variant):

```
In[ ]:= Flatten[ Solve[  $\frac{\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa == 0.0833, \beta V ] ]$ 
```

```
Out[ ]:= {  $\beta V \rightarrow 0.590208$  }
```

```
In[ ]:= TRYβV = βV / . %;
```

% increase in β:

```
In[ ]:= 100 *  $\frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta}$ 
```

```
Out[ ]:= 41.65
```

and now has no immune evasive properties. Specifically, we assume five waning classes and the variant infects only susceptibles (m=0):

```
In[ ]:= TRYn = 5;
```

```
TRYm = 0;
```

Starting equilibrium would be (r0 includes all of the n resistance classes):

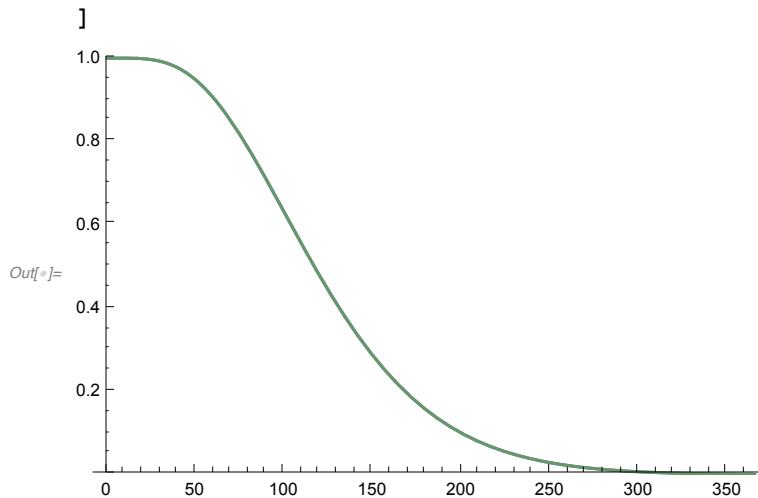
```
{ s →  $\frac{\kappa}{\beta}$ , i →  $\frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)}$  }
```

$$\text{In}[] := \text{start} = \left\{ s_0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i_0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, \right. \\ \left. r_0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right\}$$

$$\text{Out}[] := \left\{ s_0 \rightarrow \frac{12}{25}, i_0 \rightarrow \frac{1}{50}, r_0 \rightarrow \frac{1}{2} \right\}$$

Waning distribution for a population of younger and older individuals:

```
In[ ] := Show[
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ TRYn)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.4, 0.8]],
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ0 TRYn)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```



Now the susceptible and resistant classes depend only on age (not whether they carried a variant before):

[NOTE: For the ease of colouring, the first stage class is the variant.]

```
In[ ] := {ages = 2, stages = 2, n = TRYn};
```

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta O$ _,  $\kappa$ _, q_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta O$ ,  $\kappa$ , q}, start] =
    Block[{ages = 2, stages = 2, n = TRYn},
      dsdt[j_, t_] =
        (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] + n *  $\delta$ [j] * r[n, j, t] -
        Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] *
        Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
        Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 1] * i[j, 1, t];
      didt[j_, 2, t_] = Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] -
         $\kappa$ [j, 2] * i[j, 2, t];
      drdt[1, j_, t_] = q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] - n *  $\delta$ [j] * r[1, j, t];
      For[nn = 2, nn ≤ n - TRYm, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      For[nn = n + 1 - TRYm, nn ≤ n, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] -
          Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      pars = { $\beta$ [j_, 1] →  $\beta V$ ,  $\beta$ [j_, 2] →  $\beta$ ,  $\delta$ [1] →  $\delta Y$ ,  $\delta$ [2] →  $\delta O$ ,  $\kappa$ [j_, jj_] →  $\kappa$ };
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[{s[j, t], Table[i[j, jj, t], {jj, 1, stages}],
        Table[r[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      r[n, ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[Table[{D[s[j, t], t] == dsdt[j, t],
        Table[D[i[j, jj, t], t] == didt[j, jj, t], {jj, 1, stages}],
        Table[D[r[nn, j, t], t] == drdt[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0, Table[r[nn, j, 0] ==
          (frac[j, 1] + frac[j, 2])  $\frac{r0}{n}$ , {nn, 1, n}]}], {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};

```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

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

```
In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1, colours[[i]]}}, {i, 2, Length[all]}]];
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

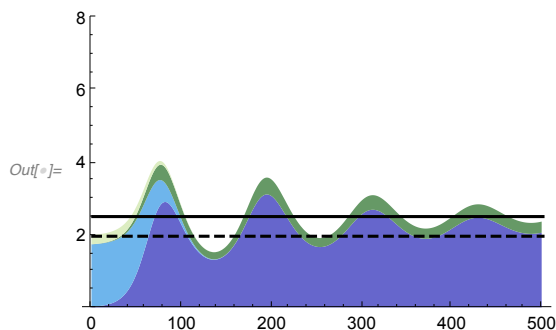
```
(
  <70,Res
  <70,Mutant
  70+,Res
  70+,Mutant
)
```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};
```

```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```
In[ ]:= plot1 = Show[
  Plot[
    Evaluate@Table[Sum[100 i[all[[c, 1]], all[[c, 2]], t] /. solution[partemp, start],
      {c, 1, jcum}], {jcum, 1, Length[all]}],
    {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
    PlotStyle -> None, Filling -> {{1 -> {0, }}, {2 -> {{1, }},
      {3 -> {{2, }}, {4 -> {{3, }}}}},
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
    PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
    {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]
```



Mutant fraction change between t=0 and t=50:

$$\text{Inf} := \frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]} /. \text{solution}[\text{partemp}, \text{start}] /. t \rightarrow 50$$

$$\text{Out}[\#] = \{0.38051\}$$

$$\text{Inf} := \text{Solve}\left[\text{Exp}[s \ 50] == \left(\frac{p50 / (1 - p50)}{p0 / (1 - p0)}\right) /. p50 \rightarrow \% /. p0 \rightarrow 1 - \text{TRYf}\right], s][[1]]$$

 **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

$$\text{Out}[\#] = \{s \rightarrow 0.0821547\}$$

This is consistent with the predicted selection coefficient:

$$\text{Inf} := \frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \frac{\text{TRY}m}{\text{TRY}n} \left(\frac{\text{TRY}\kappa \text{TRYconvert} (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right) \text{TRY}\beta V // N$$

$$\text{Out}[\#] = 0.0833$$

New equilibrium:

$$\text{Inf} := \left(\frac{(\text{TRY}\delta + \Delta\delta) (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V ((\text{TRY}\delta + \Delta\delta) + \text{TRY}\kappa \text{TRYconvert})} \right) /. \Delta\delta \rightarrow \frac{\text{TRY}m}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta // N$$

$$\text{Out}[\#] = 0.0254283$$

% rise in the endemic equilibrium:

$$\text{Inf} := 100 * \frac{(\% - \text{TRYinf})}{\text{TRYinf}}$$

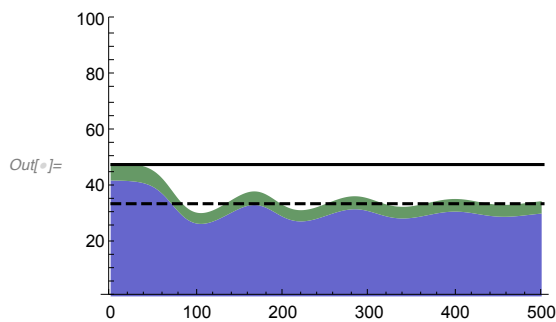
$$\text{Out}[\#] = 27.1417$$

This considers the number of susceptibles, with the black line at $1/\tilde{R}_0$ (the fraction of susceptibles that causes the disease to stop growing before the variant) and the dashed black line at $1/\tilde{R}_0^*$ (the fraction of susceptibles that causes the disease to stop growing once the variant predominates):

```

In[ ]:= Show[
  Plot[Evaluate@
    Table[Sum[100 s[c, t] /. solution[partemp, start], {c, 1, jcum}], {jcum, 1, 2}],
    {t, 0, maxtime}, PlotRange -> {Automatic, {0, 100}},
    PlotStyle -> None, Filling -> {{1 -> {0, Blue}}, {2 -> {{1}, Green}}}],
  Plot[100  $\frac{TRY\kappa}{TRY\beta}$ , {t, 0, maxtime}, PlotStyle -> {Black}],
  Plot[100  $\frac{TRY\kappa}{TRY\beta V}$ , {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  ImageSize -> 250
]

```



The first time that the number of susceptibles falls below $\frac{TRY\kappa}{TRY\beta V}$ is when we expect the number of the new variant to start declining (roughly, given that waning changes the dynamics):

$$In[]:= \left(1 + \frac{(TRY\beta V - TRY\beta)}{TRY\beta} \right)$$

Out[]:= 1.4165

```

In[ ]:= droptime = First[
  Select[Table[Flatten[{t, Sum[100 s[c, t] /. solution[partemp, start], {c, 1, 2}]}],
    {t, 0, maxtime}], #[[2]] < 100  $\frac{TRY\kappa}{TRY\beta V}$  &]]

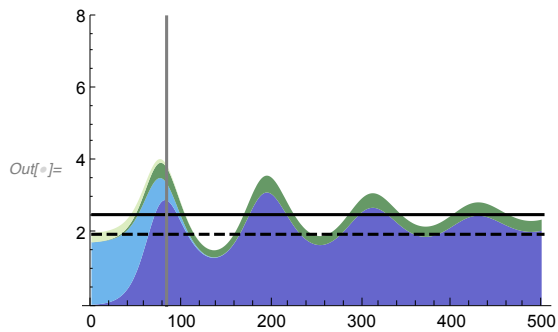
```

Out[]:= {82, 33.842}

```

In[ ]:= Show[
  plot1,
  ListPlot[{{droptime[[1]], 0}, {droptime[[1]], maxy}},
    Joined → True, PlotStyle → {Gray}],
  ImageSize → 250
]

```



The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

```

In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV,  $\frac{8}{10}$  TRYδ,  $\frac{8}{10}$  TRYδ0, TRYκ,  $\frac{8}{10}$ };

```

```

In[ ]:= solution[partemp, start];

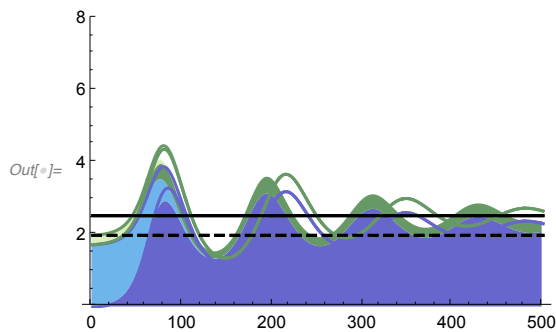
```

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n-\theta} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n-\theta} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Seroconversion affects the dynamics (curves compared to the previous shaded plot) but not the initial speed of spread of the variant (described by the selection coefficient) or the equilibrium.

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```

**Figure S1A: both persistently immune evasive and more transmissible (n=5)
Can infect last class (m=1)**

```

In[ ]:= maxtime = 500;
maxy = 8;
Parameters:

```

```

In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
TRYf = 99 / 100; (*Starting fraction of resident*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
i →  $\frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)}$ 

```

```

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

```

```

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

```

```

In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
TRYβ =  $\frac{\text{TRY} \delta \text{TRY} \kappa}{\text{TRY} \delta - \text{TRYinf} \text{TRY} \delta - \text{TRYconvert} \text{TRYinf} \text{TRY} \kappa}$ ;

```

```

 $\frac{\text{TRY} \beta}{\text{TRY} \kappa} // \text{N}$ 

```

```

Out[ ]:= 2.08333

```

Now we allow partial immune evasiveness, coupled with higher transmission. Specifically, we assume five waning classes and the variant infects one earlier resistant class (m=1):

```

In[ ]:= TRYn = 5;
TRYm = 1;

```

Variant has a higher transmissibility (set to have the same selection coefficient as for the immune evasive variant):

```

In[ ]:= Flatten[ Solve[  $\frac{\beta V - \text{TRY} \beta}{\text{TRY} \beta} \text{TRY} \kappa + \frac{\text{TRYm}}{\text{TRYn}} \left( \frac{\text{TRY} \kappa \text{TRYconvert} (\text{TRY} \beta - \text{TRY} \kappa)}{\text{TRY} \beta (\text{TRY} \delta + \text{TRY} \kappa \text{TRYconvert})} \right) \beta V == 0.0833, \beta V ] ]$ 

```

```

Out[ ]:= {  $\beta V \rightarrow 0.488448$  }

```

```

In[ ]:= TRYβV = βV / . %;

```

```

In[ ]:= TRYβ // N

```

```

Out[ ]:= 0.416667

```

```

In[ ]:= TRYβV / TRYβ // N

```

```

Out[ ]:= 1.17228

```

Starting equilibrium would be (r0 includes all of the n resistance classes):

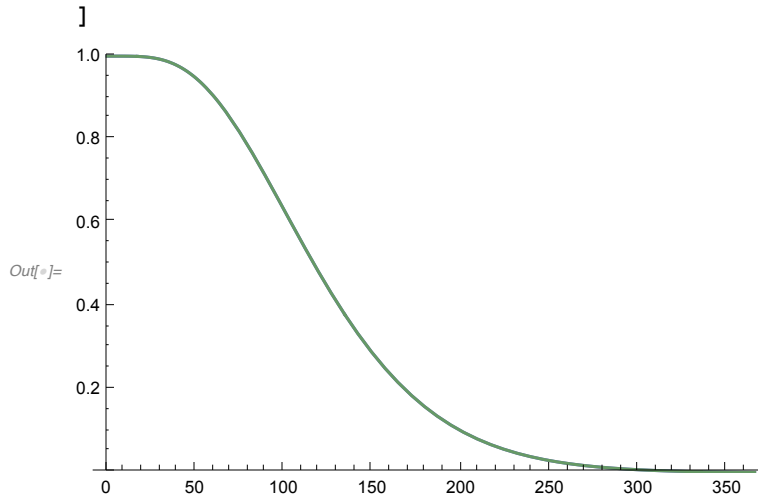
$$\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)} \right\}$$

$$\text{In}[] := \text{start} = \left\{ s_0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i_0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, \right. \\ \left. r_0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right\}$$

$$\text{Out}[] := \left\{ s_0 \rightarrow \frac{12}{25}, i_0 \rightarrow \frac{1}{50}, r_0 \rightarrow \frac{1}{2} \right\}$$

Waning distribution for a population of younger and older individuals:

```
In[ ] := Show[
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ TRYn)]], t),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.4, 0.8]],
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ0 TRYn)]], t),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```



Now the susceptible and resistant classes depend only on age (not whether they carried a variant before):

[NOTE: For the ease of colouring, the first stage class is the variant.]

```
In[ ] := {ages = 2, stages = 2, n = TRYn};
```

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta O$ _,  $\kappa$ _, q_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta O$ ,  $\kappa$ , q}, start] =
    Block[{ages = 2, stages = 2, n = TRYn},
      dsdt[j_, t_] =
        (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] + n *  $\delta$ [j] * r[n, j, t] -
        Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] *
        Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
        Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 1] * i[j, 1, t];
      didt[j_, 2, t_] = Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] -
         $\kappa$ [j, 2] * i[j, 2, t];
      drdt[1, j_, t_] = q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] - n *  $\delta$ [j] * r[1, j, t];
      For[nn = 2, nn ≤ n - TRYm, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      For[nn = n + 1 - TRYm, nn ≤ n, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] -
          Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      pars = { $\beta$ [j_, 1] →  $\beta V$ ,  $\beta$ [j_, 2] →  $\beta$ ,  $\delta$ [1] →  $\delta Y$ ,  $\delta$ [2] →  $\delta O$ ,  $\kappa$ [j_, jj_] →  $\kappa$ };
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[{s[j, t], Table[i[j, jj, t], {jj, 1, stages}],
        Table[r[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      r[n, ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[Table[{D[s[j, t], t] == dsdt[j, t],
        Table[D[i[j, jj, t], t] == didt[j, jj, t], {jj, 1, stages}],
        Table[D[r[nn, j, t], t] == drdt[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0, Table[r[nn, j, 0] ==
          (frac[j, 1] + frac[j, 2])  $\frac{r0}{n}$ , {nn, 1, n}]}], {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};

```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

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

```
In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1, colours[[i]]}}, {i, 2, Length[all]}]];
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

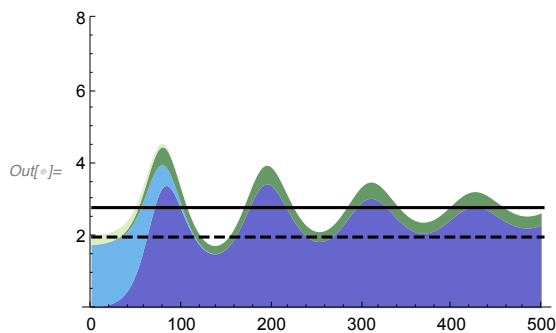
```
Out[ ]//MatrixForm=
```

```
( <70,Res <70,Mutant
  70+,Res 70+,Mutant )
```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};
```

```
In[ ]:= solution[partemp, start];
```

```
In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[
    100 Sum[i[all[[c, 1]], all[[c, 2]], t] /. solution[partemp, start], {c, 1, jcum}],
    {jcum, 1, Length[all]}], {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
    PlotStyle -> None, Filling -> {{1 -> {0, }}, {2 -> {{1, }}},
    {3 -> {{2, }}}, {4 -> {{3, }}}}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
    PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
    {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]
```



Mutant fraction change between t=0 and t=50:

```
In[ ]:= 
$$\frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]}$$
 /. solution[partemp, start] /. t -> 50
```

```
Out[ ]:= {0.382856}
```

```
In[ ]:= Solve[Exp[s 50] == 
$$\left( \frac{p50 / (1 - p50)}{p0 / (1 - p0)} \right) /. p50 \rightarrow \% /. p0 \rightarrow 1 - \text{TRYf}$$
, s][[1]]
```

 **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```
Out[ ]:= {s -> 0.0823535}
```

This is consistent with the predicted selection coefficient:

```
In[ ]:= 
$$\frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \frac{\text{TRY}m}{\text{TRY}n} \left( \frac{\text{TRY}\kappa \text{TRYconvert} (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right) \text{TRY}\beta V // N$$

```

```
Out[ ]:= 0.0833
```

New equilibrium:

```
In[ ]:= 
$$\left( \frac{(\text{TRY}\delta + \Delta\delta) (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V (\text{TRY}\delta + \Delta\delta) + \text{TRY}\kappa \text{TRYconvert}} \right) /. \Delta\delta \rightarrow \frac{\text{TRY}m}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta // N$$

```

```
Out[ ]:= 0.028121
```

% rise in the endemic equilibrium:

```
In[ ]:= 
$$100 * \frac{(\% - \text{TRYinf})}{\text{TRYinf}}$$

```

```
Out[ ]:= 40.6048
```

The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYbeta, TRYbetaV,  $\frac{8}{10} \text{TRY}\delta$ ,  $\frac{8}{10} \text{TRY}\delta 0$ , TRYkappa,  $\frac{8}{10}$ };
```

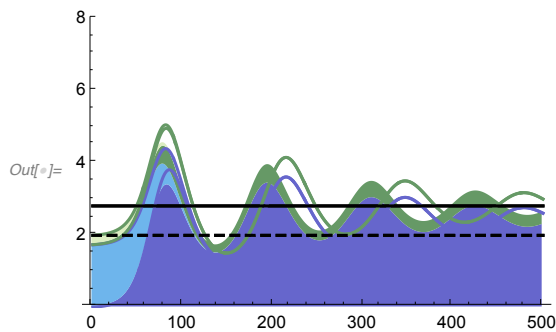
```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})}$ ,
    {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert} \right)}$ ,
    {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Seroconversion affects the dynamics (curves compared to the previous shaded plot) but not the initial speed of spread of the variant (described by the selection coefficient) or the equilibrium.

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```

Figure S1B: strongly immune evasive (transient) but less transmissible (n=5)
 → leads to a decline in cases due to the spread of the variant, but eventually the
 previous variant takes over because of its transmission advantage
 Can infect last three classes (m=3)

```

In[ ]:= maxtime = 500;
maxy = 8;
Parameters:

```

```

In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
TRYf = 99 / 100; (*Starting fraction of resident*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
i →  $\frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)}$ 

```

```

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

```

```

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

```

```

In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
TRYβ =  $\frac{\text{TRY}\delta \text{TRY}\kappa}{\text{TRY}\delta - \text{TRYinf} \text{TRY}\delta - \text{TRYconvert} \text{TRYinf} \text{TRY}\kappa}$ ;

```

```

 $\frac{\text{TRY}\beta}{\text{TRY}\kappa} // N$ 

```

```

Out[ ]:= 2.08333

```

Now we allow stronger immune evasiveness, coupled with lower transmission. Specifically, we assume five waning classes and the variant infects three earlier resistant classes (m=3):

```

In[ ]:= TRYn = 5;
TRYm = 3;

```

Variant has a lower transmissibility (set to have the same selection coefficient as for the immune evasive variant):

```

In[ ]:= Flatten[ Solve[  $\frac{\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \frac{\text{TRY}m}{\text{TRY}n} \left( \frac{\text{TRY}\kappa \text{TRYconvert} (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right) \beta V == 0.0833, \beta V ] ]$ 

```

```

Out[ ]:= {  $\beta V \rightarrow 0.363205$  }

```

```

In[ ]:= TRYβV = βV / . %;

```

```

In[ ]:= TRYβ // N

```

```

Out[ ]:= 0.416667

```

Starting equilibrium would be (r0 includes all of the n resistance classes):

```

{ s →  $\frac{\kappa}{\beta}$ , i →  $\frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)}$  }

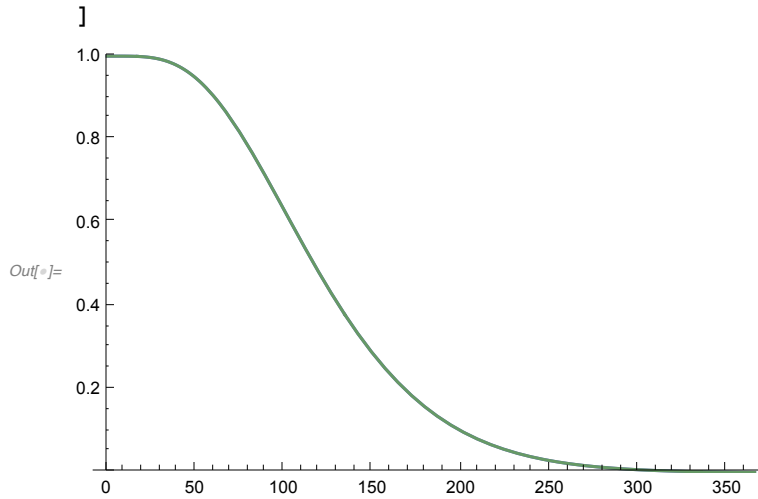
```

$$\text{In}[] := \text{start} = \left\{ s_0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i_0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, \right. \\ \left. r_0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right\}$$

$$\text{Out}[] := \left\{ s_0 \rightarrow \frac{12}{25}, i_0 \rightarrow \frac{1}{50}, r_0 \rightarrow \frac{1}{2} \right\}$$

Waning distribution for a population of younger and older individuals:

```
In[ ] := Show[
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ TRYn)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.4, 0.8]],
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ0 TRYn)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```



Now the susceptible and resistant classes depend only on age (not whether they carried a variant before):

[NOTE: For the ease of colouring, the first stage class is the variant.]

```
In[ ] := {ages = 2, stages = 2, exposures = 2, n = TRYn};
```

```
In[ ] := Clear[solution]
solution[{p_, f_, older_, β_, βV_, δY_, δ0_, κ_, q_}, start] :=
  solution[{p, f, older, β, βV, δY, δ0, κ, q}, start] =
    Block[{ages = 2, stages = 2, exposures = 2, n = TRYn},
      dsdt[j_, zz_, t_] = (1 - q) * Sum[κ[j, jj] * i[j, jj, zz, t], {jj, 1, stages}] +
        n * δ[j] * r[n, j, zz, t] - Sum[β[k, kk] * i[k, kk, kkk, t],
          {k, 1, ages}, {kk, 1, stages}, {kkk, 1, exposures}] * s[j, zz, t];
      (*For the susceptible and recovered classes,
        we introduce zz to measure whether individuals have ever
        been exposed to the new variant (zz=1) or not (zz=2),
        this allows us to model transient immunity. We assume that those who

```

```

do not seroconvert, with probability 1-c, remain in their zz class.*)
didt[j_, 1, 1, t_] = Sum[ $\beta[k, 1] * i[k, 1, kkk, t]$ , {k, 1, ages}, {kkk, 1, exposures}] *
  Sum[r[nn, j, 2, t], {nn, n+1-TRYm, n}] + Sum[ $\beta[k, 1] * i[k, 1, kkk, t]$ ,
    {k, 1, ages}, {kkk, 1, exposures}] * s[j, 1, t] -  $\kappa[j, 1] * i[j, 1, 1, t]$ ;
(*This is the variant [stage 1], but it can only infect the
  recovering individuals who have never been exposed to a variant
  infection [stage 2]. Once infected by the variant these will move into the
  first type of recovering individual [zz=1] and are no longer available*)
didt[j_, 1, 2, t_] = Sum[ $\beta[k, 1] * i[k, 1, kkk, t]$ , {k, 1, ages}, {kkk, 1, exposures}] *
  s[j, 2, t] -  $\kappa[j, 1] * i[j, 1, 2, t]$ ;
(*Although no infection with the variant lacks exposure to the variant,
  we allow this in case some fail to seroconvert, with probability 1-c.*)
didt[j_, 2, zz_, t_] = Sum[ $\beta[k, 2] * i[k, 2, kkk, t]$ , {k, 1, ages},
  {kkk, 1, exposures}] * s[j, zz, t] -  $\kappa[j, 2] * i[j, 2, zz, t]$ ;
drdt[1, j_, 1, t_] = q * ( $\kappa[j, 1] * i[j, 1, 1, t]$  +  $\kappa[j, 1] * i[j, 1, 2, t]$  +
   $\kappa[j, 2] * i[j, 2, 1, t]$ ) - n *  $\delta[j] * r[1, j, 1, t]$ ;
(*All infections with the variant move into this first resistance class only,
  as do those exposed in prior infections (i[j,2,1,t]).*)
drdt[1, j_, 2, t_] = q * ( $\kappa[j, 2] * i[j, 2, 2, t]$ ) - n *  $\delta[j] * r[1, j, 2, t]$ ;
For[nn = 2, nn ≤ n - TRYm, nn++,
  drdt[nn, j_, zz_, t_] = n *  $\delta[j] * r[nn-1, j, zz, t]$  - n *  $\delta[j] * r[nn, j, zz, t]$ ;
];
For[nn = n+1-TRYm, nn ≤ n, nn++,
  drdt[nn, j_, 1, t_] = n *  $\delta[j] * r[nn-1, j, 1, t]$  - n *  $\delta[j] * r[nn, j, 1, t]$ ;
  drdt[nn, j_, 2, t_] = n *  $\delta[j] * r[nn-1, j, 2, t]$  - Sum[ $\beta[k, 1] * i[k, 1, kkk, t]$ ,
    {k, 1, ages}, {kkk, 1, exposures}] * r[nn, j, 2, t] - n *  $\delta[j] * r[nn, j, 2, t]$ ;
  (*Only those that have not been infected before by the new variant [stage 2]
    can become infected earlier by the new variant [stage 1]*)];
pars = { $\beta[j_, 1] \rightarrow \beta V$ ,  $\beta[j_, 2] \rightarrow \beta$ ,  $\delta[1] \rightarrow \delta Y$ ,  $\delta[2] \rightarrow \delta O$ ,  $\kappa[j_, jj_] \rightarrow \kappa$ };
frac[1, 1] = (1 - older) (1 - f);
frac[2, 1] = older (1 - f);
frac[1, 2] = (1 - older) f;
frac[2, 2] = older f;
nvars = Drop[Flatten[Table[{Table[s[j, zz, t], {zz, 1, exposures}],
  Table[i[j, jj, zz, t], {jj, 1, stages}, {zz, 1, exposures}],
  Table[r[nn, j, zz, t], {nn, 1, n}, {zz, 1, exposures}]}], {j, 1, ages}]], -1];
r[n, ages, exposures, t_] = 1 - Total[nvars];
neqns = Drop[
  Flatten[Table[{Table[D[s[j, zz, t], t] == dsdt[j, zz, t], {zz, 1, exposures}],
    Table[D[i[j, jj, zz, t], t] == didt[j, jj, zz, t], {jj, 1, stages},
      {zz, 1, exposures}], Table[D[r[nn, j, zz, t], t] == drdt[nn, j, zz, t],
        {nn, 1, n}, {zz, 1, exposures}]}], {j, 1, ages}]], -1];
nstart = Drop[Flatten[Table[{

```

```

Table[i[j, jj, 1, 0] == 0, {jj, 1, stages}],
Table[i[j, jj, 2, 0] == frac[j, jj] i0, {jj, 1, stages}],
s[j, 1, 0] == 0, (*Nobody starts exposed to the variant*)
s[j, 2, 0] == (frac[j, 1] + frac[j, 2]) * s0,
Table[r[nn, j, 1, 0] == 0, {nn, 1, n}],
Table[r[nn, j, 2, 0] == (frac[j, 1] + frac[j, 2])  $\frac{r0}{n}$ , {nn, 1, n}],
{j, 1, ages}]] /. start, -1];

(*All susceptible and resistant individuals initially
susceptible to the new variant [in stage 2] *)
NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};

In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
Out[ ]:= {, , , }

In[ ]:= coltab = Join[{{1 -> {0, colours[[1]]}}},
  Table[{i -> {{i - 1}, colours[[i]]}}, {i, 2, Length[all]}]];
Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
Out[ ]:=//MatrixForm=

$$\begin{pmatrix} <70,Res & \text{blue} \\ <70,Mutant & \text{light blue} \\ 70+,Res & \text{green} \\ 70+,Mutant & \text{light green} \end{pmatrix}$$


In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};

In[ ]:= solution[partemp, start];

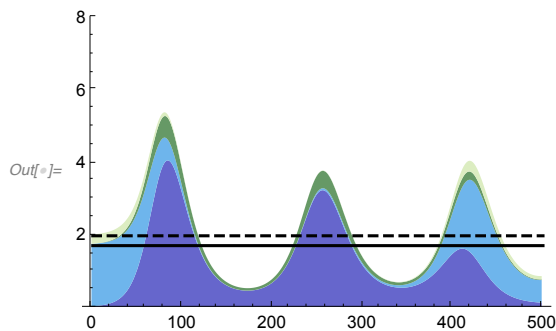
Showing the % of the population infectious:

```

```

In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[
    Sum[100 i[all[[c, 1]], all[[c, 2]], 1, t] + 100 i[all[[c, 1]], all[[c, 2]], 2, t] /.
      solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
    {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
    PlotStyle -> None, Filling -> {{1 -> {0, Blue}}, {2 -> {1, Blue}},
      {3 -> {2, Green}}, {4 -> {3, Green}}}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
    PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n-0} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n-0} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
    {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Mutant fraction change between t=0 and t=50:

```

In[ ]:= 
$$\frac{\text{Sum}[i[j, 1, zz, t], \{j, 1, \text{ages}\}, \{zz, 1, \text{exposures}\}]}{\text{Sum}[i[j, jj, zz, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}, \{zz, 1, \text{exposures}\}]} /. \text{solution}[\text{partemp}, \text{start}] /. t \rightarrow 50$$

Out[ ]:= {0.38282}

```

```

In[ ]:= Solve[Exp[s 50] ==  $\left( \frac{p50 / (1 - p50)}{p0 / (1 - p0)} \right) /. p50 \rightarrow \% /. p0 \rightarrow 1 - \text{TRY}f$ ], s][[1]]

```

Solve: Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```

Out[ ]:= {s -> 0.0823505}

```

This is consistent with the predicted selection coefficient:

$$\text{In}[*]:= \frac{\text{TRY}\beta\text{V} - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \frac{\text{TRY}m}{\text{TRY}n} \left(\frac{\text{TRY}\kappa \text{TRYconvert} (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right) \text{TRY}\beta\text{V} // \text{N}$$

Out[*]= 0.0833

New equilibrium (if resident fixed):

$$\text{In}[*]:= \left(\frac{(\text{TRY}\delta + \Delta\delta) (\text{TRY}\beta\text{V} - \text{TRY}\kappa)}{\text{TRY}\beta\text{V} ((\text{TRY}\delta + \Delta\delta) + \text{TRY}\kappa \text{TRYconvert})} \right) /. \Delta\delta \rightarrow \frac{0}{\text{TRY}n - 0} \text{TRY}\delta // \text{N}$$

Out[*]= 0.0172826

% rise in the endemic equilibrium:

$$\text{In}[*]:= 100 * \frac{(\% - \text{TRY}inf)}{\text{TRY}inf}$$

Out[*]= -13.5871

The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

$$\text{In}[*]:= \text{partemp} = \left\{ \text{TRY}p, \text{TRY}f, \text{TRY}older, \text{TRY}\beta, \text{TRY}\beta\text{V}, \frac{8}{10} \text{TRY}\delta, \frac{8}{10} \text{TRY}\delta 0, \text{TRY}\kappa, \frac{8}{10} \right\};$$

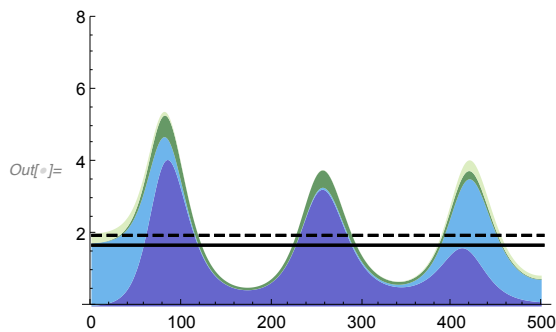
in[*]:= `solution[partemp, start];`

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n-\theta} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n-\theta} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Seroconversion affects the dynamics (curves compared to the previous shaded plot) but not the initial speed of spread of the variant (described by the selection coefficient) or the equilibrium.

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```

Figure S2A: more transmissible (n=1)

→ Less oscillatory

```

In[ ]:= maxtime = 500;
maxy = 8;

```

Parameters:

```

In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
TRYf = 99 / 100; (*Starting fraction of resident*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)

```

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

```

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

```

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

```

In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
TRYβ =  $\frac{\text{TRY}\delta \text{TRY}\kappa}{\text{TRY}\delta - \text{TRYinf} \text{TRY}\delta - \text{TRYconvert} \text{TRYinf} \text{TRY}\kappa}$ ;

```

$$\frac{\text{TRY}\beta}{\text{TRY}\kappa} // N$$

```

Out[ ]:= 2.08333

```

Variant has a higher transmissibility (set to have the same selection coefficient as for the immune evasive variant):

```

In[ ]:= Flatten[Solve[ $\frac{\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa == 0.0833, \beta V]$ ]

```

```

Out[ ]:= {βV → 0.590208}

```

```

In[ ]:= TRYβV = βV / . %;

```

% increase in β:

```

In[ ]:= 100 *  $\frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta}$ 

```

```

Out[ ]:= 41.65

```

and now has no immune evasive properties. Specifically, we assume five waning classes and the variant infects only susceptibles (m=0):

```

In[ ]:= TRYn = 1;
TRYm = 0;

```

Starting equilibrium would be (r0 includes all of the n resistance classes):

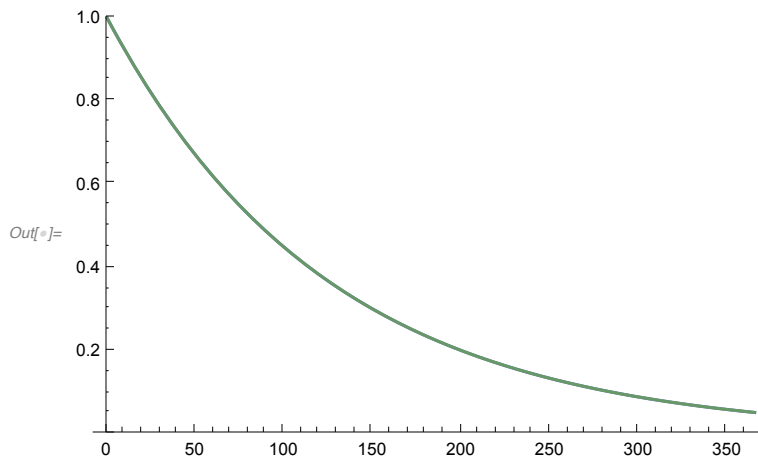
$$\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)} \right\}$$

$$\text{In}[*]:= \text{start} = \left\{ s_0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i_0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, \right. \\ \left. r_0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right\}$$

$$\text{Out}[*]:= \left\{ s_0 \rightarrow \frac{12}{25}, i_0 \rightarrow \frac{1}{50}, r_0 \rightarrow \frac{1}{2} \right\}$$

Waning distribution for a population of younger and older individuals:

```
In[*]:= Show[
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ TRYn)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.4, 0.8]],
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ0 TRYn)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```



Now the susceptible and resistant classes depend only on age (not whether they carried a variant before):

[NOTE: For the ease of colouring, the first stage class is the variant.]

```
In[*]:= {ages = 2, stages = 2, n = TRYn};
```

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta O$ _,  $\kappa$ _, q_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta O$ ,  $\kappa$ , q}, start] =
    Block[{ages = 2, stages = 2, n = TRYn},
      dsdt[j_, t_] =
        (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] + n *  $\delta$ [j] * r[n, j, t] -
        Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] *
        Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
        Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 1] * i[j, 1, t];
      didt[j_, 2, t_] = Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] -
         $\kappa$ [j, 2] * i[j, 2, t];
      drdt[1, j_, t_] = q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] - n *  $\delta$ [j] * r[1, j, t];
      For[nn = 2, nn ≤ n - TRYm, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      For[nn = n + 1 - TRYm, nn ≤ n, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] -
          Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      pars = { $\beta$ [j_, 1] →  $\beta V$ ,  $\beta$ [j_, 2] →  $\beta$ ,  $\delta$ [1] →  $\delta Y$ ,  $\delta$ [2] →  $\delta O$ ,  $\kappa$ [j_, jj_] →  $\kappa$ };
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[{s[j, t], Table[i[j, jj, t], {jj, 1, stages}],
        Table[r[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      r[n, ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[Table[{D[s[j, t], t] == dsdt[j, t],
        Table[D[i[j, jj, t], t] == didt[j, jj, t], {jj, 1, stages}],
        Table[D[r[nn, j, t], t] == drdt[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0, Table[r[nn, j, 0] ==
          (frac[j, 1] + frac[j, 2])  $\frac{r0}{n}$ , {nn, 1, n}]}], {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};

```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

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

```
In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1, colours[[i]]}}, {i, 2, Length[all]}]];
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

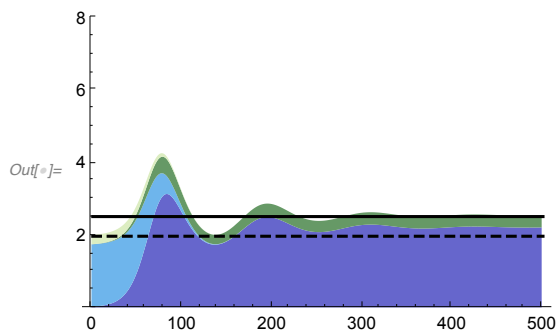
```
( <70,Res <70,Mutant
  70+,Res 70+,Mutant )
```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};
```

```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```
In[ ]:= plot1 = Show[
  Plot[
    Evaluate@Table[Sum[100 i[all[[c, 1]], all[[c, 2]], t] /. solution[partemp, start],
      {c, 1, jcum}], {jcum, 1, Length[all]}],
    {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
    PlotStyle -> None, Filling -> {{1 -> {0, }}, {2 -> {{1, }},
      {3 -> {{2, }}, {4 -> {{3, }}}}},
    Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
      PlotStyle -> {Black, Dashed}],
    Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
      {t, 0, maxtime}, PlotStyle -> {Black}],
    ImageSize -> 250
]
```



Mutant fraction change between t=0 and t=50:

$$\text{In}[] := \frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]} /. \text{solution}[\text{partemp}, \text{start}] /. t \rightarrow 50$$

$$\text{Out}[] := \{0.381045\}$$

$$\text{In}[] := \text{Solve}\left[\text{Exp}[s 50] == \left(\frac{p50 / (1 - p50)}{p0 / (1 - p0)}\right) /. p50 \rightarrow \% /. p0 \rightarrow 1 - \text{TRYf}\right], s][[1]]$$

 **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

$$\text{Out}[] := \{s \rightarrow 0.0822001\}$$

This is consistent with the predicted selection coefficient:

$$\text{In}[] := \frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \frac{\text{TRY}m}{\text{TRY}n} \left(\frac{\text{TRY}\kappa \text{TRYconvert} (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right) \text{TRY}\beta V // N$$

$$\text{Out}[] := 0.0833$$

New equilibrium:

$$\text{In}[] := \left(\frac{(\text{TRY}\delta + \Delta\delta) (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V ((\text{TRY}\delta + \Delta\delta) + \text{TRY}\kappa \text{TRYconvert})} \right) /. \Delta\delta \rightarrow \frac{\text{TRY}m}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta // N$$

$$\text{Out}[] := 0.0254283$$

% rise in the endemic equilibrium:

$$\text{In}[] := 100 * \frac{(\% - \text{TRYinf})}{\text{TRYinf}}$$

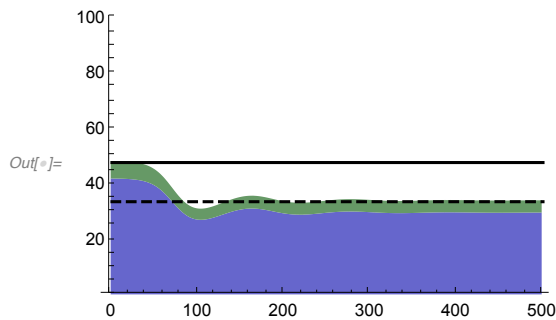
$$\text{Out}[] := 27.1417$$

This considers the number of susceptibles, with the black line at $1/\tilde{R}_0$ (the fraction of susceptibles that causes the disease to stop growing before the variant) and the dashed black line at $1/\tilde{R}_0^*$ (the fraction of susceptibles that causes the disease to stop growing once the variant predominates):

```

In[ ]:= Show[
  Plot[Evaluate@
    Table[Sum[100 s[c, t] /. solution[partemp, start], {c, 1, jcum}], {jcum, 1, 2}],
    {t, 0, maxtime}, PlotRange -> {Automatic, {0, 100}},
    PlotStyle -> None, Filling -> {{1 -> {0, #}}, {2 -> {{1}, #}}}],
  Plot[100  $\frac{\text{TRY}\kappa}{\text{TRY}\beta}$ , {t, 0, maxtime}, PlotStyle -> {Black}],
  Plot[100  $\frac{\text{TRY}\kappa}{\text{TRY}\beta V}$ , {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  ImageSize -> 250
]

```



The first time that the number of susceptibles falls below $\frac{\text{TRY}\kappa}{\text{TRY}\beta V}$ is when we expect the number of the new variant to start declining (roughly, given that waning changes the dynamics):

$$\text{In[]:= } \left(1 + \frac{(\text{TRY}\beta V - \text{TRY}\beta)}{\text{TRY}\beta} \right)$$

Out[]:= 1.4165

```

In[ ]:= droptime = First[
  Select[Table[Flatten[{t, Sum[100 s[c, t] /. solution[partemp, start], {c, 1, 2}]}],
    {t, 0, maxtime}], #[[2]] < 100  $\frac{\text{TRY}\kappa}{\text{TRY}\beta V}$  &]]

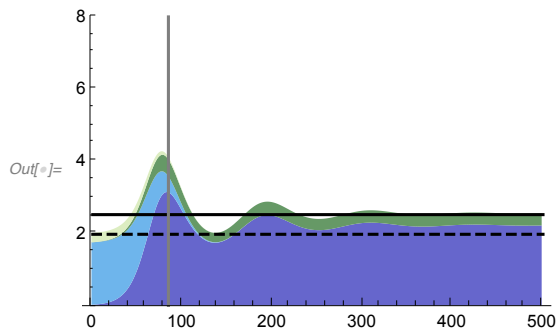
```

Out[]:= {84, 33.7945}

```

In[ ]:= Show[
  plot1,
  ListPlot[{{droptime[[1]], 0}, {droptime[[1]], maxy}},
    Joined → True, PlotStyle → {Gray}],
  ImageSize → 250
]

```



The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

```

In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV,  $\frac{8}{10}$  TRYδ,  $\frac{8}{10}$  TRYδ0, TRYκ,  $\frac{8}{10}$ };

```

```

In[ ]:= solution[partemp, start];

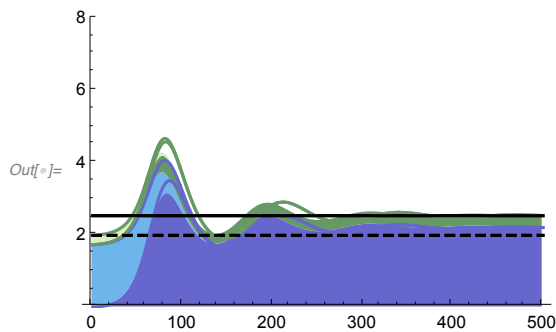
```

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n-\theta} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n-\theta} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Seroconversion affects the dynamics (curves compared to the previous shaded plot) but not the initial speed of spread of the variant (described by the selection coefficient) or the equilibrium.

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```

Figure S2C: more transmissible (n=10)

→ More oscillatory

```

In[ ]:= maxtime = 500;
maxy = 8;

```

Parameters:

```

In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
TRYf = 99 / 100; (*Starting fraction of resident*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)

```

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

```

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

```

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

```

In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
TRYβ =  $\frac{\text{TRY}\delta \text{ TRY}\kappa}{\text{TRY}\delta - \text{TRYinf } \text{TRY}\delta - \text{TRYconvert } \text{TRYinf } \text{TRY}\kappa}$ ;

```

$$\frac{\text{TRY}\beta}{\text{TRY}\kappa} // N$$

```

Out[ ]:= 2.08333

```

Variant has a higher transmissibility (set to have the same selection coefficient as for the immune evasive variant):

```

In[ ]:= Flatten[Solve[ $\frac{\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa == 0.0833, \beta V]$ ]

```

```

Out[ ]:= {βV → 0.590208}

```

```

In[ ]:= TRYβV = βV / . %;

```

% increase in β:

```

In[ ]:= 100 *  $\frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta}$ 

```

```

Out[ ]:= 41.65

```

and now has no immune evasive properties. Specifically, we assume five waning classes and the variant infects only susceptibles (m=0):

```

In[ ]:= TRYn = 10;
TRYm = 0;

```

Starting equilibrium would be (r0 includes all of the n resistance classes):

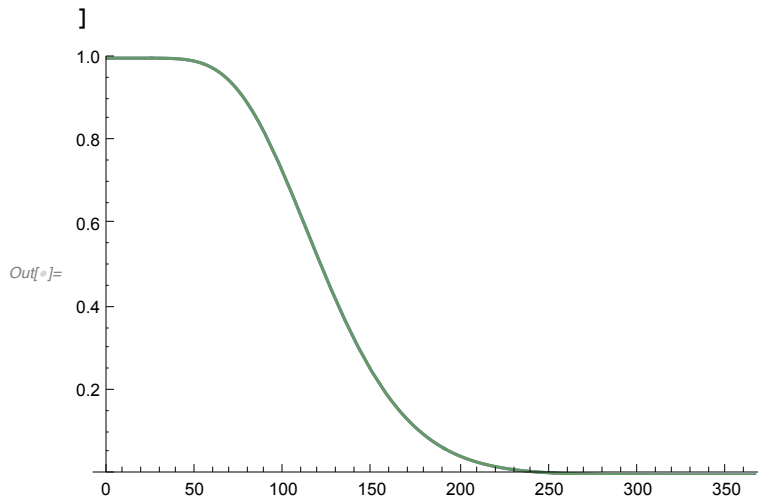
$$\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)} \right\}$$

$$In[] := \text{start} = \left\{ s0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, \right. \\ \left. r0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right\}$$

$$Out[] := \left\{ s0 \rightarrow \frac{12}{25}, i0 \rightarrow \frac{1}{50}, r0 \rightarrow \frac{1}{2} \right\}$$

Waning distribution for a population of younger and older individuals:

```
In[ ] := Show[
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ TRYn)]], t),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.4, 0.8]],
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ0 TRYn)]], t),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```



Now the susceptible and resistant classes depend only on age (not whether they carried a variant before):

[NOTE: For the ease of colouring, the first stage class is the variant.]

```
In[ ] := {ages = 2, stages = 2, n = TRYn};
```

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta O$ _,  $\kappa$ _, q_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta O$ ,  $\kappa$ , q}, start] =
    Block[{ages = 2, stages = 2, n = TRYn},
      dsdt[j_, t_] =
        (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] + n *  $\delta$ [j] * r[n, j, t] -
        Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] *
        Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
        Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 1] * i[j, 1, t];
      didt[j_, 2, t_] = Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] -
         $\kappa$ [j, 2] * i[j, 2, t];
      drdt[1, j_, t_] = q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] - n *  $\delta$ [j] * r[1, j, t];
      For[nn = 2, nn ≤ n - TRYm, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      For[nn = n + 1 - TRYm, nn ≤ n, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] -
          Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      pars = { $\beta$ [j_, 1] →  $\beta V$ ,  $\beta$ [j_, 2] →  $\beta$ ,  $\delta$ [1] →  $\delta Y$ ,  $\delta$ [2] →  $\delta O$ ,  $\kappa$ [j_, jj_] →  $\kappa$ };
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[{s[j, t], Table[i[j, jj, t], {jj, 1, stages}],
        Table[r[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      r[n, ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[Table[{D[s[j, t], t] == dsdt[j, t],
        Table[D[i[j, jj, t], t] == didt[j, jj, t], {jj, 1, stages}],
        Table[D[r[nn, j, t], t] == drdt[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0, Table[r[nn, j, 0] ==
          (frac[j, 1] + frac[j, 2])  $\frac{r0}{n}$ , {nn, 1, n}]}], {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};

```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

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

```
In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1, colours[[i]]}}, {i, 2, Length[all]}]];
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

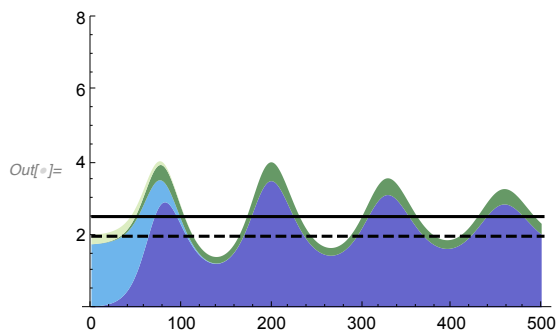
```
( <70,Res <70,Mutant
  70+,Res 70+,Mutant )
```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};
```

```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```
In[ ]:= plot1 = Show[
  Plot[
    Evaluate@Table[Sum[100 i[all[[c, 1]], all[[c, 2]], t] /. solution[partemp, start],
      {c, 1, jcum}], {jcum, 1, Length[all]}],
    {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
    PlotStyle -> None, Filling -> {{1 -> {0, }}, {2 -> {{1, }},
      {3 -> {{2, }}, {4 -> {{3, }}}}},
    Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
      PlotStyle -> {Black, Dashed}],
    Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
      {t, 0, maxtime}, PlotStyle -> {Black}],
    ImageSize -> 250
]
```



Mutant fraction change between t=0 and t=50:

$$\text{In[]:= } \frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]} /. \text{solution}[\text{partemp}, \text{start}] /. t \rightarrow 50$$

$$\text{Out[]:= } \{0.380508\}$$

$$\text{In[]:= } \text{Solve}\left[\text{Exp}[s 50] == \left(\frac{p50 / (1 - p50)}{p0 / (1 - p0)}\right) /. p50 \rightarrow \% /. p0 \rightarrow 1 - \text{TRYf}\right], s][[1]]$$

 **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

$$\text{Out[]:= } \{s \rightarrow 0.0821546\}$$

This is consistent with the predicted selection coefficient:

$$\text{In[]:= } \frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \frac{\text{TRY}m}{\text{TRY}n} \left(\frac{\text{TRY}\kappa \text{TRYconvert} (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right) \text{TRY}\beta V // N$$

$$\text{Out[]:= } 0.0833$$

New equilibrium:

$$\text{In[]:= } \left(\frac{(\text{TRY}\delta + \Delta\delta) (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V ((\text{TRY}\delta + \Delta\delta) + \text{TRY}\kappa \text{TRYconvert})} \right) /. \Delta\delta \rightarrow \frac{\text{TRY}m}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta // N$$

$$\text{Out[]:= } 0.0254283$$

% rise in the endemic equilibrium:

$$\text{In[]:= } 100 * \frac{(\% - \text{TRYinf})}{\text{TRYinf}}$$

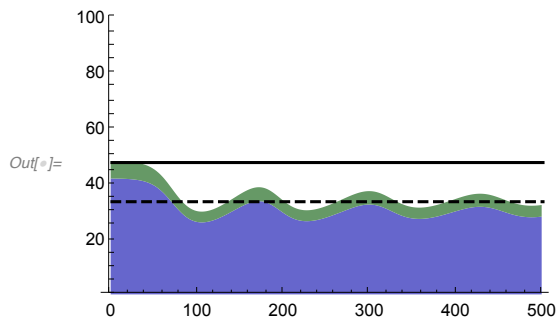
$$\text{Out[]:= } 27.1417$$

This considers the number of susceptibles, with the black line at $1/\tilde{R}_0$ (the fraction of susceptibles that causes the disease to stop growing before the variant) and the dashed black line at $1/\tilde{R}_0^*$ (the fraction of susceptibles that causes the disease to stop growing once the variant predominates):

```

In[ ]:= Show[
  Plot[Evaluate@
    Table[Sum[100 s[c, t] /. solution[partemp, start], {c, 1, jcum}], {jcum, 1, 2}],
    {t, 0, maxtime}, PlotRange -> {Automatic, {0, 100}},
    PlotStyle -> None, Filling -> {{1 -> {0, Blue}}, {2 -> {{1}, Green}}}],
  Plot[100  $\frac{TRY\kappa}{TRY\beta}$ , {t, 0, maxtime}, PlotStyle -> {Black}],
  Plot[100  $\frac{TRY\kappa}{TRY\beta V}$ , {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  ImageSize -> 250
]

```



The first time that the number of susceptibles falls below $\frac{TRY\kappa}{TRY\beta V}$ is when we expect the number of the new variant to start declining (roughly, given that waning changes the dynamics):

$$In[]:= \left(1 + \frac{(TRY\beta V - TRY\beta)}{TRY\beta} \right)$$

Out[]:= 1.4165

```

In[ ]:= droptime = First[
  Select[Table[Flatten[{t, Sum[100 s[c, t] /. solution[partemp, start], {c, 1, 2}]}],
    {t, 0, maxtime}], #[[2]] < 100  $\frac{TRY\kappa}{TRY\beta V}$  &]]

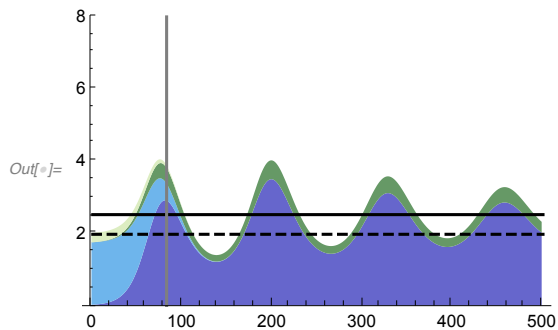
```

Out[]:= {82, 33.8}

```

In[ ]:= Show[
  plot1,
  ListPlot[{{droptime[[1]], 0}, {droptime[[1]], maxy}},
    Joined → True, PlotStyle → {Gray}],
  ImageSize → 250
]

```



The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

```

In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV,  $\frac{8}{10}$  TRYδ,  $\frac{8}{10}$  TRYδ0, TRYκ,  $\frac{8}{10}$ };

```

```

In[ ]:= solution[partemp, start];

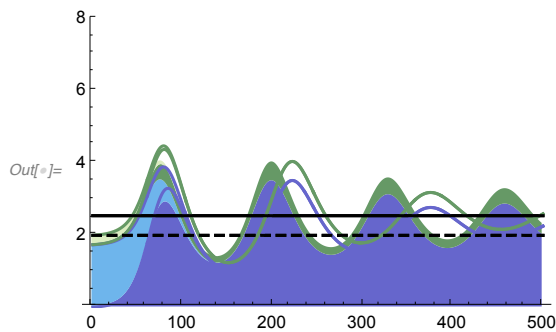
```

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
    {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n-\theta} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n-\theta} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
    {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Seroconversion affects the dynamics (curves compared to the previous shaded plot) but not the initial speed of spread of the variant (described by the selection coefficient) or the equilibrium.

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```

Alt Figure 2B: persistently immune evasive (n=10) (increases mean waning rate by 67%)

Can infect last four classes (m=4)

→ More oscillatory

```

In[ ]:= maxtime = 500;

```

```

maxy = 8;

```

Parameters:

```

In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
TRYf = 99 / 100; (*Starting fraction of resident*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)

```

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

```

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

```

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

```

In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)

```

$$\text{TRY}\beta = \frac{\text{TRY}\delta \text{TRY}\kappa}{\text{TRY}\delta - \text{TRYinf } \text{TRY}\delta - \text{TRYconvert } \text{TRYinf } \text{TRY}\kappa};$$

$$\frac{\text{TRY}\beta}{\text{TRY}\kappa} // N$$

```

Out[ ]:= 2.08333

```

Variant has the same transmissibility:

```

In[ ]:= TRYβV = TRYβ;

```

but infects earlier during waning. Specifically, we assume five waning classes and the variant infects two earlier.

```

In[ ]:= TRYn = 10;
TRYm = 4;

```

Thus, the mean waning rate (once fixed) increases by 67%:

$$\text{In[]} := \frac{\text{TRY}\delta + \Delta\delta}{\text{TRY}\delta} / \Delta\delta \rightarrow \frac{\text{TRYm}}{\text{TRYn} - \text{TRYm}} \text{TRY}\delta // N$$

```

Out[ ]:= 1.66667

```

while the mean waiting time decreases by 40%:

```

In[ ]:= 1 / %

```

```

Out[ ]:= 0.6

```

Starting equilibrium would be (r0 includes all of the n resistance classes):

$$\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)} \right\}$$

$$\text{In}[*]:= \text{start} = \left\{ s_0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i_0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, \right. \\ \left. r_0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right\}$$

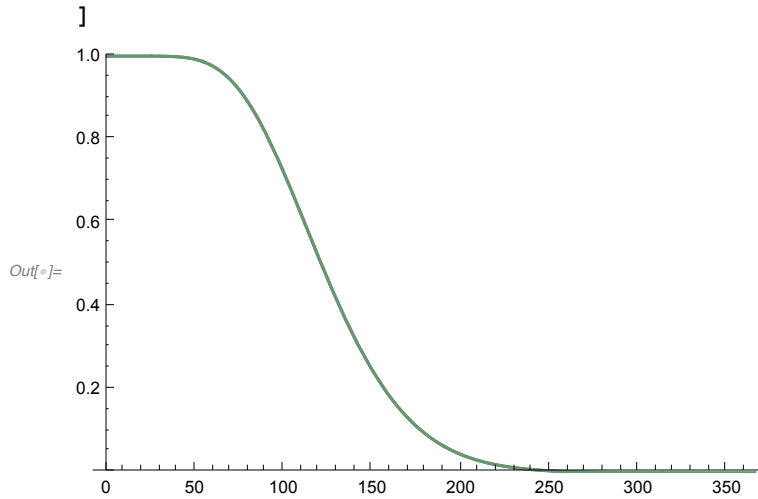
$$\text{Out}[*]:= \left\{ s_0 \rightarrow \frac{12}{25}, i_0 \rightarrow \frac{1}{50}, r_0 \rightarrow \frac{1}{2} \right\}$$

Waning distribution for a population of younger and older individuals:

```

In[*]:= Show[
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ TRYn)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.4, 0.8]],
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRYδ0 TRYn)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]

```



Now the susceptible and resistant classes depend only on age (not whether they carried a variant before):

[NOTE: For the ease of colouring, the first stage class is the variant.]

```

In[*]:= {ages = 2, stages = 2, n = TRYn};

```

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta O$ _,  $\kappa$ _, q_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta O$ ,  $\kappa$ , q}, start] =
    Block[{ages = 2, stages = 2, n = TRYn},
      dsdt[j_, t_] =
        (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] + n *  $\delta$ [j] * r[n, j, t] -
        Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] *
        Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
        Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 1] * i[j, 1, t];
      didt[j_, 2, t_] = Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] -
         $\kappa$ [j, 2] * i[j, 2, t];
      drdt[1, j_, t_] = q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] - n *  $\delta$ [j] * r[1, j, t];
      For[nn = 2, nn ≤ n - TRYm, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      For[nn = n + 1 - TRYm, nn ≤ n, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] -
          Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      pars = { $\beta$ [j_, 1] →  $\beta V$ ,  $\beta$ [j_, 2] →  $\beta$ ,  $\delta$ [1] →  $\delta Y$ ,  $\delta$ [2] →  $\delta O$ ,  $\kappa$ [j_, jj_] →  $\kappa$ };
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[{s[j, t], Table[i[j, jj, t], {jj, 1, stages}],
        Table[r[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      r[n, ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[Table[{D[s[j, t], t] == dsdt[j, t],
        Table[D[i[j, jj, t], t] == didt[j, jj, t], {jj, 1, stages}],
        Table[D[r[nn, j, t], t] == drdt[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0, Table[r[nn, j, 0] ==
          (frac[j, 1] + frac[j, 2])  $\frac{r0}{n}$ , {nn, 1, n}]}], {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};

```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

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

```
In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1, colours[[i]]}}, {i, 2, Length[all]}]];
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

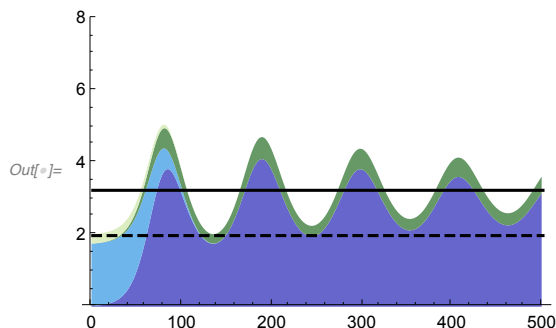
```
( <70,Res <70,Mutant
  70+,Res 70+,Mutant )
```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};
```

```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```
In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[ Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> None, Filling -> {{1 -> {0, }}, {2 -> {{1, }},
    {3 -> {{2, }}, {4 -> {{3, }}}}},
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
  PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]
```



Mutant fraction change between t=0 and t=50:

$$\text{In[]:= } \frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]} /. \text{solution}[\text{partemp}, \text{start}] /. t \rightarrow 50$$

$$\text{Out[]:= } \{0.383891\}$$

$$\text{In[]:= } \text{Solve}\left[\text{Exp}[s \, 50] == \left(\frac{p50 / (1 - p50)}{p0 / (1 - p0)} /. p50 \rightarrow \% /. p0 \rightarrow 1 - \text{TRYf}\right), s\right][[1]]$$

 **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

$$\text{Out[]:= } \{s \rightarrow 0.0824411\}$$

This is consistent with the predicted selection coefficient:

$$\text{In[]:= } \frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \frac{\text{TRY}m}{\text{TRY}n} \left(\frac{\text{TRY}\kappa \text{TRYconvert} (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right) \text{TRY}\beta V // N$$

$$\text{Out[]:= } 0.0833333$$

New equilibrium:

$$\text{In[]:= } \left(\frac{(\text{TRY}\delta + \Delta\delta) (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V (\text{TRY}\delta + \Delta\delta) + \text{TRY}\kappa \text{TRYconvert}} \right) /. \Delta\delta \rightarrow \frac{\text{TRY}m}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta // N$$

$$\text{Out[]:= } 0.0325$$

% rise in the endemic equilibrium:

$$\text{In[]:= } 100 * \frac{(\% - \text{TRYinf})}{\text{TRYinf}}$$

$$\text{Out[]:= } 62.5$$

The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

$$\text{In[]:= } \text{partemp} = \left\{ \text{TRY}p, \text{TRY}f, \text{TRY}older, \text{TRY}\beta, \text{TRY}\beta V, \frac{8}{10} \text{TRY}\delta, \frac{8}{10} \text{TRY}\delta 0, \text{TRY}\kappa, \frac{8}{10} \right\};$$

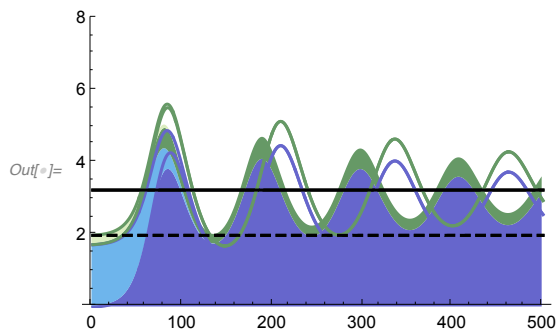
$$\text{In[]:= } \text{solution}[\text{partemp}, \text{start}];$$

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}n}{\text{TRY}n - \text{TRY}m} \text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert} \right)}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Seroconversion affects the dynamics (curves compared to the previous shaded plot) but not the initial speed of spread of the variant (described by the selection coefficient) or the equilibrium.

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```

Vaccines

Figure 6: Change in vaccinations

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/>).

Below we will explore the impact of each level of vaccination, as well as a policy limiting vaccination to older individuals.

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

```
In[ ]:= maxtime = 500;
      maxy = 3;
```

Parameters:

```
In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
      TRYf = 1; (*Starting fraction of resident*)
      TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
      (*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
      TRYκ = 1 / 5; (*Five day infectious period*)
      TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
      TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
      TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)

      i →  $\frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)}$ 
```

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

```
Out[ ]:=  $\left\{ \left\{ \beta \rightarrow - \frac{\delta \kappa}{-\delta + \text{inf } \delta + \text{inf } q \kappa} \right\} \right\}$ 
```

Incidence is expected to decline by:

```
In[ ]:=  $\frac{v}{\delta + \kappa}$  /. v → { TRYvLOW, TRYvHIGH} /. δ -> TRYδ /. κ -> TRYκ // N
```

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

```
In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
      TRYβ =  $\frac{\text{TRY} \delta \text{ TRY} \kappa}{\text{TRY} \delta - \text{TRYinf } \text{TRY} \delta - \text{TRYconvert } \text{TRYinf } \text{TRY} \kappa}$ ;
```

```
 $\frac{\text{TRY} \beta}{\text{TRY} \kappa}$  // N
```

```
Out[ ]:= 2.08333
```

We assume five waning classes and no variant (m=0):

```
In[ ]:= TRYn = 5;
      TRYm = 0;
```

```
In[ ]:= TRYβV = TRYβ;
```

Starting equilibrium would be (r0 includes all of the n resistance classes):

```
 $\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)} \right\}$ 
```

$$In[] := \text{start} = \left\{ s0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, \right. \\ \left. r0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right\}$$

$$Out[] := \left\{ s0 \rightarrow \frac{12}{25}, i0 \rightarrow \frac{1}{50}, r0 \rightarrow \frac{1}{2} \right\}$$

[NOTE: For the ease of colouring, the first stage class is the variant and the second the resident (here there are no variants).]

$$In[] := \{\text{ages} = 2, \text{stages} = 2, n = \text{TRY}n\};$$

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta O$ _,  $v Y$ _,  $v O$ _,  $\kappa$ _, q_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta O$ ,  $v Y$ ,  $v O$ ,  $\kappa$ , q}, start] =
    Block[{ages = 2, stages = 2, n = TRYn},
      dsdt[j_, t_] =
        (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] + n *  $\delta$ [j] * r[n, j, t] -
        Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t] - q * v[j];
      didt[j_, 1, t_] = Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] *
        Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
        Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 1] * i[j, 1, t];
      didt[j_, 2, t_] = Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] -
         $\kappa$ [j, 2] * i[j, 2, t];
      drdt[1, j_, t_] = q * v[j] + q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] -
        n *  $\delta$ [j] * r[1, j, t];
      For[nn = 2, nn ≤ n - TRYm, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      For[nn = n + 1 - TRYm, nn ≤ n, nn++,
        drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] -
          Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n *  $\delta$ [j] * r[nn, j, t];
      ];
      pars = { $\beta$ [j_, 1] →  $\beta V$ ,  $\beta$ [j_, 2] →  $\beta$ ,
         $\delta$ [1] →  $\delta Y$ ,  $\delta$ [2] →  $\delta O$ ,  $\kappa$ [j_, jj_] →  $\kappa$ , v[1] →  $v Y$ , v[2] →  $v O$ };
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[{s[j, t], Table[i[j, jj, t], {jj, 1, stages}],
        Table[r[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      r[n, ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[Table[{D[s[j, t], t] == dsdt[j, t],
        Table[D[i[j, jj, t], t] == didt[j, jj, t], {jj, 1, stages}],
        Table[D[r[nn, j, t], t] == drdt[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0, Table[r[nn, j, 0] ==
          (frac[j, 1] + frac[j, 2])  $\frac{r0}{n}$ , {nn, 1, n}]}], {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

```

```
In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
```

```
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}
```

```
In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};
```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],  
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

```
Out[ ]:= {■, ■, ■, ■}
```

```
In[ ]:= coltab = Join[{{1 → {0, colours[[1]]}}},  
  Table[{i -> {i - 1}, colours[[i]]}, {i, 2, Length[all]}];  
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

```
(  
  <70,Res    ■  
  <70,Mutant ■  
  70+,Res    ■  
  70+,Mutant ■  
)
```

No vaccinations:

```
In[ ]:= TRYvY = (1 - TRYolder) * 0; (*Fraction of susceptibles getting vaccinated per day*)  
  TRYv0 = TRYolder * 0;  
  (*Fraction of older susceptibles getting vaccinated per day*)
```

```
In[ ]:= partemp =  
  {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYvY, TRYv0, TRYκ, TRYconvert};
```

```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```

In[ ]:= Show[
  Plot[
    Evaluate@Table[ Sum[100 i[all[[c, 1]], all[[c, 2]], t] /. solution[partemp, start],
      {c, 1, jcum}], {jcum, 1, Length[all]}],
    {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
    PlotStyle -> None, Filling ->
      {{1 -> {0, #}}, {2 -> {{1}, #}}, {3 -> {{2}, #}}, {4 -> {{3}, #}}}],
    Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})}$ , {t, 0, maxtime},
      PlotStyle -> {Black, Dashed}],
    Plot[100  $\left( \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})} - \frac{\text{TRYvY} + \text{TRYvO}}{\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert}} \right)$ ,
      {t, 0, maxtime}, PlotStyle -> {Black}],
    ImageSize -> 250
  ]

```

The mean infection rate for <70 (top) and 70+ individuals (bottom) in the first versus last 10 time steps:

```

In[ ]:= { {Mean[
  Flatten[Table[  $\frac{i[1, 1, t] + i[1, 2, t]}{1 - \text{TRYolder}}$  /. solution[partemp, start], {t, 1, 10}]]],
  Mean[Flatten[Table[  $\frac{i[1, 1, t] + i[1, 2, t]}{1 - \text{TRYolder}}$  /. solution[partemp, start],
    {t, maxtime - 9, maxtime}]]]],
  {Mean[Flatten[Table[  $\frac{i[2, 1, t] + i[2, 2, t]}{\text{TRYolder}}$  /. solution[partemp, start],
    {t, 1, 10}]]],
  Mean[Flatten[Table[  $\frac{i[2, 1, t] + i[2, 2, t]}{\text{TRYolder}}$  /. solution[partemp, start],
    {t, maxtime - 9, maxtime}]]]]} // MatrixForm

```

Out[]:= MatrixForm=

$$\begin{pmatrix} 0.02 & 0.02 \\ 0.02 & 0.02 \end{pmatrix}$$

```

In[ ]:= TRYvY = (1 - TRYolder) TRYvLOW;
(*Fraction of younger susceptibles getting vaccinated per day*)
TRYvO = TRYolder TRYvLOW;
(*Fraction of older susceptibles getting vaccinated per day*)

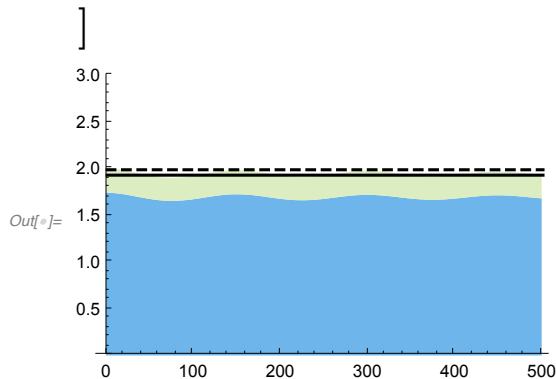
In[ ]:= partemp =
  {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYvY, TRYvO, TRYκ, TRYconvert};

In[ ]:= solution[partemp, start];

Showing the % of the population infectious:

In[ ]:= Show[
  Plot[
    Evaluate@Table[ Sum[100 i[all[[c, 1]], all[[c, 2]], t] /. solution[partemp, start],
      {c, 1, jcum}], {jcum, 1, Length[all]}],
    {t, 0, maxtime}, PlotRange → {Automatic, {0, maxy}},
    PlotStyle → None, Filling →
      {{1 → {0, Blue}}, {2 → {{1}, Blue}}, {3 → {{2}, Green}}, {4 → {{3}, LightGreen}}}],
    Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
      PlotStyle → {Black, Dashed}],
    Plot[100  $\left( \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} - \frac{\text{TRYvY} + \text{TRYvO}}{\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert}} \right)$ ,
      {t, 0, maxtime}, PlotStyle → {Black}],
    ImageSize → 250
  ]

```



The mean infection rate for <70 (top) and 70+ individuals (bottom) in the first versus last 10 time steps:

```

In[ ]:= {{Mean[
  Flatten[Table[ $\frac{i[1, 1, t] + i[1, 2, t]}{1 - \text{TRYolder}}$  /. solution[partemp, start], {t, 1, 10}]]],
  Mean[Flatten[Table[ $\frac{i[1, 1, t] + i[1, 2, t]}{1 - \text{TRYolder}}$  /. solution[partemp, start],
    {t, maxtime - 9, maxtime}]]]],
  {Mean[Flatten[Table[ $\frac{i[2, 1, t] + i[2, 2, t]}{\text{TRYolder}}$  /. solution[partemp, start],
    {t, 1, 10}]]],
  Mean[Flatten[Table[ $\frac{i[2, 1, t] + i[2, 2, t]}{\text{TRYolder}}$  /. solution[partemp, start],
    {t, maxtime - 9, maxtime}]]]]} // MatrixForm

```

Out[]//MatrixForm=

```

( 0.0199813 0.0193475 )
( 0.0199813 0.0193475 )

```

```

In[ ]:= TRYvY = (1 - TRYolder) TRYvHIGH;
(*Fraction of susceptibles getting vaccinated per day*)
TRYvO = TRYolder TRYvHIGH;
(*Fraction of older susceptibles getting vaccinated per day*)

```

```

In[ ]:= partemp =
  {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYvY, TRYvO, TRYκ, TRYconvert};

```

```

In[ ]:= solution[partemp, start];

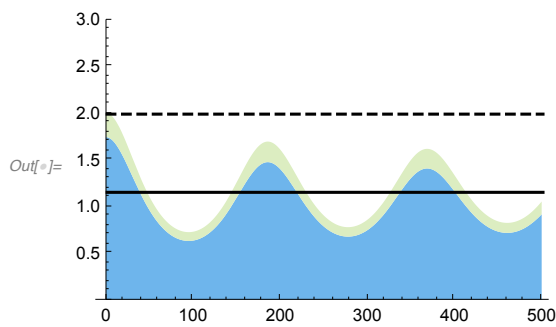
```

Showing the % of the population infectious:

```

In[ ]:= Show[
  Plot[
    Evaluate@Table[ Sum[100 i[all[[c, 1]], all[[c, 2]], t] /. solution[partemp, start],
      {c, 1, jcum}], {jcum, 1, Length[all]}],
    {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
    PlotStyle -> None, Filling ->
      {{1 -> {0, Blue}}, {2 -> {{1}, Blue}}, {3 -> {{2}, Green}}, {4 -> {{3}, Green}}}],
    Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})}$ , {t, 0, maxtime},
      PlotStyle -> {Black, Dashed}],
    Plot[100  $\left( \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})} - \frac{\text{TRYvY} + \text{TRYv0}}{\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert}} \right)$ ,
      {t, 0, maxtime}, PlotStyle -> {Black}],
    ImageSize -> 250
  ]

```



```

In[ ]:= {neweq, oldeq} /. oldeq ->  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})}$  /.
  neweq ->  $\left( \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})} - \frac{\text{TRYvY} + \text{TRYv0}}{\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert}} \right) // N$ 
```

Out[]:= {0.0116388, 0.02}

```

In[ ]:= 100  $\frac{\text{neweq} - \text{oldeq}}{\text{oldeq}}$  /. oldeq ->  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})}$  /.
  neweq ->  $\left( \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})} - \frac{\text{TRYvY} + \text{TRYv0}}{\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert}} \right) // N$ 
```

Out[]:= -41.806

The mean infection rate for <70 (top) and 70+ individuals (bottom) in the first versus last 10 time steps:

```

In[ ]:= {{Mean[
  Flatten[Table[ $\frac{i[1, 1, t] + i[1, 2, t]}{1 - \text{TRYolder}}$  /. solution[partemp, start], {t, 1, 10}]]],
  Mean[Flatten[Table[ $\frac{i[1, 1, t] + i[1, 2, t]}{1 - \text{TRYolder}}$  /. solution[partemp, start],
    {t, maxtime - 9, maxtime}]]]],
  {Mean[Flatten[Table[ $\frac{i[2, 1, t] + i[2, 2, t]}{\text{TRYolder}}$  /. solution[partemp, start],
    {t, 1, 10}]]],
  Mean[Flatten[Table[ $\frac{i[2, 1, t] + i[2, 2, t]}{\text{TRYolder}}$  /. solution[partemp, start],
    {t, maxtime - 9, maxtime}]]]]} // MatrixForm

```

Out[]//MatrixForm=

```

( 0.0197325  0.0100449 )
( 0.0197325  0.0100449 )

```

```

In[ ]:= TRYvY = 0; (*Fraction of susceptibles getting vaccinated per day*)

```

```

TRYvO = TRYolder TRYvHIGH;

```

```

(*Fraction of older susceptibles getting vaccinated per day*)

```

```

In[ ]:= partemp =

```

```

{TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYvY, TRYvO, TRYκ, TRYconvert};

```

```

In[ ]:= solution[partemp, start];

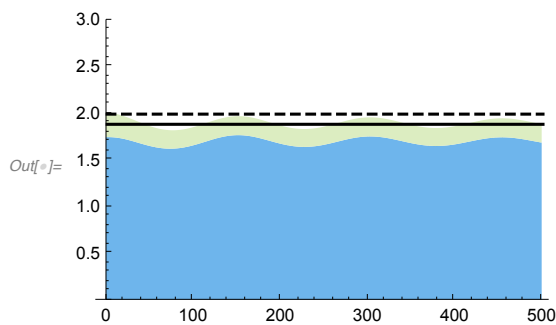
```

Showing the % of the population infectious:

```

In[ ]:= Show[
  Plot[
    Evaluate@Table[ Sum[100 i[all[[c, 1]], all[[c, 2]], t] /. solution[partemp, start],
      {c, 1, jcum}], {jcum, 1, Length[all]}],
    {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
    PlotStyle -> None, Filling ->
      {{1 -> {0, Blue}}, {2 -> {{1}, Blue}}, {3 -> {{2}, Green}}, {4 -> {{3}, LightGreen}}}],
    Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})}$ , {t, 0, maxtime},
      PlotStyle -> {Black, Dashed}],
    Plot[100  $\left( \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})} - \frac{\text{TRYvY} + \text{TRYv0}}{\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert}} \right)$ ,
      {t, 0, maxtime}, PlotStyle -> {Black}],
    ImageSize -> 250
  ]

```



The mean infection rate per capita for <70 (top) and 70+ individuals (bottom) in the first versus last 10 time steps:

```

In[ ]:= {{Mean[
  Flatten[Table[ $\frac{i[1, 1, t] + i[1, 2, t]}{1 - \text{TRYolder}}$  /. solution[partemp, start], {t, 1, 10}]]],
  Mean[Flatten[Table[ $\frac{i[1, 1, t] + i[1, 2, t]}{1 - \text{TRYolder}}$  /. solution[partemp, start],
    {t, maxtime - 9, maxtime}]]]],
  {Mean[Flatten[Table[ $\frac{i[2, 1, t] + i[2, 2, t]}{\text{TRYolder}}$  /. solution[partemp, start],
    {t, 1, 10}]]],
  Mean[Flatten[Table[ $\frac{i[2, 1, t] + i[2, 2, t]}{\text{TRYolder}}$  /. solution[partemp, start],
    {t, maxtime - 9, maxtime}]]]]} // MatrixForm

```

Out[]//MatrixForm=

```

( 0.0199874  0.019412 )
( 0.0198141  0.015192 )

```

Increasing maxtime=5000 for a more accurate estimate of the long-term impact gives

```

( 0.0199874  0.019465 )
( 0.0198141  0.0152335 )

```

so the decline in cases among <70 is 2.67% and in 70+ is 23.83%.

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```

NPIs

NPIs (f=0.5, p=0.25)

Considers impact of changing NPI from no adherence (f=0) to 50% (f=0.5) instantaneously at time 0

Parameters:

```

In[ ]:= maxtime = 500;
maxy = 8;

```

Parameters:

```

In[ ]:= TRYp = 1 / 4; (*Efficacy of masking per interaction*)
TRYf = 1 / 2; (*Additional fraction masking*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)

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

```

```

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

```

```

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

```

```

In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
TRYβ =  $\frac{\text{TRY} \delta \text{TRY} \kappa}{\text{TRY} \delta - \text{TRY} \text{inf} \text{TRY} \delta - \text{TRY} \text{convert} \text{TRY} \text{inf} \text{TRY} \kappa}$ ;

```

```

 $\frac{\text{TRY} \beta}{\text{TRY} \kappa}$  // N

```

```

Out[ ]:= 2.08333

```

Starting with no masking in the population and everybody starts masking. Starting equilibrium would be (r0 includes all of the n resistance classes):

$$\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} \right\}$$

```

In[ ]:= start = { s0 →  $\frac{\text{TRY} \kappa}{\text{TRY} \beta}$ , i0 →  $\frac{\text{TRY} \delta (\text{TRY} \beta - \text{TRY} \kappa)}{\text{TRY} \beta (\text{TRY} \delta + \text{TRY} \kappa \text{TRY} \text{convert})}$ ,
r0 →  $1 - \frac{\text{TRY} \kappa}{\text{TRY} \beta} - \frac{\text{TRY} \delta (\text{TRY} \beta - \text{TRY} \kappa)}{\text{TRY} \beta (\text{TRY} \delta + \text{TRY} \kappa \text{TRY} \text{convert})}$  }

```

```

Out[ ]:= { s0 →  $\frac{12}{25}$ , i0 →  $\frac{1}{50}$ , r0 →  $\frac{1}{2}$  }

```

```

In[ ]:= { ages = 2, stages = 2, n = 5 };

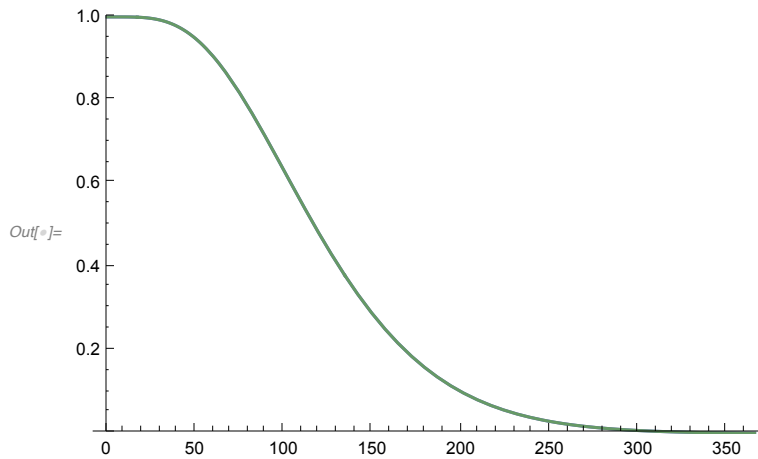
```

Waning distribution

```

In[ ]:= Show[
  Plot[TRYconvert * (1 - CDF[GammaDistribution[n, 1 / (TRYδ n)], t]), {t, 0, 365},
    PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.4, 0.8]],
  Plot[TRYconvert * (1 - CDF[GammaDistribution[n, 1 / (TRYδ0 n)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]

```



The two stages in this case correspond to those who do (jj=2) or do not (jj=1) engage in the protective NPI measures.

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\delta Y$ _,  $\delta 0$ _,  $\kappa$ _, q_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\delta Y$ ,  $\delta 0$ ,  $\kappa$ , q}, start] =
    Block[{ages = 2, stages = 2, n = 5},
      dsdt[j_, jj_, t_] = (1 - q) *  $\kappa$ [j, jj] * i[j, jj, t] + n *  $\delta$ [j, jj] * r[n, j, jj, t] - Sum[
        m[jj_, kk_] *  $\beta$ [jj_, kk_] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, jj, t];
      didt[j_, jj_, t_] = Sum[m[jj_, kk_] *  $\beta$ [jj_, kk_] * i[k, kk, t], {k, 1, ages},
        {kk, 1, stages}] * s[j, jj, t] -  $\kappa$ [j, jj] * i[j, jj, t];
      drdt[1, j_, jj_, t_] = q *  $\kappa$ [j, jj] * i[j, jj, t] - n *  $\delta$ [j, jj] * r[1, j, jj, t];
      For[nn = 2, nn ≤ n, nn++,
        drdt[nn, j_, jj_, t_] =
          n *  $\delta$ [j, jj] * r[nn - 1, j, jj, t] - n *  $\delta$ [j, jj] * r[nn, j, jj, t];
      ];
      pars = {m[jj_, kk_] → (1 - p)  $^{jj+kk-2}$ ,
         $\beta$ [j_, k_] →  $\beta$ ,  $\delta$ [1, jj_] →  $\delta Y$ ,  $\delta$ [2, jj_] →  $\delta 0$ ,  $\kappa$ [j_, jj_] →  $\kappa$ };
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars =
        Drop[Flatten[Table[{s[j, jj, t], i[j, jj, t], Table[r[nn, j, jj, t], {nn, 1, n}]}],
          {j, 1, ages}, {jj, 1, stages}]], -1];
      r[n, ages, stages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[
        Table[{D[s[j, jj, t], t] == dsdt[j, jj, t], D[i[j, jj, t], t] == didt[j, jj, t],
          Table[D[r[nn, j, jj, t], t] == drdt[nn, j, jj, t], {nn, 1, n}]}],
          {j, 1, ages}, {jj, 1, stages}]], -1];
      nstart = Drop[Flatten[Table[{s[j, jj, 0] == frac[j, jj] s0,
        i[j, jj, 0] == frac[j, jj] i0,
        Table[r[nn, j, jj, 0] == frac[j, jj]  $\frac{r0}{n}$ , {nn, 1, n}]}],
        {j, 1, ages}, {jj, 1, stages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,None", "<70,NPI", "70+,None", "70+,NPI"};

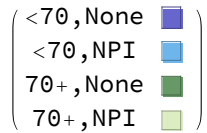
```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

```
Out[ ]:= {, , , 
```

```
In[ ]:= coltab = Join[{{1 -> {0, colours[[1]]}}},
  Table[{i -> {{i - 1}, colours[[i]]}}, {i, 2, Length[all]}]];
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

```
()
```

Equilibrium with a heterogeneous population (allowing some fraction of seroconversion, q):

```
In[ ]:= neweq[{p_, f_, older_, β_, δY_, δ0_, κ_, q_}] =
  1
  2 (-1 + p)2 β (δ + q κ) δ ( (1 + f (-2 + p)) (-1 + p) p β - (2 + (-2 + p) p) κ +
  2 √(4 (-1 + f) (-1 + p) p β κ + ((-1 + p) (-1 + f p) β - p κ)2 -
  p √(4 (-1 + f) (-1 + p) p β κ + ((-1 + p) (-1 + f p) β - p κ)2 ) /. δ -> δY
  (*Doesn't consider age differences here in waning*);
```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYδ, TRYδ0, TRYκ, TRYconvert};
```

Equilibrium number of cases:

```
In[ ]:= 100 neweq[partemp] // N
```

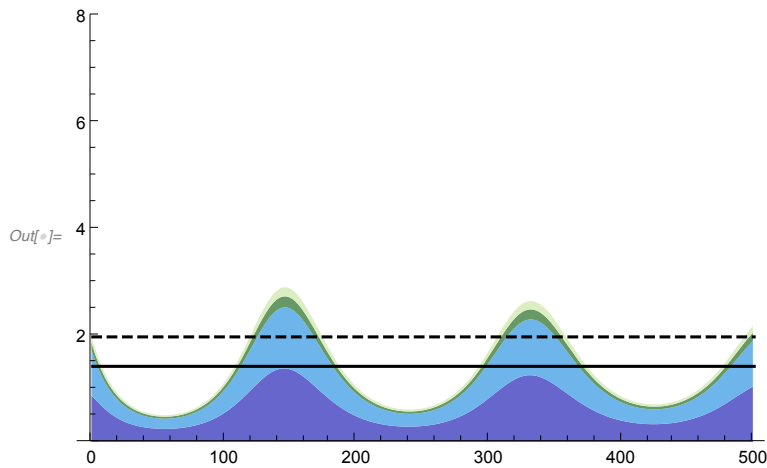
```
Out[ ]:= 1.4468
```

```
In[ ]:= solution[partemp, start];
```

```

In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[
    100 Sum[i[all[[c, 1]], all[[c, 2]], t] /. solution[partemp, start], {c, 1, jcum}],
    {jcum, 1, Length[all]}], {t, 0, maxtime}, PlotRange -> {All, {0, maxy}},
    PlotStyle -> None, Filling -> {{1 -> {0, Blue}}, {2 -> {1, Blue}},
    {3 -> {2, Green}}, {4 -> {3, Green}}}],
  Plot[100  $\frac{\text{TRY}\delta (1 - p) \text{TRY}\beta - \text{TRY}\kappa}{(1 - p) \text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$  /. p -> 0,
    {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100 neweq[partemp] /. p -> TRYp /. f -> TRYf /.  $\beta$  -> TRY $\beta$  /.  $\kappa$  -> TRY $\kappa$  /.  $\delta$  -> TRY $\delta$  /.
    q -> TRYconvert, {t, 0, maxtime}, PlotStyle -> {Black}]
]

```



The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

```

In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRY $\beta$ ,  $\frac{8}{10} \text{TRY}\delta$ ,  $\frac{8}{10} \text{TRY}\delta 0$ , TRY $\kappa$ ,  $\frac{8}{10}}$ ;

```

Equilibrium number of cases:

```

In[ ]:= 100 neweq[partemp] // N

```

```

Out[ ]:= 1.4468

```

```

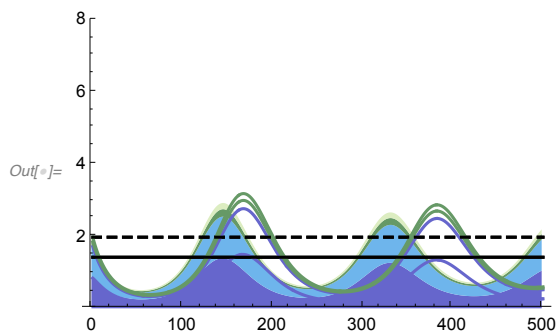
In[ ]:= solution[partemp, start];

```

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100 neweq[partemp] /. p -> TRYp /. f -> TRYf /.  $\beta$  -> TRY $\beta$  /.  $\kappa$  -> TRY $\kappa$  /.  $\delta$  ->  $\frac{8}{10} \text{TRY}\delta$  /.
  q ->  $\frac{8}{10} \text{TRYconvert}$ , {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]
```



```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];
```

NPIs (f=0.5, p=0.25) - moves between classes

Allows switching between masking and non-masking (1% per day), with initial population not masking

Parameters:

```

In[ ]:= maxtime = 500;
```

```
maxy = 8;
```

Parameters:

```

In[ ]:= TRYp = 1 / 4; (*Efficacy of masking per interaction*)
```

```
TRYf = 1 / 2; (*Additional fraction masking*)
```

```
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
```

```
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
```

```
TRY $\kappa$  = 1 / 5; (*Five day infectious period*)
```

```
TRY $\delta$  = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
```

```
TRY $\delta$ 0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
```

```
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

Adding in a rate of switching classes:

`In[ ]:= TRYrate = 1 / 100; (*Rate of switching NPI classes*)`

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

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

`In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)`

$$\text{TRY}\beta = \frac{\text{TRY}\delta \text{ TRY}\kappa}{\text{TRY}\delta - \text{TRYinf } \text{TRY}\delta - \text{TRYconvert } \text{TRYinf } \text{TRY}\kappa};$$

$$\frac{\text{TRY}\beta}{\text{TRY}\kappa} // \text{N}$$

`Out[ ]:= 2.08333`

Starting with no masking in the population and everybody starts masking. Starting equilibrium would be (r0 includes all of the n resistance classes):

$$\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} \right\}$$

$$\text{In[]:= start} = \left\{ s0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})}, \right. \\ \left. r0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})} \right\}$$

$$\text{Out[]:= } \left\{ s0 \rightarrow \frac{12}{25}, i0 \rightarrow \frac{1}{50}, r0 \rightarrow \frac{1}{2} \right\}$$

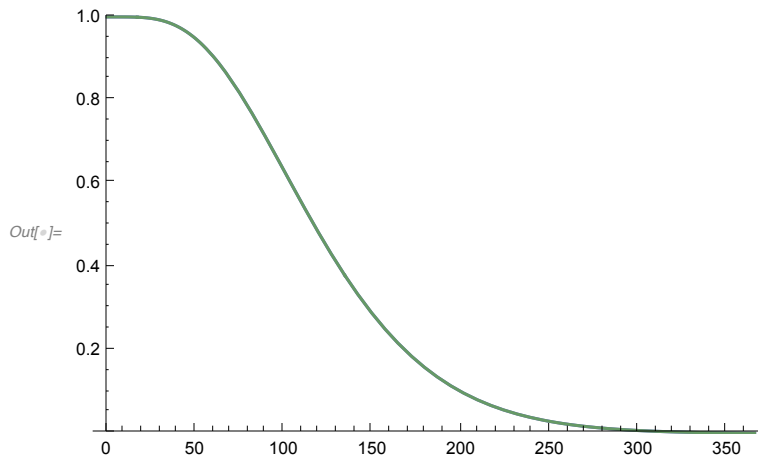
`In[ ]:= {ages = 2, stages = 2, n = 5};`

Waning distribution

```

In[ ]:= Show[
  Plot[TRYconvert * (1 - CDF[GammaDistribution[n, 1 / (TRYδ n)], t]), {t, 0, 365},
    PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.4, 0.8]],
  Plot[TRYconvert * (1 - CDF[GammaDistribution[n, 1 / (TRYδ0 n)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]

```



The two stages in this case correspond to those who do ($jj=2$) or do not ($jj=1$) engage in the protective NPI measures.

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\delta Y$ _,  $\delta 0$ _,  $\kappa$ _, q_, rate_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\delta Y$ ,  $\delta 0$ ,  $\kappa$ , q, rate}, start] =
    Block[{ages = 2, stages = 2, n = 5},
      dsdt[j_, jj_, t_] = (1 - q) *  $\kappa$ [j, jj] * i[j, jj, t] + n *  $\delta$ [j, jj] * r[n, j, jj, t] - Sum[
        m[jj, kk] *  $\beta$ [jj, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, jj, t] -
        If[jj == 1, f, 1 - f] rate s[j, jj, t] + If[jj == 1, 1 - f, f]
        rate s[j, Mod[jj, 2] + 1, t];
      didt[j_, jj_, t_] = Sum[m[jj, kk] *  $\beta$ [jj, kk] * i[k, kk, t], {k, 1, ages},
        {kk, 1, stages}] * s[j, jj, t] -  $\kappa$ [j, jj] * i[j, jj, t] -
        If[jj == 1, f, 1 - f] rate i[j, jj, t] + If[jj == 1, 1 - f, f]
        rate i[j, Mod[jj, 2] + 1, t];
      drdt[1, j_, jj_, t_] = q *  $\kappa$ [j, jj] * i[j, jj, t] - n *  $\delta$ [j, jj] * r[1, j, jj, t] -
        If[jj == 1, f, 1 - f] rate r[1, j, jj, t] +
        If[jj == 1, 1 - f, f] rate r[1, j, Mod[jj, 2] + 1, t];
      For[nn = 2, nn ≤ n, nn++,
        drdt[nn, j_, jj_, t_] =
          n *  $\delta$ [j, jj] * r[nn - 1, j, jj, t] - n *  $\delta$ [j, jj] * r[nn, j, jj, t] -
          If[jj == 1, f, 1 - f] rate r[nn, j, jj, t] +
          If[jj == 1, 1 - f, f] rate r[nn, j, Mod[jj, 2] + 1, t];
      ];
      pars = {m[jj_, kk_] → (1 - p)jj+kk-2,
         $\beta$ [j_, k_] →  $\beta$ ,  $\delta$ [1, jj_] →  $\delta Y$ ,  $\delta$ [2, jj_] →  $\delta 0$ ,  $\kappa$ [j_, jj_] →  $\kappa$ };
      frac[1, 1] = (1 - older);
      frac[2, 1] = older;
      frac[1, 2] = 0;
      frac[2, 2] = 0;
      nvars =
        Drop[Flatten[Table[{s[j, jj, t], i[j, jj, t], Table[r[nn, j, jj, t], {nn, 1, n}]}],
          {j, 1, ages}, {jj, 1, stages}]], -1];
      r[n, ages, stages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[
        Table[{D[s[j, jj, t], t] == dsdt[j, jj, t], D[i[j, jj, t], t] == didt[j, jj, t],
          Table[D[r[nn, j, jj, t], t] == drdt[nn, j, jj, t], {nn, 1, n}]}],
          {j, 1, ages}, {jj, 1, stages}]], -1];
      nstart = Drop[Flatten[Table[{s[j, jj, 0] == frac[j, jj] s0,
        i[j, jj, 0] == frac[j, jj] i0,
        Table[r[nn, j, jj, 0] == frac[j, jj]  $\frac{r0}{n}$ , {nn, 1, n}]}],
        {j, 1, ages}, {jj, 1, stages}]] /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

```

```
In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
```

```
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}
```

```
In[ ]:= labels = {"<70,None", "<70,NPI", "70+,None", "70+,NPI"};
```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],  
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

```
Out[ ]:= {, , , 
```

```
In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},  
  Table[{i -> {i - 1}, colours[[i]]}, {i, 2, Length[all]}];  
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

```
(

|          |                                                                                   |
|----------|-----------------------------------------------------------------------------------|
| <70,None |  |
| <70,NPI  |  |
| 70+,None |  |
| 70+,NPI  |  |

)
```

Equilibrium with a heterogeneous population (allowing some fraction of seroconversion, q):

```
In[ ]:= neweq[{p_, f_, older_, β_, δY_, δ0_, κ_, q_, rate_}] =
```

$$\frac{1}{2(-1+p)^2\beta(\delta+q\kappa)}\delta\left((1+f(-2+p))(-1+p)p\beta-(2+(-2+p)p)\kappa+\right. \\ \left.2\sqrt{4(-1+f)(-1+p)p\beta\kappa+((-1+p)(-1+fp)\beta-p\kappa)^2}-\right. \\ \left.p\sqrt{4(-1+f)(-1+p)p\beta\kappa+((-1+p)(-1+fp)\beta-p\kappa)^2}\right)/\delta\rightarrow\delta Y$$

(*Doesn't consider age differences here in waning*);

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYδ, TRYδ0, TRYκ, TRYconvert, TRYrate};
```

```
In[ ]:= 100 neweq[partemp] // N
```

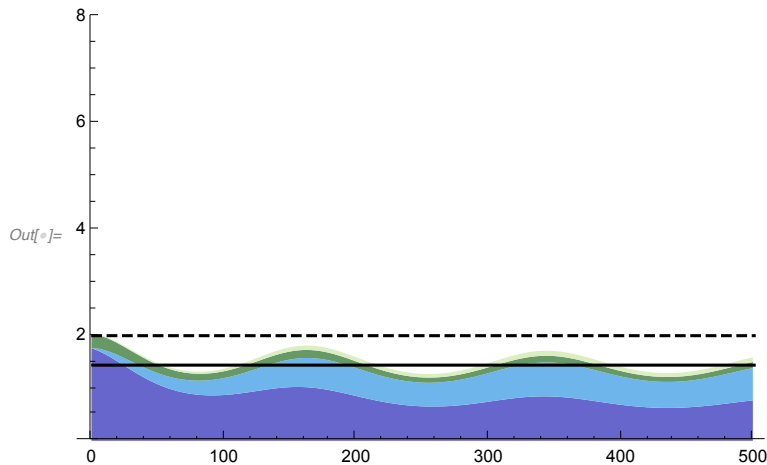
```
Out[ ]:= 1.4468
```

```
In[ ]:= solution[partemp, start];
```

```

In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[
    100 Sum[i[all[[c, 1]], all[[c, 2]], t] /. solution[partemp, start], {c, 1, jcum}],
    {jcum, 1, Length[all]}], {t, 0, maxtime}, PlotRange -> {All, {0, maxy}},
    PlotStyle -> None, Filling -> {{1 -> {0, Blue}}, {2 -> {1, LightBlue}},
    {3 -> {2, Green}}, {4 -> {3, LightGreen}}}],
  Plot[100  $\frac{\text{TRY}\delta ((1-p) \text{TRY}\beta - \text{TRY}\kappa)}{(1-p) \text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$  /. p -> 0,
    {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100 neweq[partemp], {t, 0, maxtime}, PlotStyle -> {Black}]
]

```



The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

```

In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ,  $\frac{8}{10} \text{TRY}\delta$ ,  $\frac{8}{10} \text{TRY}\delta 0$ , TRYκ,  $\frac{8}{10}$ , TRYrate};

```

```

In[ ]:= 100 neweq[partemp] // N

```

```

Out[ ]:= 1.4468

```

```

In[ ]:= solution[partemp, start];

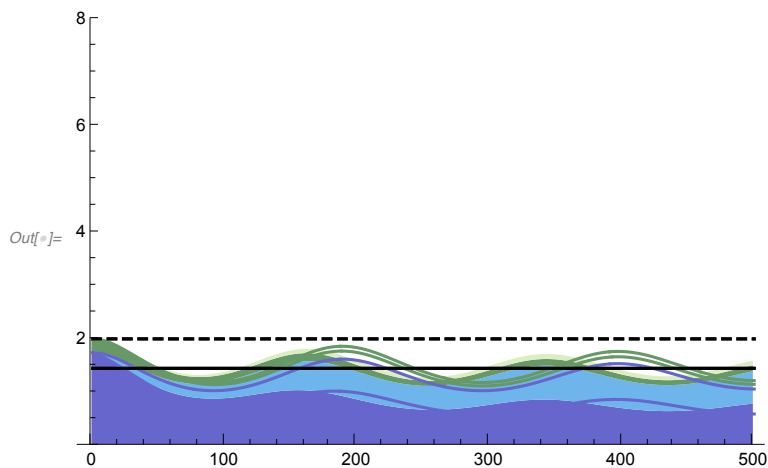
```

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100 neweq[partemp], {t, 0, maxtime}, PlotStyle -> {Black}]
]

```



In[]:=

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```

NPIs ($f=0.25$, $p=0.5$) - moves between classes (similar result since $f \cdot p$ is constant)

Allows switching between masking and non-masking (1% per day), with initial population not masking

Parameters:

```

In[ ]:= maxtime = 500;
maxy = 8;

```

Parameters:

```

In[ ]:= TRYp = 1 / 2; (*Efficacy of masking per interaction*)
TRYf = 1 / 4; (*Additional fraction masking*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)

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

```

Adding in a rate of switching classes:

```

In[ ]:= TRYrate = 1 / 100; (*Rate of switching NPI classes*)

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

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

In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
TRYβ =  $\frac{\text{TRY} \delta \text{TRY} \kappa}{\text{TRY} \delta - \text{TRYinf} \text{TRY} \delta - \text{TRYconvert} \text{TRYinf} \text{TRY} \kappa}$ ;

 $\frac{\text{TRY} \beta}{\text{TRY} \kappa} // N$ 

Out[ ]:= 2.08333

```

Starting with no masking in the population and everybody starts masking. Starting equilibrium would be (r0 includes all of the n resistance classes):

```

 $\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} \right\}$ 

In[ ]:= start =  $\left\{ s0 \rightarrow \frac{\text{TRY} \kappa}{\text{TRY} \beta}, i0 \rightarrow \frac{\text{TRY} \delta (\text{TRY} \beta - \text{TRY} \kappa)}{\text{TRY} \beta (\text{TRY} \delta + \text{TRY} \kappa \text{TRYconvert})}, \right.$ 
 $\left. r0 \rightarrow 1 - \frac{\text{TRY} \kappa}{\text{TRY} \beta} - \frac{\text{TRY} \delta (\text{TRY} \beta - \text{TRY} \kappa)}{\text{TRY} \beta (\text{TRY} \delta + \text{TRY} \kappa \text{TRYconvert})} \right\}$ 

Out[ ]:=  $\left\{ s0 \rightarrow \frac{12}{25}, i0 \rightarrow \frac{1}{50}, r0 \rightarrow \frac{1}{2} \right\}$ 

In[ ]:= {ages = 2, stages = 2, n = 5};

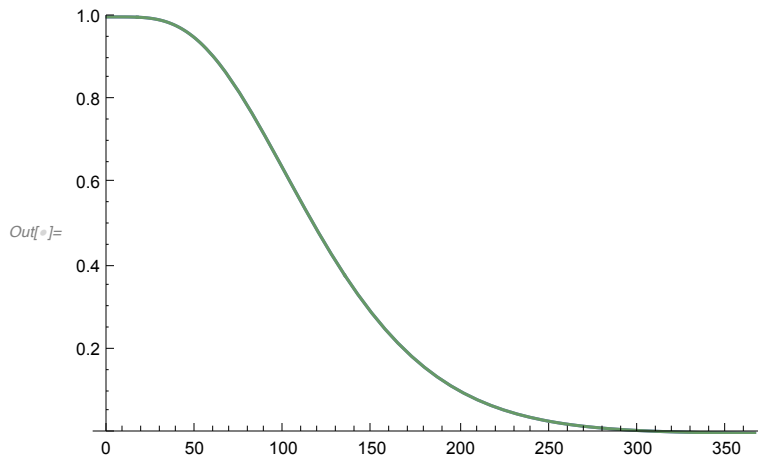
```

Waning distribution

```

In[ ]:= Show[
  Plot[TRYconvert * (1 - CDF[GammaDistribution[n, 1 / (TRYδ n)], t]), {t, 0, 365},
    PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.4, 0.8]],
  Plot[TRYconvert * (1 - CDF[GammaDistribution[n, 1 / (TRYδ0 n)], t]),
    {t, 0, 365}, PlotRange -> {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]

```



The two stages in this case correspond to those who do (jj=2) or do not (jj=1) engage in the protective NPI measures.

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\delta Y$ _,  $\delta 0$ _,  $\kappa$ _, q_, rate_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\delta Y$ ,  $\delta 0$ ,  $\kappa$ , q, rate}, start] =
    Block[{ages = 2, stages = 2, n = 5},
      dsdt[j_, jj_, t_] = (1 - q) *  $\kappa$ [j, jj] * i[j, jj, t] + n *  $\delta$ [j, jj] * r[n, j, jj, t] - Sum[
        m[jj, kk] *  $\beta$ [jj, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, jj, t] -
        If[jj == 1, f, 1 - f] rate s[j, jj, t] + If[jj == 1, 1 - f, f]
        rate s[j, Mod[jj, 2] + 1, t];
      didt[j_, jj_, t_] = Sum[m[jj, kk] *  $\beta$ [jj, kk] * i[k, kk, t], {k, 1, ages},
        {kk, 1, stages}] * s[j, jj, t] -  $\kappa$ [j, jj] * i[j, jj, t] -
        If[jj == 1, f, 1 - f] rate i[j, jj, t] + If[jj == 1, 1 - f, f]
        rate i[j, Mod[jj, 2] + 1, t];
      drdt[1, j_, jj_, t_] = q *  $\kappa$ [j, jj] * i[j, jj, t] - n *  $\delta$ [j, jj] * r[1, j, jj, t] -
        If[jj == 1, f, 1 - f] rate r[1, j, jj, t] +
        If[jj == 1, 1 - f, f] rate r[1, j, Mod[jj, 2] + 1, t];
      For[nn = 2, nn ≤ n, nn++,
        drdt[nn, j_, jj_, t_] =
          n *  $\delta$ [j, jj] * r[nn - 1, j, jj, t] - n *  $\delta$ [j, jj] * r[nn, j, jj, t] -
          If[jj == 1, f, 1 - f] rate r[nn, j, jj, t] +
          If[jj == 1, 1 - f, f] rate r[nn, j, Mod[jj, 2] + 1, t];
      ];
      pars = {m[jj_, kk_] → (1 - p)jj+kk-2,
         $\beta$ [j_, k_] →  $\beta$ ,  $\delta$ [1, jj_] →  $\delta Y$ ,  $\delta$ [2, jj_] →  $\delta 0$ ,  $\kappa$ [j_, jj_] →  $\kappa$ };
      frac[1, 1] = (1 - older);
      frac[2, 1] = older;
      frac[1, 2] = 0;
      frac[2, 2] = 0;
      nvars =
        Drop[Flatten[Table[{s[j, jj, t], i[j, jj, t], Table[r[nn, j, jj, t], {nn, 1, n}]}],
          {j, 1, ages}, {jj, 1, stages}]], -1];
      r[n, ages, stages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[
        Table[{D[s[j, jj, t], t] == dsdt[j, jj, t], D[i[j, jj, t], t] == didt[j, jj, t],
          Table[D[r[nn, j, jj, t], t] == drdt[nn, j, jj, t], {nn, 1, n}]}],
          {j, 1, ages}, {jj, 1, stages}]], -1];
      nstart = Drop[Flatten[Table[{s[j, jj, 0] == frac[j, jj] s0,
        i[j, jj, 0] == frac[j, jj] i0,
        Table[r[nn, j, jj, 0] == frac[j, jj]  $\frac{r0}{n}$ , {nn, 1, n}]}],
        {j, 1, ages}, {jj, 1, stages}]] /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

```

```
In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
```

```
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}
```

```
In[ ]:= labels = {"<70,None", "<70,NPI", "70+,None", "70+,NPI"};
```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],  
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

```
Out[ ]:= {■, ■, ■, ■}
```

```
In[ ]:= coltab = Join[{1 → {0, colours[[1]]}},  
  Table[{i → {{i - 1}, colours[[i]]}}, {i, 2, Length[all]}]],  
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

```
(  
  <70,None ■  
  <70,NPI ■  
  70+,None ■  
  70+,NPI ■  
)
```

Equilibrium with a heterogeneous population (allowing some fraction of seroconversion, q):

```
In[ ]:= neweq[{p_, f_, older_, β_, δY_, δ0_, κ_, q_, rate_}] =
```

$$\frac{1}{2(-1+p)^2\beta(\delta+q\kappa)}\delta\left((1+f(-2+p))(-1+p)p\beta-(2+(-2+p)p)\kappa+\right. \\ \left.2\sqrt{4(-1+f)(-1+p)p\beta\kappa+((-1+p)(-1+fp)\beta-p\kappa)^2}-\right. \\ \left.p\sqrt{4(-1+f)(-1+p)p\beta\kappa+((-1+p)(-1+fp)\beta-p\kappa)^2}\right)/\delta\rightarrow\delta Y$$

(*Doesn't consider age differences here in waning*);

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYδ, TRYδ0, TRYκ, TRYconvert, TRYrate};
```

```
In[ ]:= 100 neweq[partemp] // N
```

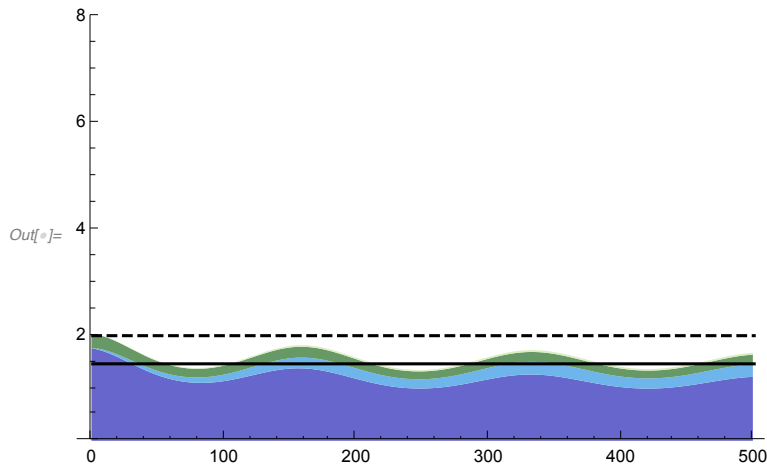
```
Out[ ]:= 1.47119
```

```
In[ ]:= solution[partemp, start];
```

```

In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[
    100 Sum[i[all[[c, 1]], all[[c, 2]], t] /. solution[partemp, start], {c, 1, jcum}],
    {jcum, 1, Length[all]}], {t, 0, maxtime}, PlotRange -> {All, {0, maxy}},
    PlotStyle -> None, Filling -> {{1 -> {0, Blue}}, {2 -> {1, Blue}},
    {3 -> {2, Green}}, {4 -> {3, Green}}}],
  Plot[100  $\frac{\text{TRY}\delta ((1-p) \text{TRY}\beta - \text{TRY}\kappa)}{(1-p) \text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$  /. p -> 0,
    {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100 neweq[partemp], {t, 0, maxtime}, PlotStyle -> {Black}]
]

```



The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

```

In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ,  $\frac{8}{10} \text{TRY}\delta$ ,  $\frac{8}{10} \text{TRY}\delta 0$ , TRYκ,  $\frac{8}{10}$ , TRYrate};

```

```

In[ ]:= 100 neweq[partemp] // N

```

```

Out[ ]:= 1.47119

```

```

In[ ]:= solution[partemp, start];

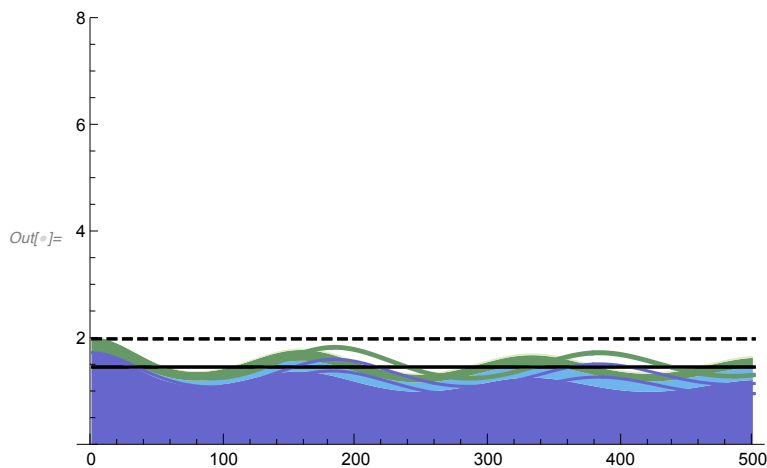
```

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100 neweq[partemp], {t, 0, maxtime}, PlotStyle -> {Black}]
]

```



In[]:=

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```

Alternative: SIR_n model (with leaky variants)

→ Consistent results (accounting for impact on resistant classes)

Alt Figure 3: leaky immunity & more transmissible (n=5)

In[]:= maxtime = 500;

maxy = 8;

Parameters:

```

In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
TRYf = 99 / 100; (*Starting fraction of resident*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10;
(*Only this fraction of cases seroconvert or boost immunity*)
TRYleak = 1 / 10;

```

Now the $R[j, t]$ classes are no longer equal in frequency at equilibrium and must be numerically calculated:

```

In[ ]:= Flatten[{0 == 5 δ R[5, t] - β I I[t] × S[t],
  0 == -κ I I[t] + leak β I I[t] × Sum[R[j, t], {j, 1, 5}] + β I I[t] × S[t],
  0 == κ I I[t] - 5 δ R[1, t] - leak β I I[t] × R[1, t],
  Table[0 == 5 δ R[-1 + j, t] - 5 δ R[j, t] - leak β I I[t] × R[j, t], {j, 2, 5}]}]

```

```

Out[ ]:= {0 == 5 δ R[5, t] - β I I[t] × S[t], 0 ==
  -κ I I[t] + leak β I I[t] (R[1, t] + R[2, t] + R[3, t] + R[4, t] + R[5, t]) + β I I[t] × S[t],
  0 == κ I I[t] - 5 δ R[1, t] - leak β I I[t] × R[1, t],
  0 == 5 δ R[1, t] - 5 δ R[2, t] - leak β I I[t] × R[2, t],
  0 == 5 δ R[2, t] - 5 δ R[3, t] - leak β I I[t] × R[3, t],
  0 == 5 δ R[3, t] - 5 δ R[4, t] - leak β I I[t] × R[4, t],
  0 == 5 δ R[4, t] - 5 δ R[5, t] - leak β I I[t] × R[5, t]}

```

```

In[ ]:= Solve[%, Flatten[{S[t], I I[t], Table[R[j, t], {j, 1, 5}]}]] // Simplify

```

 **Solve:** Equations may not give solutions for all "solve" variables.

```

Out[ ]:= {{I I[t] → 0, R[1, t] → 0, R[2, t] → 0, R[3, t] → 0, R[4, t] → 0, R[5, t] → 0},
  {S[t] →  $\frac{3125 \delta^5 \kappa}{\beta I (5 \delta + \text{leak } \beta I I[t])^5}$ , R[1, t] →  $\frac{\kappa I I[t]}{5 \delta + \text{leak } \beta I I[t]}$ ,
  R[2, t] →  $\frac{5 \delta \kappa I I[t]}{(5 \delta + \text{leak } \beta I I[t])^2}$ , R[3, t] →  $\frac{25 \delta^2 \kappa I I[t]}{(5 \delta + \text{leak } \beta I I[t])^3}$ ,
  R[4, t] →  $\frac{125 \delta^3 \kappa I I[t]}{(5 \delta + \text{leak } \beta I I[t])^4}$ , R[5, t] →  $\frac{625 \delta^4 \kappa I I[t]}{(5 \delta + \text{leak } \beta I I[t])^5}$ }}

```

```

In[ ]:= startme = %[[2]];

```

Finding the value of β that gives the target incidence (TRYinf):

```
In[ ]:= Solve[(S[t] + I1[t] + Sum[R[j, t], {j, 1, 5}] /. startme /. I1[t] -> TRYinf /.  $\delta \rightarrow \text{TRY}\delta$  /.  $\kappa \rightarrow \text{TRY}\kappa$  /. leak  $\rightarrow \text{TRYleak}$ ) == 1,  $\beta 1$ ]
```

```
Out[ ]:= {{ $\beta 1 \rightarrow -4.47\dots$ }, { $\beta 1 \rightarrow 0.361\dots$ }, { $\beta 1 \rightarrow -29.4\dots - 6.27\dots i$ },  
{ $\beta 1 \rightarrow -29.4\dots + 6.27\dots i$ }, { $\beta 1 \rightarrow -17.5\dots - 11.8\dots i$ }, { $\beta 1 \rightarrow -17.5\dots + 11.8\dots i$ }}
```

```
In[ ]:=  $\text{TRY}\beta = \beta 1 /. \%$ [[2]]
```

```
Out[ ]:= 0.361...
```

```
In[ ]:= (* $\text{TRY}\beta = \frac{\text{TRY}\delta \text{ TRY}\kappa}{\text{TRY}\delta - \text{TRYinf} \text{ TRY}\delta - \text{TRYconvert} \text{ TRYinf} \text{ TRY}\kappa}$ *)
```

```
 $\frac{\text{TRY}\beta}{\text{TRY}\kappa} // \text{N}$ 
```

```
Out[ ]:= 1.807
```

Variant has a higher transmissibility (set to have the same selection coefficient as for the immune evasive variant):

```
In[ ]:= Flatten[Solve[ $\frac{\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa == 0.0833$ ,  $\beta V$ ]]
```

```
Out[ ]:= { $\beta V \rightarrow 0.511924$ }
```

```
In[ ]:=  $\text{TRY}\beta V = \beta V /. \%$ ;
```

% increase in β :

```
In[ ]:=  $100 * \frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta}$ 
```

```
Out[ ]:= 41.65
```

and now has no immune evasive properties. Specifically, we assume five waning classes and the variant infects only susceptibles ($m=0$):

```
In[ ]:=  $\text{TRYn} = 5$ ;
```

```
 $\text{TRYm} = 0$ ;
```

Equilibrium once variant fixes:

```

In[ ]:= Sort[Solve[
  (S[t] + I1[t] + Sum[R[j], t], {j, 1, TRYn - TRYm}] /. startme /.  $\delta \rightarrow \text{TRY}\delta$  /.  $\kappa \rightarrow \text{TRY}\kappa$  /.
  leak  $\rightarrow \text{TRYleak}$  /.  $\beta_1 \rightarrow \text{TRY}\beta_V$ ) == 1, I1[t]] // N]
neweq =
  I1[
    t] /.
  Last[
    %]

```

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

```

Out[ ]:= { {I1[t]  $\rightarrow$  -2.92923}, {I1[t]  $\rightarrow$  -1.48102 - 0.598745 i},
  {I1[t]  $\rightarrow$  -1.48102 + 0.598745 i}, {I1[t]  $\rightarrow$  -0.475548 - 0.774942 i},
  {I1[t]  $\rightarrow$  -0.475548 + 0.774942 i}, {I1[t]  $\rightarrow$  0.0287181} }

```

```

Out[ ]:= 0.0287181

```

Starting equilibrium would be (r0 includes all of the n resistance classes and is just an approximate start):

```

In[ ]:= start = {s0  $\rightarrow$  S[t], i0  $\rightarrow$  TRYinf, r0  $\rightarrow$  1 - S[t] - TRYinf} /. startme /. I1[t]  $\rightarrow$  TRYinf /.
   $\delta \rightarrow \text{TRY}\delta$  /.  $\kappa \rightarrow \text{TRY}\kappa$  /. leak  $\rightarrow \text{TRYleak}$  /.  $\beta_1 \rightarrow \text{TRY}\beta$ ;

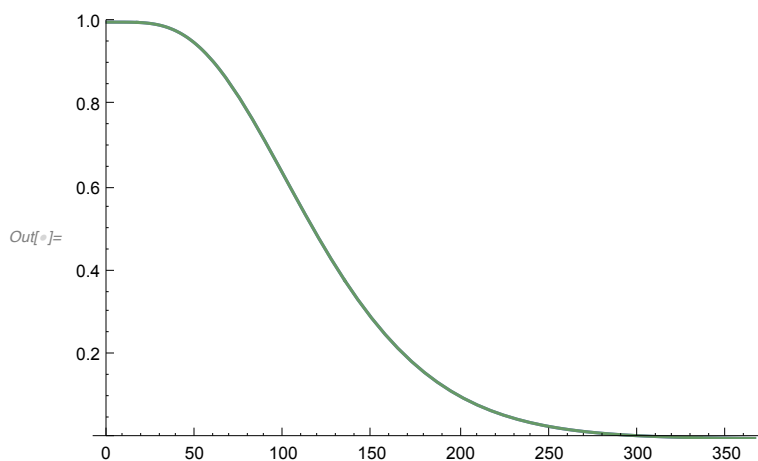
```

Waning distribution for a population of younger and older individuals:

```

In[ ]:= Show[
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRY $\delta$  TRYn)], t]),
    {t, 0, 365}, PlotRange  $\rightarrow$  {All, {0, 1}}, PlotStyle  $\rightarrow$  RGBColor[0.4, 0.4, 0.8]],
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRY $\delta_0$  TRYn)], t]),
    {t, 0, 365}, PlotRange  $\rightarrow$  {All, {0, 1}}, PlotStyle  $\rightarrow$  RGBColor[0.4, 0.6, 0.4]]
]

```



Now the susceptible and resistant classes depend only on age (not whether they carried a variant before):

[NOTE: For the ease of colouring, the first stage class is the variant.]

```

In[ ]:= {ages = 2, stages = 2, n = TRYn};

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta O$ _,  $\kappa$ _, q_}, start] :=
solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta O$ ,  $\kappa$ , q}, start] =
Block[{ages = 2, stages = 2, n = TRYn},
  dsdt[j_, t_] =
    (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] + n *  $\delta$ [j] * r[n, j, t] -
    Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
  didt[j_, 1, t_] = Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] *
    Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] + Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] *
    s[j, t] + TRYleak * Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] *
    Sum[r[nn, j, t], {nn, 1, TRYn}] -  $\kappa$ [j, 1] * i[j, 1, t];
  didt[j_, 2, t_] = Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] +
    TRYleak * Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] *
    Sum[r[nn, j, t], {nn, 1, TRYn}] -  $\kappa$ [j, 2] * i[j, 2, t];
  drdt[1, j_, t_] = q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] -
    n *  $\delta$ [j] * r[1, j, t] -
    TRYleak * Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * r[1, j, t];
  For[nn = 2, nn ≤ n - TRYm, nn++,
    drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] - n *  $\delta$ [j] * r[nn, j, t] -
      TRYleak * Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * r[nn, j, t];
  ];
  For[nn = n + 1 - TRYm, nn ≤ n, nn++,
    drdt[nn, j_, t_] =
      n *  $\delta$ [j] * r[nn - 1, j, t] - Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] -
      TRYleak * Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * r[nn, j, t] -
      n *  $\delta$ [j] * r[nn, j, t];
  ];
  pars = { $\beta$ [j_, 1] →  $\beta V$ ,  $\beta$ [j_, 2] →  $\beta$ ,  $\delta$ [1] →  $\delta Y$ ,  $\delta$ [2] →  $\delta O$ ,  $\kappa$ [j_, jj_] →  $\kappa$ };
  frac[1, 1] = (1 - older) (1 - f);
  frac[2, 1] = older (1 - f);
  frac[1, 2] = (1 - older) f;
  frac[2, 2] = older f;
  nvars = Drop[Flatten[Table[{s[j, t], Table[i[j, jj, t], {jj, 1, stages}],
    Table[r[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
  r[n, ages, t_] = 1 - Total[nvars];
  neqns = Drop[Flatten[Table[{D[s[j, t], t] == dsdt[j, t],
    Table[D[i[j, jj, t], t] == didt[j, jj, t], {jj, 1, stages}],
    Table[D[r[nn, j, t], t] == drdt[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
  nstart = Drop[Flatten[Table[{
    Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
    s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0, Table[r[nn, j, 0] ==

```

```

      (frac[j, 1] + frac[j, 2])  $\frac{r_0}{n}$ , {nn, 1, n}]]}, {j, 1, ages}]] /. start, -1];
    NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
  ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
Out[ ]:= { , , , }

In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1}, colours[[i]]}, {i, 2, Length[all]}]];
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
Out[ ]//MatrixForm=

$$\begin{pmatrix} <70, \text{Res} & \\ <70, \text{Mutant} & \\ 70+, \text{Res} & \\ 70+, \text{Mutant} & \end{pmatrix}$$

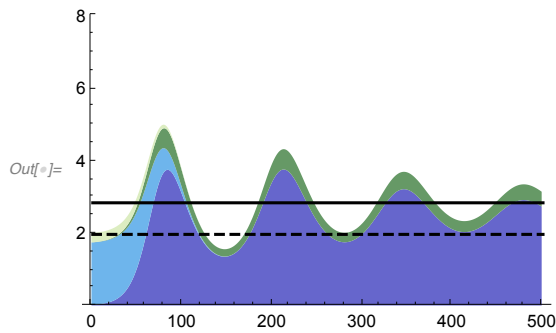

In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRY $\beta$ , TRY $\beta$ V, TRY $\delta$ , TRY $\delta$ 0, TRY $\kappa$ , TRYconvert};
In[ ]:= solution[partemp, start];
  Showing the % of the population infectious:

```

```

In[ ]:= plot1 = Show[
  Plot[
    Evaluate@Table[ Sum[100 i[all[[c, 1]], all[[c, 2]], t] /. solution[partemp, start],
      {c, 1, jcum}], {jcum, 1, Length[all]}],
    {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
    PlotStyle -> None, Filling -> {{1 -> {0, Blue}}, {2 -> {1, Blue}},
      {3 -> {2, Green}}, {4 -> {3, Green}}}],
    Plot[100 TRYinf, {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
    Plot[100 neweq, {t, 0, maxtime}, PlotStyle -> {Black}],
    ImageSize -> 250
  ]

```



Mutant fraction change between t=0 and t=50:

```

In[ ]:= Sum[i[j, 1, t], {j, 1, ages}]
Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}] /. solution[partemp, start] /. t -> 50

```

Out[]:= {0.385458}

```

In[ ]:= Solve[Exp[s 50] == (p50 / (1 - p50)) /. p50 -> % /. p0 -> 1 - TRYf], s][[1]]

```

Solve: Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

Out[]:= {s -> 0.0825735}

This is consistent with the predicted selection coefficient (updating the last part for the leaky model):

```

In[ ]:= (TRYβV - TRYβ) / TRYβ * TRYκ + Sum[R[j, t], {j, 1 + TRYn - TRYm, TRYn}] TRYβV /. startme /.
  I1[t] -> TRYinf /. δ -> TRYδ /. κ -> TRYκ /. leak -> TRYleak /. β1 -> TRYβV // N

```

Out[]:= 0.0833

New equilibrium:

```

In[ ]:= neweq // N

```

Out[]:= 0.0287181

% rise in the endemic equilibrium:

```
In[ ]:= 100 * 
$$\frac{(\% - \text{TRYinf})}{\text{TRYinf}}$$

```

```
Out[ ]:= 43.5903
```

```
In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];
```

Alt Figure 3: leaky immunity & more permanently immune evasive (m=2, n=5)

```
In[ ]:= maxtime = 500;
```

```
maxy = 8;
```

Parameters:

```
In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
```

```
TRYf = 99 / 100; (*Starting fraction of resident*)
```

```
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
```

```
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
```

```
TRYκ = 1 / 5; (*Five day infectious period*)
```

```
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
```

```
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
```

```
TRYconvert = 10 / 10;
```

```
(*Only this fraction of cases seroconvert or boost immunity*)
```

```
TRYleak = 1 / 10;
```

```
In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
```

Now the R[j,t] classes are no longer equal in frequency at equilibrium and must be numerically calculated:

```
In[ ]:= Flatten[{0 == 5 δ R[5, t] - β1 I1[t] × S[t],
```

```
0 == -κ I1[t] + leak β1 I1[t] × Sum[R[j, t], {j, 1, 5}] + β1 I1[t] × S[t],
```

```
0 == κ I1[t] - 5 δ R[1, t] - leak β1 I1[t] × R[1, t],
```

```
Table[0 == 5 δ R[-1 + j, t] - 5 δ R[j, t] - leak β1 I1[t] × R[j, t], {j, 2, 5}]]]
```

```
Out[ ]:= {0 == 5 δ R[5, t] - β1 I1[t] × S[t], 0 ==
```

```
-κ I1[t] + leak β1 I1[t] (R[1, t] + R[2, t] + R[3, t] + R[4, t] + R[5, t]) + β1 I1[t] × S[t],
```

```
0 == κ I1[t] - 5 δ R[1, t] - leak β1 I1[t] × R[1, t],
```

```
0 == 5 δ R[1, t] - 5 δ R[2, t] - leak β1 I1[t] × R[2, t],
```

```
0 == 5 δ R[2, t] - 5 δ R[3, t] - leak β1 I1[t] × R[3, t],
```

```
0 == 5 δ R[3, t] - 5 δ R[4, t] - leak β1 I1[t] × R[4, t],
```

```
0 == 5 δ R[4, t] - 5 δ R[5, t] - leak β1 I1[t] × R[5, t]}
```

```
In[ ]:= Solve[%, Flatten[{S[t], I1[t], Table[R[j, t], {j, 1, 5}]}]] // Simplify
```

 **Solve:** Equations may not give solutions for all "solve" variables.

```
Out[ ]:= { {I1[t] -> 0, R[1, t] -> 0, R[2, t] -> 0, R[3, t] -> 0, R[4, t] -> 0, R[5, t] -> 0},
  {S[t] ->  $\frac{3125 \delta^5 \kappa}{\beta 1 (5 \delta + \text{leak} \beta 1 I1[t])^5}$ , R[1, t] ->  $\frac{\kappa I1[t]}{5 \delta + \text{leak} \beta 1 I1[t]}$ ,
  R[2, t] ->  $\frac{5 \delta \kappa I1[t]}{(5 \delta + \text{leak} \beta 1 I1[t])^2}$ , R[3, t] ->  $\frac{25 \delta^2 \kappa I1[t]}{(5 \delta + \text{leak} \beta 1 I1[t])^3}$ ,
  R[4, t] ->  $\frac{125 \delta^3 \kappa I1[t]}{(5 \delta + \text{leak} \beta 1 I1[t])^4}$ , R[5, t] ->  $\frac{625 \delta^4 \kappa I1[t]}{(5 \delta + \text{leak} \beta 1 I1[t])^5}$ }}
```

```
In[ ]:= startme = %[[2]];
```

Finding the value of β that gives the target incidence (TRYinf):

```
In[ ]:= Solve[(S[t] + I1[t] + Sum[R[j, t], {j, 1, 5}] /. startme /. I1[t] -> TRYinf /.  $\delta \rightarrow \text{TRY}\delta$  /.
   $\kappa \rightarrow \text{TRY}\kappa$  /. leak -> TRYleak) == 1,  $\beta 1$ ]
```

```
Out[ ]:= {{ $\beta 1 \rightarrow -4.47...$ }, { $\beta 1 \rightarrow 0.361...$ }, { $\beta 1 \rightarrow -29.4... - 6.27... i$ },
  { $\beta 1 \rightarrow -29.4... + 6.27... i$ }, { $\beta 1 \rightarrow -17.5... - 11.8... i$ }, { $\beta 1 \rightarrow -17.5... + 11.8... i$ }}
```

```
In[ ]:= TRY $\beta$  =  $\beta 1$  /. %[[2]]
```

```
Out[ ]:= 0.361...
```

```
In[ ]:= (*TRY $\beta$  =  $\frac{\text{TRY}\delta \text{ TRY}\kappa}{\text{TRY}\delta - \text{TRYinf} \text{ TRY}\delta - \text{TRYconvert} \text{ TRYinf} \text{ TRY}\kappa}$ ; *)
```

$\frac{\text{TRY}\beta}{\text{TRY}\kappa}$ // N

```
Out[ ]:= 1.807
```

Variant has the same transmissibility:

```
In[ ]:= TRY $\beta$ V = TRY $\beta$ ;
```

but is more immune evasive:

```
In[ ]:= TRYn = 5;
```

```
TRYm = 2;
```

Equilibrium once variant fixes:

```

In[ ]:= Sort[Solve[
  (S[t] + I1[t] + Sum[R[j], t], {j, 1, TRYn - TRYm}) /. startme /.  $\delta \rightarrow \text{TRY}\delta$  /.  $\kappa \rightarrow \text{TRY}\kappa$  /.
  leak  $\rightarrow \text{TRYleak}$  /.  $\beta 1 \rightarrow \text{TRY}\beta V$ ) == 1, I1[t]] // N]
neweq =
  I1[
    t] /.
    Last[
      %]
Out[ ]:= {{I1[t]  $\rightarrow$  -4.6949}, {I1[t]  $\rightarrow$  -1.60065 - 1.25807 i}, {I1[t]  $\rightarrow$  -1.60065 + 1.25807 i},
  {I1[t]  $\rightarrow$  -1.45384}, {I1[t]  $\rightarrow$  -0.752823}, {I1[t]  $\rightarrow$  0.034828}}
Out[ ]:= 0.034828

```

Starting equilibrium would be (r0 includes all of the n resistance classes and is just an approximate start):

```

In[ ]:= start = {s0  $\rightarrow$  S[t], i0  $\rightarrow$  TRYinf, r0  $\rightarrow$  1 - S[t] - TRYinf} /. startme /. I1[t]  $\rightarrow$  TRYinf /.
   $\delta \rightarrow \text{TRY}\delta$  /.  $\kappa \rightarrow \text{TRY}\kappa$  /. leak  $\rightarrow \text{TRYleak}$  /.  $\beta 1 \rightarrow \text{TRY}\beta$ ;

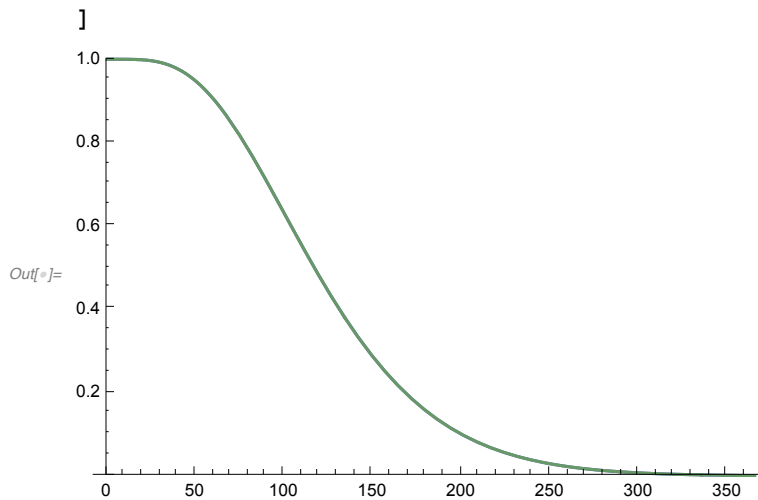
```

Waning distribution for a population of younger and older individuals:

```

In[ ]:= Show[
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRY $\delta$  TRYn)], t]),
    {t, 0, 365}, PlotRange  $\rightarrow$  {All, {0, 1}}, PlotStyle  $\rightarrow$  RGBColor[0.4, 0.4, 0.8]],
  Plot[TRYconvert * (1 - CDF[GammaDistribution[TRYn, 1 / (TRY $\delta 0$  TRYn)], t]),
    {t, 0, 365}, PlotRange  $\rightarrow$  {All, {0, 1}}, PlotStyle  $\rightarrow$  RGBColor[0.4, 0.6, 0.4]]
]

```



Now the susceptible and resistant classes depend only on age (not whether they carried a variant before):

[NOTE: For the ease of colouring, the first stage class is the variant.]

```

In[ ]:= {ages = 2, stages = 2, n = TRYn};
In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta 0$ _,  $\kappa$ _, q_}, start] :=

```

```

solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta 0$ ,  $\kappa$ , q}, start] =
Block[{ages = 2, stages = 2, n = TRYn},
  dsdt[j_, t_] =
    (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] + n *  $\delta$ [j] * r[n, j, t] -
    Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
  didt[j_, 1, t_] = Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] *
    Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] + Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] *
    s[j, t] + TRYleak * Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] *
    Sum[r[nn, j, t], {nn, 1, TRYn}] -  $\kappa$ [j, 1] * i[j, 1, t];
  didt[j_, 2, t_] = Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] +
    TRYleak * Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] *
    Sum[r[nn, j, t], {nn, 1, TRYn}] -  $\kappa$ [j, 2] * i[j, 2, t];
  drdt[1, j_, t_] = q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] -
    n *  $\delta$ [j] * r[1, j, t] -
    TRYleak * Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * r[1, j, t];
  For[nn = 2, nn ≤ n - TRYm, nn++,
    drdt[nn, j_, t_] = n *  $\delta$ [j] * r[nn - 1, j, t] - n *  $\delta$ [j] * r[nn, j, t] -
      TRYleak * Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * r[nn, j, t];
  ];
  For[nn = n + 1 - TRYm, nn ≤ n, nn++,
    drdt[nn, j_, t_] =
      n *  $\delta$ [j] * r[nn - 1, j, t] - Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] -
      TRYleak * Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * r[nn, j, t] -
      n *  $\delta$ [j] * r[nn, j, t];
  ];
  pars = { $\beta$ [j_, 1] →  $\beta V$ ,  $\beta$ [j_, 2] →  $\beta$ ,  $\delta$ [1] →  $\delta Y$ ,  $\delta$ [2] →  $\delta 0$ ,  $\kappa$ [j_, jj_] →  $\kappa$ };
  frac[1, 1] = (1 - older) (1 - f);
  frac[2, 1] = older (1 - f);
  frac[1, 2] = (1 - older) f;
  frac[2, 2] = older f;
  nvars = Drop[Flatten[Table[{s[j, t], Table[i[j, jj, t], {jj, 1, stages}],
    Table[r[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
  r[n, ages, t_] = 1 - Total[nvars];
  neqns = Drop[Flatten[Table[{D[s[j, t], t] == dsdt[j, t],
    Table[D[i[j, jj, t], t] == didt[j, jj, t], {jj, 1, stages}],
    Table[D[r[nn, j, t], t] == drdt[nn, j, t], {nn, 1, n}]}], {j, 1, ages}]], -1];
  nstart = Drop[Flatten[Table[{
    Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
    s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0, Table[r[nn, j, 0] ==
      (frac[j, 1] + frac[j, 2])  $\frac{r0}{n}$ , {nn, 1, n}]}], {j, 1, ages}]], /. start, -1];
  NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
]

```

```
In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
```

```
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}
```

```
In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};
```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],  
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

```
Out[ ]:= {■, ■, ■, ■}
```

```
In[ ]:= coltab = Join[{1 → {0, colours[[1]]}},  
  Table[{i → {{i - 1}, colours[[i]]}}, {i, 2, Length[all]}],  
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

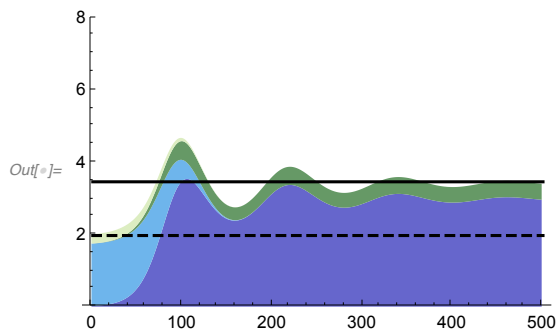
```
(  
  <70,Res    ■  
  <70,Mutant ■  
  70+,Res    ■  
  70+,Mutant ■  
)
```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRY $\beta$ , TRY $\beta$ V, TRY $\delta$ , TRY $\delta$ 0, TRY $\kappa$ , TRYconvert};
```

```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```
In[ ]:= plot1 = Show[  
  Plot[  
    Evaluate@Table[Sum[100 i[all[[c, 1]], all[[c, 2]], t] /. solution[partemp, start],  
      {c, 1, jcum}], {jcum, 1, Length[all]}],  
    {t, 0, maxtime}, PlotRange → {Automatic, {0, maxy}},  
    PlotStyle → None, Filling → {{1 → {0, ■}}, {2 → {{1}, ■}},  
      {3 → {{2}, ■}}, {4 → {{3}, ■}}}],  
    Plot[100 TRYinf, {t, 0, maxtime}, PlotStyle → {Black, Dashed}],  
    Plot[100 neweq, {t, 0, maxtime}, PlotStyle → {Black}],  
    ImageSize → 250  
  ]
```



Mutant fraction change between t=0 and t=50:

```
In[ ]:= 
$$\frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]}$$
 /. solution[partemp, start] /. t → 50
```

```
Out[ ]:= {0.223271}
```

```
In[ ]:= Solve[Exp[s 50] == 
$$\left( \frac{p50 / (1 - p50)}{p0 / (1 - p0)} \right) /. p50 \rightarrow \% /. p0 \rightarrow 1 - \text{TRYf}$$
, s][[1]]
```

 **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```
Out[ ]:= {s → 0.0669682}
```

This is consistent with the predicted selection coefficient (updating the last part for the leaky model):

```
In[ ]:= 
$$\frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \text{Sum}[R[j, t], \{j, 1 + \text{TRY}n - \text{TRY}m, \text{TRY}n\}] \text{TRY}\beta V /. \text{startme} /. \\ I1[t] \rightarrow \text{TRY}inf /. \delta \rightarrow \text{TRY}\delta /. \kappa \rightarrow \text{TRY}\kappa /. \text{leak} \rightarrow \text{TRY}leak /. \beta1 \rightarrow \text{TRY}\beta V // N$$

```

```
Out[ ]:= 0.0666864
```

New equilibrium:

```
In[ ]:= neweq // N
```

```
Out[ ]:= 0.034828
```

% rise in the endemic equilibrium:

```
In[ ]:= 
$$100 * \frac{(\% - \text{TRY}inf)}{\text{TRY}inf}$$

```

```
Out[ ]:= 74.1399
```

```
In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];
```

Alternative: SIR model (with leaky variants)

→ Consistent results (accounting for impact on resistant classes)

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

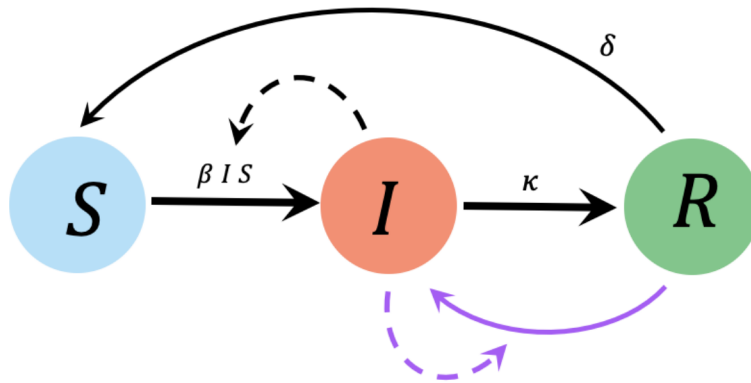


Figure S2A: more transmissible (equivalent to $n=1$ explored above)

```
In[ ]:= maxtime = 500;
```

```
maxy = 8;
```

Parameters:

```
In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
```

```
TRYf = 99 / 100; (*Starting fraction of resident*)
```

```
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
```

```
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
```

```
TRYκ = 1 / 5; (*Five day infectious period*)
```

```
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
```

```
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
```

```
TRYconvert = 10 / 10;
```

```
(*Only this fraction of cases seroconvert or boost immunity*)
```

```
TRYleak = 0;
```

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

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

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

```
In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
```

$$\text{TRY}\beta = \frac{\text{TRY}\delta \text{ TRY}\kappa}{\text{TRY}\delta - \text{TRYinf } \text{TRY}\delta - \text{TRYconvert } \text{TRYinf } \text{TRY}\kappa};$$

$$\frac{\text{TRY}\beta}{\text{TRY}\kappa} // N$$

```
Out[ ]:= 2.08333
```

Variant has a higher transmissibility (set to have the same selection coefficient as for the immune

evasive variant):

$$\text{In}[*]:= \text{Flatten}\left[\text{Solve}\left[\frac{\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa == 0.0833, \beta V\right]\right]$$

$$\text{Out}[*]:= \{\beta V \rightarrow 0.590208\}$$

$$\text{In}[*]:= \text{TRY}\beta V = \beta V /. \%;$$

% increase in β :

$$\text{In}[*]:= 100 * \frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta}$$

$$\text{Out}[*]:= 41.65$$

and now has no immune evasive properties (neither the resident nor the variant can infect individuals in the RL class).

New equilibrium is the same as in the SIR_n model when there is no leakiness:

$$\text{In}[*]:= \text{Limit}\left[\frac{\text{leak } \beta 2 - \delta - \kappa + \sqrt{\text{leak}^2 \beta 2^2 + 2 \text{leak } \beta 2 (\delta - \kappa) - 4 \text{leak } \delta \kappa + (\delta + \kappa)^2}}{2 \text{leak } \beta 2} /. \beta 2 \rightarrow \text{TRY}\beta V /. \delta \rightarrow \text{TRY}\delta /. \kappa \rightarrow \text{TRY}\kappa, \text{leak} \rightarrow 0\right]$$

$$\text{Out}[*]:= 0.0254283$$

$$\text{In}[*]:= \left(\frac{\text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}\right)$$

$$\text{Out}[*]:= 0.0254283$$

Starting equilibrium would be ($r0$ includes all of the resistance classes):

$$\left\{s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)}\right\}$$

$$\text{In}[*]:= \text{start} = \left\{s0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, r0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}\right\}$$

$$\text{Out}[*]:= \left\{s0 \rightarrow \frac{12}{25}, i0 \rightarrow \frac{1}{50}, r0 \rightarrow \frac{1}{2}\right\}$$

[NOTE: For the ease of colouring, the first stage class is the variant.]

$$\text{In}[*]:= \{\text{ages} = 2, \text{stages} = 2\};$$

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta O$ _,  $\kappa$ _, q_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta O$ ,  $\kappa$ , q}, start] =
    Block[{ages = 2, stages = 2},
      dsdt[j_, t_] = (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] +  $\delta$ [j] * r[j, t] -
        Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = TRYleak Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t] +
        Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 1] * i[j, 1, t];
      didt[j_, 2, t_] =
        Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 2] * i[j, 2, t];
      drdt[j_, t_] = q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] -
         $\delta$ [j] * r[j, t] - TRYleak Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t];
      pars = { $\beta$ [j_, 1]  $\rightarrow$   $\beta V$ ,  $\beta$ [j_, 2]  $\rightarrow$   $\beta$ ,  $\delta$ [1]  $\rightarrow$   $\delta Y$ ,  $\delta$ [2]  $\rightarrow$   $\delta O$ ,  $\kappa$ [j_, jj_]  $\rightarrow$   $\kappa$ };
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[
        {s[j, t], Table[i[j, jj, t], {jj, 1, stages}], r[j, t]}, {j, 1, ages}]], -1];
      r[ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[
        Table[{D[s[j, t], t] == dsdt[j, t], Table[D[i[j, jj, t], t] == didt[j, jj, t],
          {jj, 1, stages}], D[r[j, t], t] == drdt[j, t]}, {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0,
        r[j, 0] == (frac[j, 1] + frac[j, 2]) r0}, {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};

In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}

Out[ ]:= {, , , }

```

```

In[ ]:= coltab = Join[{{1 -> {0, colours[[1]]}}},
  Table[{i -> {{i - 1}, colours[[i]]}}, {i, 2, Length[all]}]];
Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm

```

Out[]:=MatrixForm=

```

(
  <70,Res    (blue square)
  <70,Mutant  (light blue square)
  70+,Res     (green square)
  70+,Mutant  (light green square)
)

```

```

In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};

```

```

In[ ]:= solution[partemp, start];

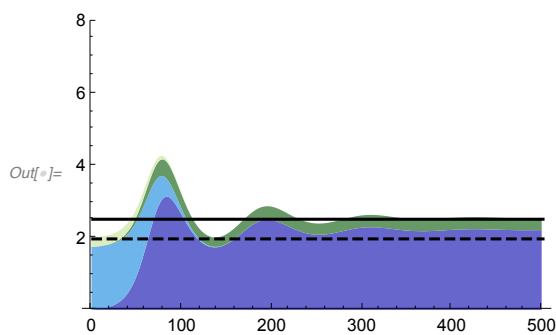
```

Showing the % of the population infectious:

```

In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> None, Filling -> {{1 -> {0, (blue square)}}, {2 -> {{1}, (light blue square)}},
    {3 -> {{2}, (green square)}}, {4 -> {{3}, (light green square)}}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
    PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Mutant fraction change between t=0 and t=50:

```

In[ ]:= 
$$\frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]} /. \text{solution}[\text{partemp}, \text{start}] /. t \rightarrow 50$$


```

Out[]:= {0.381045}

```
In[ ]:= Solve[Exp[s 50] == (p50 / (1 - p50) /. p50 -> % /. p0 -> 1 - TRYf), s][[1]]
```

--- **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```
Out[ ]:= {s -> 0.0822001}
```

This is consistent with the predicted selection coefficient:

```
In[ ]:= (TRYβV - TRYβ) / TRYβ * TRYκ + TRYleak * (TRYκ TRYconvert (TRYβ - TRYκ) / (TRYβ (TRYδ + TRYκ TRYconvert))) * TRYβV // N
```

```
Out[ ]:= 0.0833
```

New equilibrium:

```
In[ ]:= (TRYδ (TRYβV - TRYκ) / (TRYβV (TRYδ + TRYκ TRYconvert))) // N
```

```
Out[ ]:= 0.0254283
```

% rise in the endemic equilibrium:

```
In[ ]:= 100 * ((% - TRYinf) / TRYinf)
```

```
Out[ ]:= 27.1417
```

```
In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];
```

Figure S3A: more transmissible & immune evasive (variant causes leakiness: R class 10% as infective as S class)

```
In[ ]:= maxtime = 500;
```

```
maxy = 12;
```

Parameters:

```
In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
```

```
TRYf = 99 / 100; (*Starting fraction of resident*)
```

```
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
```

```
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
```

```
TRYκ = 1 / 5; (*Five day infectious period*)
```

```
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
```

```
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
```

```
TRYconvert = 10 / 10;
```

```
(*Only this fraction of cases seroconvert or boost immunity*)
```

```
TRYleak = 1 / 10;
```

```
i -> δ (β - κ) / β (δ + q κ)
```

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

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

$\text{In}[*]:= \text{TRYinf} = 1 / 50; (*\text{Assumed initial endemic frequency of infected individuals}*)$

$$\text{TRY}\beta = \frac{\text{TRY}\delta \text{TRY}\kappa}{\text{TRY}\delta - \text{TRYinf } \text{TRY}\delta - \text{TRYconvert } \text{TRYinf } \text{TRY}\kappa};$$

$$\frac{\text{TRY}\beta}{\text{TRY}\kappa} // \text{N}$$

$\text{Out}[*]= 2.08333$

Variant has a higher transmissibility (set to have the same selection coefficient as for the immune evasive variant):

$$\text{In}[*]:= \text{Flatten}\left[\text{Solve}\left[\text{TRYleak} \left(1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}\right) \beta V + \frac{\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa = 0.0833, \beta V\right]\right]$$

$\text{Out}[*]= \{\beta V \rightarrow 0.534528\}$

$\text{In}[*]:= \text{TRY}\beta V = \beta V /. \%;$

% increase in β :

$$\text{In}[*]:= 100 * \frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta}$$

$\text{Out}[*]= 28.2868$

and now has some immune evasive properties (through leaky immunity)

New equilibrium:

$$\text{In}[*]:= \text{neweq} = \frac{\text{leak } \beta 2 - \delta - \kappa + \sqrt{\text{leak}^2 \beta 2^2 + 2 \text{leak } \beta 2 (\delta - \kappa) - 4 \text{leak } \delta \kappa + (\delta + \kappa)^2}}{2 \text{leak } \beta 2} /. \beta 2 \rightarrow \text{TRY}\beta V /. \kappa \rightarrow \text{TRY}\kappa /. \delta \rightarrow \text{TRY}\delta /. \text{leak} \rightarrow \text{TRYleak}$$

$\text{Out}[*]= 0.0320409$

Starting equilibrium would be (r0 includes all of the resistance classes):

$$\left\{s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)}\right\}$$

$$\text{In[]:= start} = \left\{ s_0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i_0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, \right. \\ \left. r_0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right\}$$

$$\text{Out[]:= } \left\{ s_0 \rightarrow \frac{12}{25}, i_0 \rightarrow \frac{1}{50}, r_0 \rightarrow \frac{1}{2} \right\}$$

[NOTE: For the ease of colouring, the first stage class is the variant.]

`In[ ]:= {ages = 2, stages = 2};`

```
In[ ]:= Clear[solution]
solution[{p_, f_, older_, β_, βV_, δY_, δ0_, κ_, q_}, start] :=
  solution[{p, f, older, β, βV, δY, δ0, κ, q}, start] =
    Block[{ages = 2, stages = 2},
      dsdt[j_, t_] = (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] + δ[j] * r[j, t] -
        Sum[β[k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = TRYleak Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t] +
        Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] - κ[j, 1] * i[j, 1, t];
      didt[j_, 2, t_] =
        Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] - κ[j, 2] * i[j, 2, t];
      drdt[j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] -
        δ[j] * r[j, t] - TRYleak Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t];
      pars = {β[j_, 1] → βV, β[j_, 2] → β, δ[1] → δY, δ[2] → δ0, κ[j_, jj_] → κ};
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[
        {s[j, t], Table[i[j, jj, t], {jj, 1, stages}], r[j, t]}, {j, 1, ages}]], -1];
      r[ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[
        Table[{D[s[j, t], t] == dsdt[j, t], Table[D[i[j, jj, t], t] == didt[j, jj, t],
          {jj, 1, stages}], D[r[j, t], t] == drdt[j, t]}, {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0,
        r[j, 0] == (frac[j, 1] + frac[j, 2]) r0}, {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]
```

`In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]`

`Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}`

`In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};`

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

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

```
In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1, colours[[i]]}}, {i, 2, Length[all]}]];
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

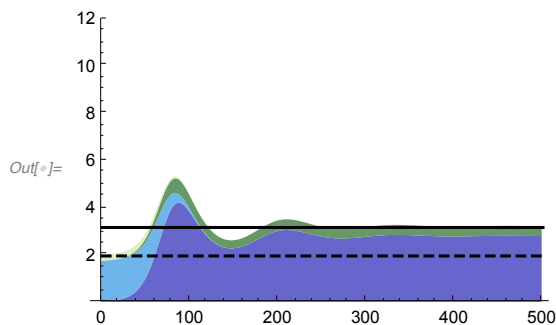
```
( <70,Res <70,Mutant
  70+,Res 70+,Mutant )
```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};
```

```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```
In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> None, Filling -> {{1 -> {0, }}, {2 -> {{1, }},
    {3 -> {{2, }}, {4 -> {{3, }}}}},
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
  PlotStyle -> {Black, Dashed}],
  Plot[100 neweq, {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]
```



Mutant fraction change between t=0 and t=50:

```
In[ ]:= 
$$\frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]} /. \text{solution}[\text{partemp}, \text{start}] /. t \rightarrow 50$$

```

```
Out[ ]:= {0.388291}
```

```
In[ ]:= Solve[Exp[s 50] ==  $\left( \frac{p50 / (1 - p50)}{p0 / (1 - p0)} \right) /. p50 \rightarrow \% /. p0 \rightarrow 1 - \text{TRYf}$ , s][[1]]
```

 **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```
Out[ ]:= {s -> 0.0828123}
```

This is consistent with the predicted selection coefficient:

```
In[ ]:= 
$$\frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \text{TRY}\text{leak} \left( \frac{\text{TRY}\kappa \text{TRYconvert} (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right) \text{TRY}\beta V // N$$

```

```
Out[ ]:= 0.0833
```

% rise in the endemic equilibrium:

```
In[ ]:= 100 * 
$$\frac{(\text{neweq} - \text{TRYinf})}{\text{TRYinf}}$$

```

```
Out[ ]:= 60.2045
```

```
In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];
```

Figure S3B: more transmissible & immune evasive (variant causes leakiness: R class 20% as infective as S class)

```
In[ ]:= maxtime = 500;
```

```
maxy = 12;
```

Parameters:

```
In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
```

```
TRYf = 99 / 100; (*Starting fraction of resident*)
```

```
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
```

```
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
```

```
TRYκ = 1 / 5; (*Five day infectious period*)
```

```
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
```

```
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
```

```
TRYconvert = 10 / 10;
```

```
(*Only this fraction of cases seroconvert or boost immunity*)
```

```
TRYleak = 1 / 5;
```

```
i -> 
$$\frac{\delta (\beta - \kappa)}{\beta (\delta + \eta \kappa)}$$

```

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

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

$In[] := \text{TRYinf} = 1 / 50; (*\text{Assumed initial endemic frequency of infected individuals}*)$

$$\text{TRY}\beta = \frac{\text{TRY}\delta \text{TRY}\kappa}{\text{TRY}\delta - \text{TRYinf} \text{TRY}\delta - \text{TRYconvert} \text{TRYinf} \text{TRY}\kappa};$$

$$\frac{\text{TRY}\beta}{\text{TRY}\kappa} // N$$

$Out[] := 2.08333$

Variant has a higher transmissibility (set to have the same selection coefficient as for the immune evasive variant):

$$In[] := \text{Flatten}\left[\text{Solve}\left[\text{TRYleak} \left(1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}\right) \beta V + \frac{\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa = 0.0833, \beta V\right]\right]$$

$Out[] := \{\beta V \rightarrow 0.488448\}$

$In[] := \text{TRY}\beta V = \beta V /. \%;$

% increase in β :

$$In[] := 100 * \frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta}$$

$Out[] := 17.2276$

and now has some immune evasive properties (through leaky immunity)

New equilibrium:

$$In[] := \text{neweq} = \frac{\text{leak } \beta 2 - \delta - \kappa + \sqrt{\text{leak}^2 \beta 2^2 + 2 \text{leak } \beta 2 (\delta - \kappa) - 4 \text{leak } \delta \kappa + (\delta + \kappa)^2}}{2 \text{leak } \beta 2} /. \beta 2 \rightarrow \text{TRY}\beta V /. \kappa \rightarrow \text{TRY}\kappa /. \delta \rightarrow \text{TRY}\delta$$

$\delta \rightarrow \text{TRY}\delta /. \kappa \rightarrow \text{TRY}\kappa /. \text{leak} \rightarrow \text{TRYleak}$

$Out[] := 0.0413158$

Starting equilibrium would be (r0 includes all of the resistance classes):

$$\left\{s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)}\right\}$$

$$In[] := \text{start} = \left\{ s_0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i_0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, \right. \\ \left. r_0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right\}$$

$$Out[] := \left\{ s_0 \rightarrow \frac{12}{25}, i_0 \rightarrow \frac{1}{50}, r_0 \rightarrow \frac{1}{2} \right\}$$

[NOTE: For the ease of colouring, the first stage class is the variant.]

```
In[ ] := {ages = 2, stages = 2};
```

```
In[ ] := Clear[solution]
solution[{p_, f_, older_, β_, βV_, δY_, δ0_, κ_, q_}, start] :=
  solution[{p, f, older, β, βV, δY, δ0, κ, q}, start] =
    Block[{ages = 2, stages = 2},
      dsdt[j_, t_] = (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] + δ[j] * r[j, t] -
        Sum[β[k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = TRYleak Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t] +
        Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] - κ[j, 1] * i[j, 1, t];
      didt[j_, 2, t_] =
        Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] - κ[j, 2] * i[j, 2, t];
      drdt[j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] -
        δ[j] * r[j, t] - TRYleak Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t];
      pars = {β[j_, 1] → βV, β[j_, 2] → β, δ[1] → δY, δ[2] → δ0, κ[j_, jj_] → κ};
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[
        {s[j, t], Table[i[j, jj, t], {jj, 1, stages}], r[j, t]}, {j, 1, ages}]], -1];
      r[ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[
        Table[{D[s[j, t], t] == dsdt[j, t], Table[D[i[j, jj, t], t] == didt[j, jj, t],
          {jj, 1, stages}], D[r[j, t], t] == drdt[j, t]}, {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0,
        r[j, 0] == (frac[j, 1] + frac[j, 2]) r0}, {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]
```

```
In[ ] := all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
```

```
Out[ ] := {{1, 1}, {1, 2}, {2, 1}, {2, 2}}
```

```
In[ ] := labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};
```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

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

```
In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1, colours[[i]]}}, {i, 2, Length[all]}]];
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

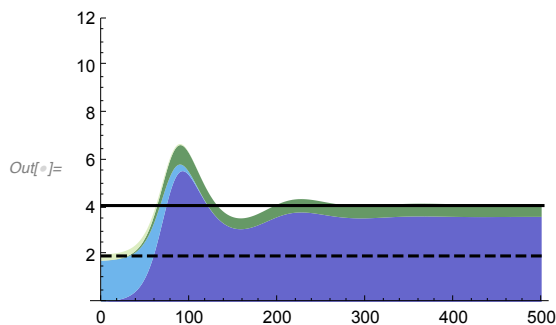
```
( <70,Res <70,Mutant
  70+,Res 70+,Mutant )
```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};
```

```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```
In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> None, Filling -> {{1 -> {0, }}, {2 -> {{1, }},
    {3 -> {{2, }}, {4 -> {{3, }}}}},
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
  PlotStyle -> {Black, Dashed}],
  Plot[100 neweq, {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]
```



Mutant fraction change between t=0 and t=50:

```
In[ ]:= 
$$\frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]}$$
 /. solution[partemp, start] /. t → 50
```

```
Out[ ]:= {0.393131}
```

```
In[ ]:= Solve[Exp[s 50] == 
$$\left( \frac{p50 / (1 - p50)}{p0 / (1 - p0)} \right) /. p50 \rightarrow \% /. p0 \rightarrow 1 - \text{TRYf}$$
, s][[1]]
```

 **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```
Out[ ]:= {s → 0.083219}
```

This is consistent with the predicted selection coefficient:

```
In[ ]:= 
$$\frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \text{TRY}\text{leak} \left( \frac{\text{TRY}\kappa \text{TRYconvert} (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right) \text{TRY}\beta V // N$$

```

```
Out[ ]:= 0.0833
```

% rise in the endemic equilibrium:

```
In[ ]:= 100 * 
$$\frac{(\text{neweq} - \text{TRYinf})}{\text{TRYinf}}$$

```

```
Out[ ]:= 106.579
```

```
In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];
```

Figure S3C: persistently immune evasive (variant causes leakiness: R class 40% as infective as S class)

```
In[ ]:= maxtime = 500;
```

```
maxy = 12;
```

Parameters:

```
In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
```

```
TRYf = 99 / 100; (*Starting fraction of resident*)
```

```
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
```

```
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
```

```
TRYκ = 1 / 5; (*Five day infectious period*)
```

```
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
```

```
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
```

```
TRYconvert = 10 / 10;
```

```
(*Only this fraction of cases seroconvert or boost immunity*)
```

```
TRYleak = 2 / 5;
```

```
i → 
$$\frac{\delta (\beta - \kappa)}{\beta (\delta + \eta \kappa)}$$

```

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

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

$\text{In}[*]:= \text{TRYinf} = 1 / 50; (*\text{Assumed initial endemic frequency of infected individuals}*)$

$$\text{TRY}\beta = \frac{\text{TRY}\delta \text{TRY}\kappa}{\text{TRY}\delta - \text{TRYinf} \text{TRY}\delta - \text{TRYconvert} \text{TRYinf} \text{TRY}\kappa};$$

$$\frac{\text{TRY}\beta}{\text{TRY}\kappa} // \text{N}$$

$\text{Out}[*]:= 2.08333$

Variant has the same transmissibility:

$\text{In}[*]:= \text{TRY}\beta\text{V} = \text{TRY}\beta;$

but infects earlier during waning by allowing leaky immunity.

New equilibrium:

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

$$\frac{\text{leak } \beta 2 - \delta - \kappa + \sqrt{\text{leak}^2 \beta 2^2 + 2 \text{leak } \beta 2 (\delta - \kappa) - 4 \text{leak } \delta \kappa + (\delta + \kappa)^2}}{2 \text{leak } \beta 2} /. \text{leak} \rightarrow \text{TRYleak} /.$$

$$\beta 2 \rightarrow \text{TRY}\beta\text{V} /. \delta \rightarrow \text{TRY}\delta /. \kappa \rightarrow \text{TRY}\kappa // \text{N}$$

$\text{Out}[*]:= 0.0768382$

Starting equilibrium would be (r0 includes all of the resistance classes):

$$\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)} \right\}$$

$$\text{In}[*]:= \text{start} = \left\{ s0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, \right.$$

$$\left. r0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right\}$$

$$\text{Out}[*]:= \left\{ s0 \rightarrow \frac{12}{25}, i0 \rightarrow \frac{1}{50}, r0 \rightarrow \frac{1}{2} \right\}$$

[NOTE: For the ease of colouring, the first stage class is the variant.]

$\text{In}[*]:= \{\text{ages} = 2, \text{stages} = 2\};$

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta O$ _,  $\kappa$ _, q_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta O$ ,  $\kappa$ , q}, start] =
    Block[{ages = 2, stages = 2},
      dsdt[j_, t_] = (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] +  $\delta$ [j] * r[j, t] -
        Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = TRYleak Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t] +
        Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 1] * i[j, 1, t];
      didt[j_, 2, t_] =
        Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 2] * i[j, 2, t];
      drdt[j_, t_] = q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] -
         $\delta$ [j] * r[j, t] - TRYleak Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t];
      pars = { $\beta$ [j_, 1]  $\rightarrow$   $\beta V$ ,  $\beta$ [j_, 2]  $\rightarrow$   $\beta$ ,  $\delta$ [1]  $\rightarrow$   $\delta Y$ ,  $\delta$ [2]  $\rightarrow$   $\delta O$ ,  $\kappa$ [j_, jj_]  $\rightarrow$   $\kappa$ };
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[
        {s[j, t], Table[i[j, jj, t], {jj, 1, stages}], r[j, t]}, {j, 1, ages}]], -1];
      r[ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[
        Table[{D[s[j, t], t] == dsdt[j, t], Table[D[i[j, jj, t], t] == didt[j, jj, t],
          {jj, 1, stages}], D[r[j, t], t] == drdt[j, t]}, {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0,
        r[j, 0] == (frac[j, 1] + frac[j, 2]) r0}, {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};

In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}

Out[ ]:= {, , , }

```

```

In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1, colours[[i]]}}, {i, 2, Length[all]}]];
Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm

```

Out[]//MatrixForm=

```

(
  <70,Res    (blue square)
  <70,Mutant  (light blue square)
  70+,Res     (green square)
  70+,Mutant  (light green square)
)

```

```

In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};

```

```

In[ ]:= solution[partemp, start];

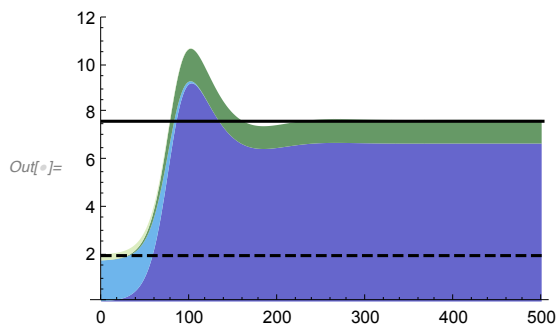
```

Showing the % of the population infectious:

```

In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> None, Filling -> {{1 -> {0, (blue square)}}, {2 -> {{1}, (light blue square)}},
    {3 -> {{2}, (green square)}}, {4 -> {{3}, (light green square)}}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
    PlotStyle -> {Black, Dashed}],
  Plot[100 neweq, {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Mutant fraction change between t=0 and t=50:

```

In[ ]:= 
$$\frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]}$$
 /. solution[partemp, start] /. t -> 50

```

Out[]:= {0.398831}

```
In[ ]:= Solve[Exp[s 50] ==  $\left( \frac{p50 / (1 - p50)}{p0 / (1 - p0)} \right) /. p50 \rightarrow \% /. p0 \rightarrow 1 - TRYf$ , s] [[1]]
```

 **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```
Out[ ]:= {s -> 0.0836956}
```

This is consistent with the predicted selection coefficient:

```
In[ ]:= 
$$\frac{TRY\beta V - TRY\beta}{TRY\beta} TRY\kappa + TRYleak \left( \frac{TRY\kappa TRYconvert (TRY\beta - TRY\kappa)}{TRY\beta (TRY\delta + TRY\kappa TRYconvert)} \right) TRY\beta V // N$$

```

```
Out[ ]:= 0.0833333
```

% rise in the endemic equilibrium:

```
In[ ]:= 100 * 
$$\frac{(neweq - TRYinf)}{TRYinf}$$

```

```
Out[ ]:= 284.191
```

The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRY\beta, TRY\beta V,  $\frac{8}{10} TRY\delta$ ,  $\frac{8}{10} TRY\delta 0$ , TRY\kappa,  $\frac{8}{10}}$ ;
```

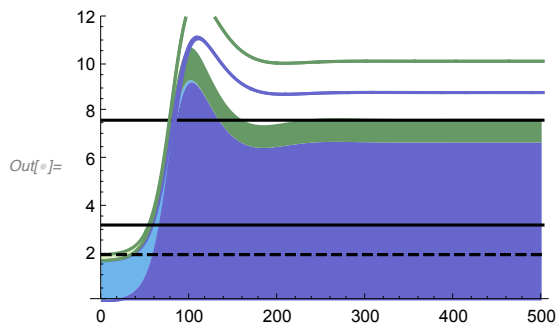
```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {■, ■, ■, ■}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}\delta}{1-\text{TRY}\kappa} (\text{TRY}\beta\text{V} - \text{TRY}\kappa)}{\text{TRY}\beta\text{V} \left( \frac{\text{TRY}\delta}{1-\text{TRY}\kappa} + \text{TRY}\kappa \text{TRYconvert} \right)}$ , {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Seroconversion affects the dynamics (curves compared to the previous shaded plot) but not the initial speed of spread of the variant (described by the selection coefficient) or the equilibrium.

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```

Alt Figure S3A: more transmissible & immune evasive (resident and variant leaky)

```

In[ ]:= maxtime = 500;

```

```

maxy = 20;

```

Parameters:

```

In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
TRYf = 99 / 100; (*Starting fraction of resident*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10;
(*Only this fraction of cases seroconvert or boost immunity*)
TRYleak = 1 / 10;
TRYleakV = 0.153;

In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
Now the equilibrium must be numerically calculated:

```

```

In[ ]:= Simplify[Solve[{0 == δ R - β1 S I1,
    0 == β1 S I1 + ξ1 β1 R I1 - κ I1,
    0 == κ I1 - δ R - ξ1 β1 R I1,
    1 == S + I1 + R}], {S, I1, R}], {β1 > 0, ξ1 > 0, δ > 0, κ > 0}]

Out[ ]:= { {S → 1, I1 → 0, R → 0}, {S →  $\frac{\delta - \kappa + \beta_1 \xi_1 + \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 (-1 + \xi_1)}$ ,
    I1 →  $-\frac{\delta + \kappa - \beta_1 \xi_1 + \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 \xi_1}$ ,
    R →  $-\frac{\delta + \kappa + \beta_1 \xi_1 - 2 \kappa \xi_1 + \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 (-1 + \xi_1) \xi_1}$  } },
    {S →  $\frac{\delta - \kappa + \beta_1 \xi_1 - \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 (-1 + \xi_1)}$ ,
    I1 →  $\frac{-\delta - \kappa + \beta_1 \xi_1 + \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 \xi_1}$ ,
    R →  $-\frac{\delta + \kappa + \beta_1 \xi_1 - 2 \kappa \xi_1 - \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 (-1 + \xi_1) \xi_1}$  } } }

```

```

In[ ]:= startme = %[[3]];

```

Finding the value of β that gives the target incidence (TRYinf):

```

In[ ]:= Solve[
    (S + I1 + R /. I1 -> TRYinf /. startme /. δ -> TRYδ /. κ -> TRYκ /. ξ1 -> TRYleak) == 1, β1]

Out[ ]:= { {β1 →  $\frac{2}{49} (-24 - \sqrt{1066})$  }, {β1 →  $\frac{2}{49} (-24 + \sqrt{1066})$  } }

```

In[]:= $\text{TRY}\beta = \beta 1 / . \% [2]$

Out[]:= $\frac{2}{49} (-24 + \sqrt{1066})$

In[]:= $(\ast \text{TRY}\beta = \frac{\text{TRY}\delta \text{ TRY}\kappa}{\text{TRY}\delta - \text{TRYinf} \text{ TRY}\delta - \text{TRYconvert} \text{ TRYinf} \text{ TRY}\kappa}; \ast)$

$\frac{\text{TRY}\beta}{\text{TRY}\kappa} // \text{N}$

Out[]:= 1.76524

Starting equilibrium would be:

In[]:= $\text{start} = \{\text{s0} \rightarrow \text{S}, \text{i0} \rightarrow \text{I1}, \text{r0} \rightarrow \text{R}\} /. \text{startme} /. \delta \rightarrow \text{TRY}\delta /. \kappa \rightarrow \text{TRY}\kappa /. \xi 1 \rightarrow \text{TRYleak} /. \beta 1 \rightarrow \text{TRY}\beta;$

$\text{N}[\text{start}]$

Out[]:= $\{\text{s0} \rightarrow 0.520552, \text{i0} \rightarrow 0.02, \text{r0} \rightarrow 0.459448\}$

Variant has a higher transmissibility (set to have the same selection coefficient as for the immune evasive variant):

In[]:= $\text{Flatten}[\text{Solve}[(\text{TRYleakV} - \text{TRYleak}) (\text{r0} /. \text{start}) \beta \text{V} + \frac{\beta \text{V} - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa == 0.0833, \beta \text{V}]]$

Out[]:= $\{\beta \text{V} \rightarrow 0.479481\}$

In[]:= $\text{TRY}\beta \text{V} = \beta \text{V} / . \%;$

and infects earlier during waning by allowing leaky immunity.

New equilibrium:

In[]:= $\text{neweq} = \frac{-\delta - \kappa + \beta 1 \xi 1 + \sqrt{\delta^2 + (\kappa - \beta 1 \xi 1)^2 + 2 \delta (\kappa + \beta 1 \xi 1 - 2 \kappa \xi 1)}}{2 \beta 1 \xi 1} /. \xi 1 \rightarrow \text{TRYleakV} /. \beta 1 \rightarrow \text{TRY}\beta \text{V} /. \delta \rightarrow \text{TRY}\delta /. \kappa \rightarrow \text{TRY}\kappa // \text{N}$

Out[]:= 0.0340037

[NOTE: For the ease of colouring, the first stage class is the variant.]

In[]:= $\{\text{ages} = 2, \text{stages} = 2\};$

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta O$ _,  $\kappa$ _, q_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta O$ ,  $\kappa$ , q}, start] =
    Block[{ages = 2, stages = 2},
      dsdt[j_, t_] = (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] +  $\delta$ [j] * r[j, t] -
        Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = TRYleakV Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t] +
        Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 1] * i[j, 1, t];
      didt[j_, 2, t_] = TRYleak Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * r[j, t] +
        Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 2] * i[j, 2, t];
      drdt[j_, t_] = q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] -
         $\delta$ [j] * r[j, t] - TRYleakV Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t] -
        TRYleak Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * r[j, t];
      pars = { $\beta$ [j_, 1]  $\rightarrow$   $\beta V$ ,  $\beta$ [j_, 2]  $\rightarrow$   $\beta$ ,  $\delta$ [1]  $\rightarrow$   $\delta Y$ ,  $\delta$ [2]  $\rightarrow$   $\delta O$ ,  $\kappa$ [j_, jj_]  $\rightarrow$   $\kappa$ };
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[
        {s[j, t], Table[i[j, jj, t], {jj, 1, stages}], r[j, t]}, {j, 1, ages}]], -1];
      r[ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[
        Table[{D[s[j, t], t] == dsdt[j, t], Table[D[i[j, jj, t], t] == didt[j, jj, t],
          {jj, 1, stages}], D[r[j, t], t] == drdt[j, t]}, {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0,
        r[j, 0] == (frac[j, 1] + frac[j, 2]) r0}, {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
Out[ ]:= {}

```

```

In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1}, colours[[i]]}, {i, 2, Length[all]}]];
Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm

```

Out[]//MatrixForm=

```

(
  <70,Res    (dark blue square)
  <70,Mutant  (light blue square)
  70+,Res     (dark green square)
  70+,Mutant  (light green square)
)

```

```

In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};

```

```

In[ ]:= solution[partemp, start];

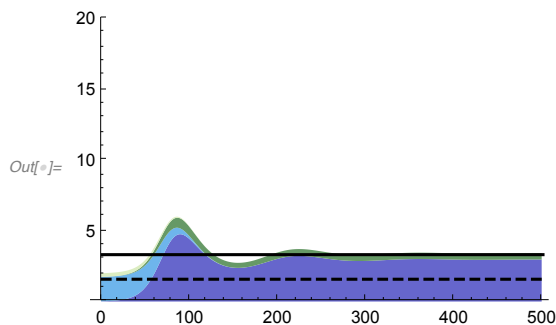
```

Showing the % of the population infectious:

```

In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> None, Filling -> {{1 -> {0, (dark blue square)}}, {2 -> {{1}, (light blue square)}},
    {3 -> {{2}, (dark green square)}}, {4 -> {{3}, (light green square)}}},
  Plot[100 * (TRYδ (TRYβ - TRYκ) / (TRYβ (TRYδ + TRYκ TRYconvert))), {t, 0, maxtime},
    PlotStyle -> {Black, Dashed}],
  Plot[100 neweq, {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Mutant fraction change between t=0 and t=50:

```

In[ ]:= (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}]) /. solution[partemp, start] /. t -> 50

```

Out[]:= {0.386835}

```
In[ ]:= Solve[Exp[s 50] == (p50 / (1 - p50) /. p50 -> % /. p0 -> 1 - TRYf), s][[1]]
```

... **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```
Out[ ]:= {s -> 0.0826897}
```

This is consistent with the predicted selection coefficient:

```
In[ ]:= (TRYβV - TRYβ) / TRYβ * TRYκ + (TRYleakV - TRYleak) (r0 /. start) TRYβV // N
```

```
Out[ ]:= 0.0833
```

Adjusted leakiness of variant to get target selection coefficient in Alt Figure S3C):

```
In[ ]:= Solve[
  ( (TRYβV - TRYβ) / TRYβ * TRYκ + (leakV - TRYleak) (r0 /. start) TRYβV == 0.0833 ), leakV]
```

```
Out[ ]:= {{leakV -> 0.613542}}
```

% rise in the endemic equilibrium:

```
In[ ]:= 100 * (neweq - TRYinf) / TRYinf
```

```
Out[ ]:= 70.0184
```

```
In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];
```

Alt Figure S3B: more transmissible & immune evasive (resident and variant leaky)

```
In[ ]:= maxtime = 500;
```

```
maxy = 20;
```

Parameters:

```
In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
```

```
TRYf = 99 / 100; (*Starting fraction of resident*)
```

```
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
```

```
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
```

```
TRYκ = 1 / 5; (*Five day infectious period*)
```

```
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
```

```
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
```

```
TRYconvert = 10 / 10;
```

```
(*Only this fraction of cases seroconvert or boost immunity*)
```

```
TRYleak = 1 / 10;
```

```
TRYleakV = 0.307;
```

In[*]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)

Now the equilibrium must be numerically calculated:

In[*]:= Simplify[Solve[{0 == δ R - β1 S I1,

$$0 = \beta_1 S I_1 + \xi_1 \beta_1 R I_1 - \kappa I_1,$$

$$0 == \kappa I_1 - \delta R - \xi_1 \beta_1 R I_1,$$

$$1 = S + I_1 + R], \{S, I_1, R\}], \{\beta_1 > 0, \xi_1 > 0, \delta > 0, \kappa > 0\}]$$

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

$$I_1 \rightarrow -\frac{\delta + \kappa - \beta_1 \xi_1 + \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 \xi_1},$$

$$R \rightarrow -\frac{\delta + \kappa + \beta_1 \xi_1 - 2 \kappa \xi_1 + \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 (-1 + \xi_1) \xi_1} \left. \right\},$$

$$\left\{ S \rightarrow \frac{\delta - \kappa + \beta_1 \xi_1 - \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 (-1 + \xi_1)}, \right.$$

$$I_1 \rightarrow \frac{-\delta - \kappa + \beta_1 \xi_1 + \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 \xi_1},$$

$$R \rightarrow -\frac{\delta + \kappa + \beta_1 \xi_1 - 2 \kappa \xi_1 - \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 (-1 + \xi_1) \xi_1} \left. \right\}$$

In[*]:= startme = %[[3]];

Finding the value of β that gives the target incidence (TRYinf):

In[*]:= Solve[

$$(S + I_1 + R /. I_1 \rightarrow \text{TRYinf} /. \text{startme} /. \delta \rightarrow \text{TRY}\delta /. \kappa \rightarrow \text{TRY}\kappa /. \xi_1 \rightarrow \text{TRY}\xi_1) == 1, \beta_1]$$

$$\text{Out[*]} = \left\{ \left\{ \beta_1 \rightarrow \frac{2}{49} (-24 - \sqrt{1066}) \right\}, \left\{ \beta_1 \rightarrow \frac{2}{49} (-24 + \sqrt{1066}) \right\} \right\}$$

In[*]:= TRYβ = β1 /. %[[2]]

$$\text{Out[*]} = \frac{2}{49} (-24 + \sqrt{1066})$$

In[*]:= (*TRYβ = $\frac{\text{TRY}\delta \text{ TRY}\kappa}{\text{TRY}\delta - \text{TRYinf} \text{ TRY}\delta - \text{TRYconvert} \text{ TRYinf} \text{ TRY}\kappa}$;*)

$$\frac{\text{TRY}\beta}{\text{TRY}\kappa} // N$$

$$\text{Out[*]} = 1.76524$$

Starting equilibrium would be:

```
In[ ]:= start = {s0 → S, i0 → I1, r0 → R} /. startme /. δ → TRYδ /. κ → TRYκ /. ξ1 → TRYleak /.  
β1 -> TRYβ;
```

```
N[  
start]
```

```
Out[ ]:= {s0 → 0.520552, i0 → 0.02, r0 → 0.459448}
```

Variant has a higher transmissibility (set to have the same selection coefficient as for the immune evasive variant):

```
In[ ]:= Flatten[Solve[(TRYleakV - TRYleak) (r0 /. start) βV +  $\frac{\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa = 0.0833, \beta V]$ ]
```

```
Out[ ]:= {βV → 0.428203}
```

```
In[ ]:= TRYβV = βV /. %;
```

and infects earlier during waning by allowing leaky immunity.

New equilibrium:

```
In[ ]:= neweq =  

$$\frac{-\delta - \kappa + \beta 1 \xi 1 + \sqrt{\delta^2 + (\kappa - \beta 1 \xi 1)^2 + 2 \delta (\kappa + \beta 1 \xi 1 - 2 \kappa \xi 1)}}{2 \beta 1 \xi 1} /. \xi 1 \rightarrow \text{TRYleakV} /. \beta 1 \rightarrow \text{TRY}\beta V /.  
δ \rightarrow \text{TRY}\delta /. \kappa \rightarrow \text{TRY}\kappa // N$$

```

```
Out[ ]:= 0.051199
```

[NOTE: For the ease of colouring, the first stage class is the variant.]

```
In[ ]:= {ages = 2, stages = 2};
```

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta O$ _,  $\kappa$ _, q_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta O$ ,  $\kappa$ , q}, start] =
    Block[{ages = 2, stages = 2},
      dsdt[j_, t_] = (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] +  $\delta$ [j] * r[j, t] -
        Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = TRYleakV Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t] +
        Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 1] * i[j, 1, t];
      didt[j_, 2, t_] = TRYleak Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * r[j, t] +
        Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 2] * i[j, 2, t];
      drdt[j_, t_] = q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] -
         $\delta$ [j] * r[j, t] - TRYleakV Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t] -
        TRYleak Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * r[j, t];
      pars = { $\beta$ [j_, 1]  $\rightarrow$   $\beta V$ ,  $\beta$ [j_, 2]  $\rightarrow$   $\beta$ ,  $\delta$ [1]  $\rightarrow$   $\delta Y$ ,  $\delta$ [2]  $\rightarrow$   $\delta O$ ,  $\kappa$ [j_, jj_]  $\rightarrow$   $\kappa$ };
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[
        {s[j, t], Table[i[j, jj, t], {jj, 1, stages}], r[j, t]}, {j, 1, ages}]], -1];
      r[ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[
        Table[{D[s[j, t], t] == dsdt[j, t], Table[D[i[j, jj, t], t] == didt[j, jj, t],
          {jj, 1, stages}], D[r[j, t], t] == drdt[j, t]}, {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0,
        r[j, 0] == (frac[j, 1] + frac[j, 2]) r0}, {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
Out[ ]:= {, , , }

```

```

In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1}, colours[[i]]}, {i, 2, Length[all]}]];
Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm

```

Out[]//MatrixForm=

```

( <70,Res    <70,Mutant  70+,Res    70+,Mutant
  {0,Blue}   {1,Blue}   {2,Green}   {3,LightGreen} )

```

```

In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};

```

```

In[ ]:= solution[partemp, start];

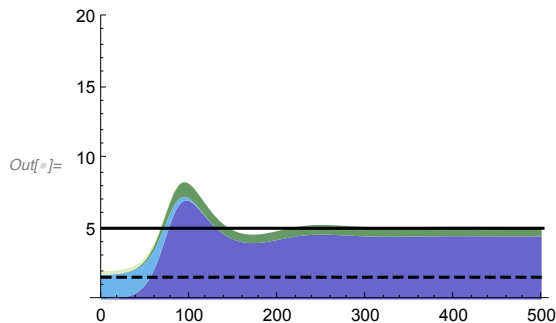
```

Showing the % of the population infectious:

```

In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> None, Filling -> {{1 -> {0, Blue}}, {2 -> {{1}, Blue}},
  {3 -> {{2}, Green}}, {4 -> {{3}, LightGreen}}}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
  PlotStyle -> {Black, Dashed}],
  Plot[100 neweq, {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Mutant fraction change between t=0 and t=50:

```

In[ ]:= 
$$\frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]}$$
 /. solution[partemp, start] /. t -> 50

```

Out[]:= {0.392738}

```
In[ ]:= Solve[Exp[s 50] == (p50 / (1 - p50) /. p50 -> % /. p0 -> 1 - TRYf), s][[1]]
```

... **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```
Out[ ]:= {s -> 0.0831861}
```

This is consistent with the predicted selection coefficient:

```
In[ ]:= (TRYβV - TRYβ) / TRYβ * TRYκ + (TRYleakV - TRYleak) (r0 /. start) TRYβV // N
```

```
Out[ ]:= 0.0833
```

Adjusted leakiness of variant to get target selection coefficient:

```
In[ ]:= Solve[
  ( (TRYβV - TRYβ) / TRYβ * TRYκ + (leakV - TRYleak) (r0 /. start) TRYβV == 0.0833 ), leakV]
```

```
Out[ ]:= {{leakV -> 0.613542}}
```

% rise in the endemic equilibrium:

```
In[ ]:= 100 * (neweq - TRYinf) / TRYinf
```

```
Out[ ]:= 155.995
```

```
In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];
```

Alt Figure S3C: persistently immune evasive (resident and variant leaky)

```
In[ ]:= maxtime = 500;
```

```
maxy = 20;
```

Parameters:

```
In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
```

```
TRYf = 99 / 100; (*Starting fraction of resident*)
```

```
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
```

```
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
```

```
TRYκ = 1 / 5; (*Five day infectious period*)
```

```
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
```

```
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
```

```
TRYconvert = 10 / 10;
```

```
(*Only this fraction of cases seroconvert or boost immunity*)
```

```
TRYleak = 1 / 10;
```

```
TRYleakV = 0.614;
```

```
In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
```

Now the equilibrium must be numerically calculated:

```
In[ ]:= Simplify[Solve[{0 == δ R - β1 S I1,
    0 == β1 S I1 + ξ1 β1 R I1 - κ I1,
    0 == κ I1 - δ R - ξ1 β1 R I1,
    1 == S + I1 + R}], {S, I1, R}], {β1 > 0, ξ1 > 0, δ > 0, κ > 0}]
```

$$\text{Out[]} = \left\{ \left\{ S \rightarrow 1, I1 \rightarrow 0, R \rightarrow 0 \right\}, \left\{ S \rightarrow \frac{\delta - \kappa + \beta1 \xi1 + \sqrt{\delta^2 + (\kappa - \beta1 \xi1)^2 + 2 \delta (\kappa + \beta1 \xi1 - 2 \kappa \xi1)}}{2 \beta1 (-1 + \xi1)}, \right. \right.$$

$$I1 \rightarrow - \frac{\delta + \kappa - \beta1 \xi1 + \sqrt{\delta^2 + (\kappa - \beta1 \xi1)^2 + 2 \delta (\kappa + \beta1 \xi1 - 2 \kappa \xi1)}}{2 \beta1 \xi1},$$

$$R \rightarrow - \frac{\delta + \kappa + \beta1 \xi1 - 2 \kappa \xi1 + \sqrt{\delta^2 + (\kappa - \beta1 \xi1)^2 + 2 \delta (\kappa + \beta1 \xi1 - 2 \kappa \xi1)}}{2 \beta1 (-1 + \xi1) \xi1} \left. \right\},$$

$$\left\{ S \rightarrow \frac{\delta - \kappa + \beta1 \xi1 - \sqrt{\delta^2 + (\kappa - \beta1 \xi1)^2 + 2 \delta (\kappa + \beta1 \xi1 - 2 \kappa \xi1)}}{2 \beta1 (-1 + \xi1)}, \right.$$

$$I1 \rightarrow \frac{-\delta - \kappa + \beta1 \xi1 + \sqrt{\delta^2 + (\kappa - \beta1 \xi1)^2 + 2 \delta (\kappa + \beta1 \xi1 - 2 \kappa \xi1)}}{2 \beta1 \xi1},$$

$$R \rightarrow - \frac{\delta + \kappa + \beta1 \xi1 - 2 \kappa \xi1 - \sqrt{\delta^2 + (\kappa - \beta1 \xi1)^2 + 2 \delta (\kappa + \beta1 \xi1 - 2 \kappa \xi1)}}{2 \beta1 (-1 + \xi1) \xi1} \left. \right\}$$

```
In[ ]:= startme = %[[3]];
```

Finding the value of β that gives the target incidence (TRYinf):

```
In[ ]:= Solve[
    (S + I1 + R /. I1 -> TRYinf /. startme /. δ -> TRYδ /. κ -> TRYκ /. ξ1 -> TRYξ1) == 1, β1]
```

```
Out[ ]:= {{β1 -> 2/49 (-24 - sqrt[1066])}, {β1 -> 2/49 (-24 + sqrt[1066])}}
```

```
In[ ]:= TRYβ = β1 /. %[[2]]
```

```
Out[ ]:= 2/49 (-24 + sqrt[1066])
```

```
In[ ]:= (*TRYβ = TRYδ TRYκ / (TRYδ - TRYinf TRYδ - TRYconvert TRYinf TRYκ);*)
```

```
TRYβ / N
```

```
Out[ ]:= 1.76524
```

Variant has the same transmissibility:

```
In[ ]:= TRYβV = TRYβ;
```

but infects earlier during waning by allowing leaky immunity.

New equilibrium:

```
In[ ]:= neweq =

$$\frac{-\delta - \kappa + \beta_1 \xi_1 + \sqrt{\delta^2 + (\kappa - \beta_1 \xi_1)^2 + 2 \delta (\kappa + \beta_1 \xi_1 - 2 \kappa \xi_1)}}{2 \beta_1 \xi_1} /. \xi_1 \rightarrow \text{TRYleakV} /. \beta_1 \rightarrow \text{TRY}\beta V /. \\ \delta \rightarrow \text{TRY}\delta /. \kappa \rightarrow \text{TRY}\kappa // N$$

```

```
Out[ ]:= 0.148324
```

Starting equilibrium would be:

```
In[ ]:= start = {s0 → S, i0 → I1, r0 → R} /. startme /. δ → TRYδ /. κ → TRYκ /. ξ1 → TRYleak /. \\ β1 → TRYβ;
```

```
N[
start]
```

```
Out[ ]:= {s0 → 0.520552, i0 → 0.02, r0 → 0.459448}
```

[NOTE: For the ease of colouring, the first stage class is the variant.]

```
In[ ]:= {ages = 2, stages = 2};
```

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_,  $\beta$ _,  $\beta V$ _,  $\delta Y$ _,  $\delta O$ _,  $\kappa$ _, q_}, start] :=
  solution[{p, f, older,  $\beta$ ,  $\beta V$ ,  $\delta Y$ ,  $\delta O$ ,  $\kappa$ , q}, start] =
    Block[{ages = 2, stages = 2},
      dsdt[j_, t_] = (1 - q) * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] +  $\delta$ [j] * r[j, t] -
        Sum[ $\beta$ [k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = TRYleakV Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t] +
        Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 1] * i[j, 1, t];
      didt[j_, 2, t_] = TRYleak Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * r[j, t] +
        Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] -  $\kappa$ [j, 2] * i[j, 2, t];
      drdt[j_, t_] = q * Sum[ $\kappa$ [j, jj] * i[j, jj, t], {jj, 1, stages}] -
         $\delta$ [j] * r[j, t] - TRYleakV Sum[ $\beta$ [k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t] -
        TRYleak Sum[ $\beta$ [k, 2] * i[k, 2, t], {k, 1, ages}] * r[j, t];
      pars = { $\beta$ [j_, 1]  $\rightarrow$   $\beta V$ ,  $\beta$ [j_, 2]  $\rightarrow$   $\beta$ ,  $\delta$ [1]  $\rightarrow$   $\delta Y$ ,  $\delta$ [2]  $\rightarrow$   $\delta O$ ,  $\kappa$ [j_, jj_]  $\rightarrow$   $\kappa$ };
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[
        {s[j, t], Table[i[j, jj, t], {jj, 1, stages}], r[j, t]}, {j, 1, ages}]], -1];
      r[ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[
        Table[{D[s[j, t], t] == dsdt[j, t], Table[D[i[j, jj, t], t] == didt[j, jj, t],
          {jj, 1, stages}], D[r[j, t], t] == drdt[j, t]}, {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0,
        r[j, 0] == (frac[j, 1] + frac[j, 2]) r0}, {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
Out[ ]:= {, , , }

```

```

In[8]:= coltab = Join[{{1 -> {0, colours[[1]]}}},
    Table[{i -> {{i - 1}, colours[[i]]}}, {i, 2, Length[all]}]];
Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm

```

`Out[•]//MatrixForm=`

$\left(\begin{array}{ll} <70, \text{Res} & \text{Blue} \\ <70, \text{Mutant} & \text{Light Blue} \\ 70+, \text{Res} & \text{Green} \\ 70+, \text{Mutant} & \text{Light Green} \end{array} \right)$

```
ln[*]:= partemp = {TRYp, TRYf, TRYolder, TRY $\beta$ , TRY $\beta$ V, TRY $\delta$ , TRY $\delta$ 0, TRY $\kappa$ , TRYconvert};
```

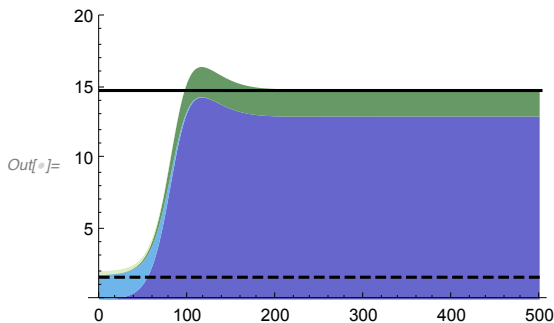
```
ln[•]:= solution[partemp, start];
```

Showing the % of the population infectious:

```

In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[ Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange → {Automatic, {0, maxy}},
  PlotStyle → None, Filling → {{1 → {0, }}, {2 → {{1}, }},
    {3 → {{2}, }}, {4 → {{3}, }}}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
    PlotStyle → {Black, Dashed}],
  Plot[100 neweq, {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
]

```



Mutant fraction change between t=0 and t=50:

$$\ln[e] := \frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]} /. \text{solution}[\text{partemp}, \text{start}] /. t \rightarrow 50$$
$$Out[\bullet]= \{0.399126\}$$

```
In[ ]:= Solve[Exp[s 50] == (p50 / (1 - p50)) /. p50 -> % /. p0 -> 1 - TRYf], s][[1]]
```

... **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```
Out[ ]:= {s -> 0.0837202}
```

This is consistent with the predicted selection coefficient:

```
In[ ]:= (TRYβV - TRYβ) / TRYβ * TRYκ + (TRYleakV - TRYleak) (r0 /. start) TRYβV // N
```

```
Out[ ]:= 0.0833744
```

Adjusted leakiness of variant to get target selection coefficient:

```
In[ ]:= Solve[
  ( (TRYβV - TRYβ) / TRYβ * TRYκ + (leakV - TRYleak) (r0 /. start) TRYβV == 0.0833 ), leakV]
```

```
Out[ ]:= {{leakV -> 0.613542}}
```

% rise in the endemic equilibrium:

```
In[ ]:= 100 * (neweq - TRYinf) / TRYinf
```

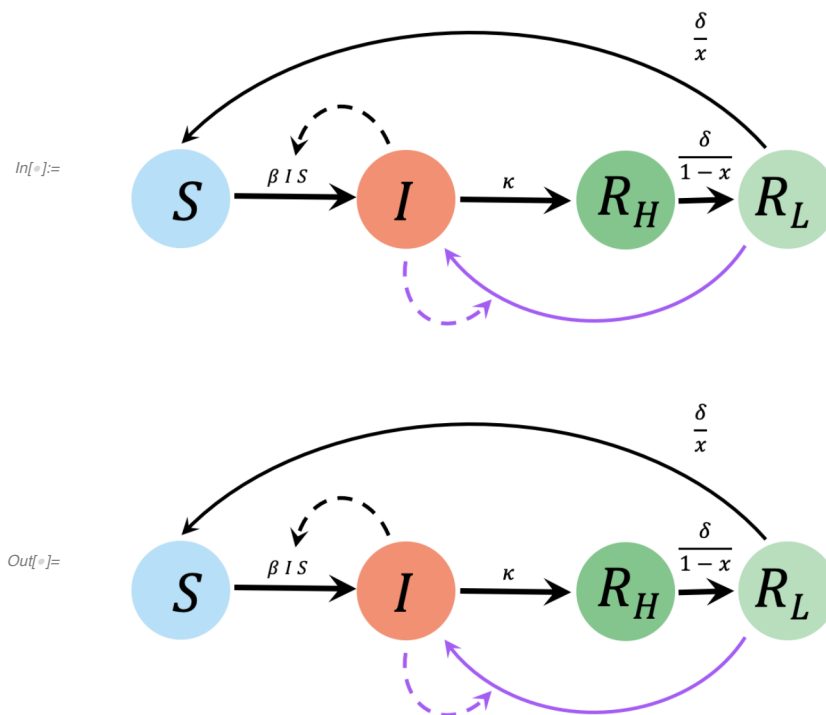
```
Out[ ]:= 641.621
```

```
In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];
```

Alternative: SIR₂ model

→ Less oscillatory

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.



We let the waning rate in the two classes be:

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

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

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

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

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

Figure S2D: more transmissible

`In[*]:= maxtime = 500;`

`maxy = 8;`

Parameters:

```

In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
TRYf = 99 / 100; (*Starting fraction of resident*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10;
(*Only this fraction of cases seroconvert or boost immunity*)
TRYx = 2 / 5;

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

In[ ]:= Solve[ $\frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)} == \text{inf}, \beta]$ 
Out[ ]:=  $\left\{ \left\{ \beta \rightarrow -\frac{\delta \kappa}{-\delta + \text{inf } \delta + \text{inf } q \kappa} \right\} \right\}$ 
In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)

$$\text{TRY}\beta = \frac{\text{TRY}\delta \text{TRY}\kappa}{\text{TRY}\delta - \text{TRYinf} \text{TRY}\delta - \text{TRYconvert} \text{TRYinf} \text{TRY}\kappa};$$


$$\frac{\text{TRY}\beta}{\text{TRY}\kappa} // N$$

Out[ ]:= 2.08333

```

Variant has a higher transmissibility (set to have the same selection coefficient as for the immune evasive variant):

```

In[ ]:= Flatten[Solve[ $\frac{\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa == 0.0833, \beta V]$ ]
Out[ ]:= { $\beta V \rightarrow 0.590208$ }
In[ ]:= TRYβV = βV /. %;
% increase in β:
In[ ]:= 100 *  $\frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta}$ 
Out[ ]:= 41.65

```

and now has no immune evasive properties (neither the resident nor the variant can infect individuals in the RL class).

Starting equilibrium would be (r0 includes all of the resistance classes):

$$\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + q \kappa)} \right\}$$

$$In[] := \text{start} = \left\{ s_0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i_0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, \right. \\ \left. r_0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right\}$$

$$Out[] := \left\{ s_0 \rightarrow \frac{12}{25}, i_0 \rightarrow \frac{1}{50}, r_0 \rightarrow \frac{1}{2} \right\}$$

[NOTE: For the ease of colouring, the first stage class is the variant.]

```
In[ ] := {ages = 2, stages = 2};
```

```
In[ ] := Clear[solution]
```

```
solution[{p_, f_, older_, β_, βV_, δY_, δ0_, κ_, q_}, start] :=
```

```
solution[{p, f, older, β, βV, δY, δ0, κ, q}, start] =
```

```
Block[{ages = 2, stages = 2},
```

```
dsdt[j_, t_] = (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] +  $\frac{\delta[j]}{\text{TRY}\kappa}$  * rL[j, t] -
```

```
Sum[β[k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
```

```
didt[j_, 1, t_] = Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] -
```

```
κ[j, 1] * i[j, 1, t];
```

```
didt[j_, 2, t_] = Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] -
```

```
κ[j, 2] * i[j, 2, t];
```

```
drHdt[j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] -  $\frac{\delta[j]}{1 - \text{TRY}\kappa}$  * rH[j, t];
```

```
drLdt[j_, t_] =  $\frac{\delta[j]}{1 - \text{TRY}\kappa}$  * rH[j, t] -  $\frac{\delta[j]}{\text{TRY}\kappa}$  * rL[j, t];
```

```
pars = {β[j_, 1] → βV, β[j_, 2] → β, δ[1] → δY, δ[2] → δ0, κ[j_, jj_] → κ};
```

```
frac[1, 1] = (1 - older) (1 - f);
```

```
frac[2, 1] = older (1 - f);
```

```
frac[1, 2] = (1 - older) f;
```

```
frac[2, 2] = older f;
```

```
nvars = Drop[Flatten[Table[{s[j, t],
```

```
Table[i[j, jj, t], {jj, 1, stages}], rH[j, t], rL[j, t}], {j, 1, ages}]], -1];
```

```
rL[ages, t_] = 1 - Total[nvars];
```

```
neqns = Drop[Flatten[Table[{D[s[j, t], t] == dsdt[j, t],
```

```
Table[D[i[j, jj, t], t] == didt[j, jj, t], {jj, 1, stages}], D[rH[j, t], t] ==
```

```
drHdt[j, t], D[rL[j, t], t] == drLdt[j, t]], {j, 1, ages}]], -1];
```

```
nstart = Drop[Flatten[Table[{
```

```
Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
```

```
s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0,
```

```
rH[j, 0] == (frac[j, 1] + frac[j, 2]) (1 - TRYκ) r0,
```

```
rL[j, 0] == (frac[j, 1] + frac[j, 2]) TRYκ r0}], {j, 1, ages}]] /. start, -1];
```

```
NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
```

```
]
```

```
In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
```

```
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}
```

```
In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};
```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],  
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

```
Out[ ]:= {, , , 
```

```
In[ ]:= coltab = Join[{{1 -> {0, colours[[1]]}}},  
  Table[{i -> {i - 1}, colours[[i]]}, {i, 2, Length[all]}];  
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

```
(

|            |                                                                                   |
|------------|-----------------------------------------------------------------------------------|
| <70,Res    |  |
| <70,Mutant |  |
| 70+,Res    |  |
| 70+,Mutant |  |

)
```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRY $\beta$ , TRY $\beta$ V, TRY $\delta$ , TRY $\delta$ 0, TRY $\kappa$ , TRYconvert};
```

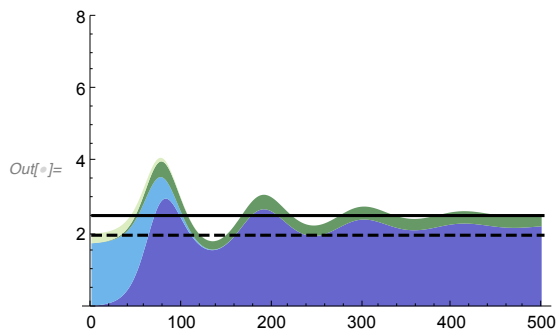
```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```

In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[ Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> None, Filling -> {{1 -> {0, Blue}}, {2 -> {1, Blue}},
    {3 -> {2, Green}}, {4 -> {3, Green}}}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})}$ , {t, 0, maxtime},
  PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})}$ , {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Mutant fraction change between t=0 and t=50:

```

In[ ]:= 
$$\frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]}$$
 /. solution[partemp, start] /. t -> 50
Out[ ]:= {0.380632}

```

```

In[ ]:= Solve[Exp[s 50] ==  $\left( \frac{p50 / (1 - p50)}{p0 / (1 - p0)} \right)$  /. p50 -> % /. p0 -> 1 - TRYf], s][[1]]

```

Solve: Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```

Out[ ]:= {s -> 0.0821651}

```

This is consistent with the predicted selection coefficient:

```

In[ ]:= 
$$\frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \text{TRY}\kappa \left( \frac{\text{TRY}\kappa \text{ TRYconvert} (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{ TRYconvert})} \right) \text{TRY}\beta V // N$$


```

```

Out[ ]:= 0.201342

```

New equilibrium:

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

Out[*]= 0.041321

% rise in the endemic equilibrium:

$$\text{In}[*]:= 100 * \frac{(\% - \text{TRYinf})}{\text{TRYinf}}$$

Out[*]= 106.605

The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

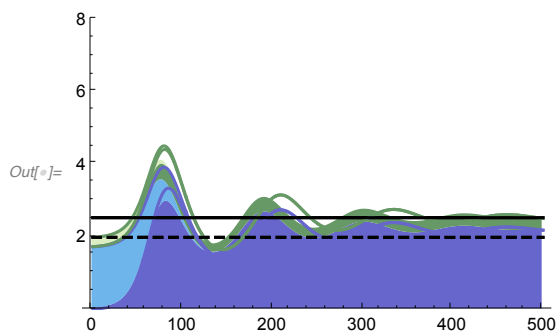
$$\text{In}[*]:= \text{partemp} = \left\{ \text{TRYp}, \text{TRYf}, \text{TRYolder}, \text{TRY}\beta, \text{TRY}\beta\text{V}, \frac{8}{10} \text{TRY}\delta, \frac{8}{10} \text{TRY}\delta\text{O}, \text{TRY}\kappa, \frac{8}{10} \right\};$$

solu[tion][partemp, start];

Showing the % of the population infectious:

```

In[*]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solu[tion][partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
    {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta\text{V} - \text{TRY}\kappa)}{\text{TRY}\beta\text{V} (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]
```



Seroconversion affects the dynamics (curves compared to the previous shaded plot) but not the initial speed of spread of the variant (described by the selection coefficient) or the equilibrium.

Clear[solu[tion], i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

Figure S2E: persistently immune evasive (increases mean waning rate by 67%)

```
In[ ]:= maxtime = 500;
```

```
maxy = 8;
```

Parameters:

```
In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
```

```
TRYf = 99 / 100; (*Starting fraction of resident*)
```

```
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
```

```
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
```

```
TRYκ = 1 / 5; (*Five day infectious period*)
```

```
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
```

```
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
```

```
TRYconvert = 10 / 10;
```

```
(*Only this fraction of cases seroconvert or boost immunity*)
```

```
TRYx = 2 / 5;
```

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

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

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

```
In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
```

$$\text{TRY}\beta = \frac{\text{TRY}\delta \text{TRY}\kappa}{\text{TRY}\delta - \text{TRYinf } \text{TRY}\delta - \text{TRYconvert } \text{TRYinf } \text{TRY}\kappa};$$

$$\frac{\text{TRY}\beta}{\text{TRY}\kappa} // \text{N}$$

```
Out[ ]:= 2.08333
```

Variant has the same transmissibility:

```
In[ ]:= TRYβV = TRYβ;
```

but infects earlier during waning.

Specifically, the mean waning rate (once fixed) increases by 67%:

```
In[ ]:= TRYδ / (1 - x) - TRYδ // Factor
```

$$\text{Out[]} = -\frac{x}{125 (-1 + x)}$$

$$\text{In[]} := \frac{\text{TRY}\delta + \Delta\delta}{\text{TRY}\delta} /. \Delta\delta \rightarrow \frac{\text{TRY}x}{1 - \text{TRY}x} \text{TRY}\delta // \text{N}$$

```
Out[ ]:= 1.66667
```

while the mean waiting time decreases by 40%:

$ln[] := 1 / \%$

$Out[] := 0.6$

Starting equilibrium would be (r_0 includes all of the resistance classes):

$$\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} \right\}$$

$$ln[] := \text{start} = \left\{ s_0 \rightarrow \frac{\text{TRY}\kappa}{\text{TRY}\beta}, i_0 \rightarrow \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}, \right.$$

$$\left. r_0 \rightarrow 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right\}$$

$$Out[] := \left\{ s_0 \rightarrow \frac{12}{25}, i_0 \rightarrow \frac{1}{50}, r_0 \rightarrow \frac{1}{2} \right\}$$

[NOTE: For the ease of colouring, the first stage class is the variant.]

$ln[] := \{\text{ages} = 2, \text{stages} = 2\};$

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_, β_, βV_, δY_, δO_, κ_, q_}, start] :=
  solution[{p, f, older, β, βV, δY, δO, κ, q}, start] =
    Block[{ages = 2, stages = 2},

      dsdt[j_, t_] = (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] +  $\frac{\delta[j]}{\text{TRYx}}$  * rL[j, t] -
        Sum[β[k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * rL[j, t] +
        Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] - κ[j, 1] * i[j, 1, t];
      didt[j_, 2, t_] =
        Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] - κ[j, 2] * i[j, 2, t];
      drHdt[j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] -  $\frac{\delta[j]}{1 - \text{TRYx}}$  * rH[j, t];
      drLdt[j_, t_] =  $\frac{\delta[j]}{1 - \text{TRYx}}$  * rH[j, t] -
         $\frac{\delta[j]}{\text{TRYx}}$  * rL[j, t] - Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * rL[j, t];
      pars = {β[j_, 1] → βV, β[j_, 2] → β, δ[1] → δY, δ[2] → δO, κ[j_, jj_] → κ};
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[{s[j, t],
        Table[i[j, jj, t], {jj, 1, stages}], rH[j, t], rL[j, t]}, {j, 1, ages}]], -1];
      rL[ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[Table[{D[s[j, t], t] == dsdt[j, t],
        Table[D[i[j, jj, t], t] == didt[j, jj, t], {jj, 1, stages}], D[rH[j, t], t] ==
          drHdt[j, t], D[rL[j, t], t] == drLdt[j, t]}, {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0,
        rH[j, 0] == (frac[j, 1] + frac[j, 2]) (1 - TRYx) r0,
        rL[j, 0] == (frac[j, 1] + frac[j, 2]) TRYx r0}, {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};

```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

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

```
In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1, colours[[i]]}}, {i, 2, Length[all]}]];
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

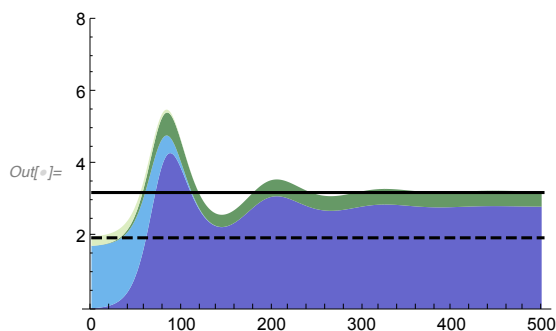
```
( <70,Res <70,Mutant
  70+,Res 70+,Mutant )
```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};
```

```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```
In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[ Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> None, Filling -> {{1 -> {0, }}, {2 -> {{1, }},
    {3 -> {{2, }}, {4 -> {{3, }}}}},
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
  PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}\delta}{1 - \text{TRY}\kappa} (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}\delta}{1 - \text{TRY}\kappa} + \text{TRY}\kappa \text{TRYconvert} \right)}$ , {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]
```



Mutant fraction change between t=0 and t=50:

```
In[ ]:= 
$$\frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]}$$
 /. solution[partemp, start] /. t -> 50
```

```
Out[ ]:= {0.385766}
```

```
In[ ]:= Solve[Exp[s 50] == 
$$\left( \frac{p50 / (1 - p50)}{p0 / (1 - p0)} \right) /. p50 \rightarrow \% /. p0 \rightarrow 1 - \text{TRYf}$$
, s][[1]]
```

 **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```
Out[ ]:= {s -> 0.0825995}
```

This is consistent with the predicted selection coefficient:

```
In[ ]:= 
$$\frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \text{TRY}\kappa \left( \frac{\text{TRY}\kappa \text{TRYconvert} (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right) \text{TRY}\beta V // N$$

```

```
Out[ ]:= 0.0833333
```

New equilibrium:

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

```

```
Out[ ]:= 0.0325
```

% rise in the endemic equilibrium:

```
In[ ]:= 
$$100 * \frac{(\% - \text{TRYinf})}{\text{TRYinf}}$$

```

```
Out[ ]:= 62.5
```

The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYbeta, TRYbetaV,  $\frac{8}{10} \text{TRY}\delta$ ,  $\frac{8}{10} \text{TRY}\delta 0$ , TRYkappa,  $\frac{8}{10}$ };
```

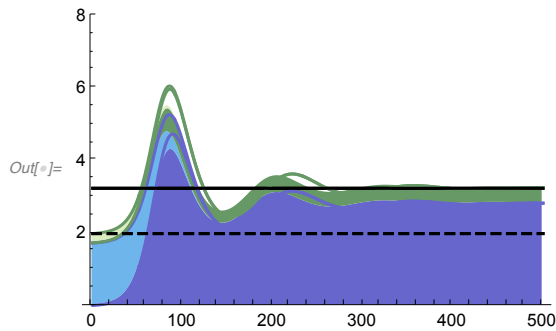
```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[ Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}\delta}{1-\text{TRY}\kappa} (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}\delta}{1-\text{TRY}\kappa} + \text{TRY}\kappa \text{TRYconvert} \right)}$ , {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Seroconversion affects the dynamics (curves compared to the previous shaded plot) but not the initial speed of spread of the variant (described by the selection coefficient) or the equilibrium.

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```

Figure S2F: more transmissible and persistently immune evasive (increases mean waning rate by 25%)

```

In[ ]:= maxtime = 500;
maxy = 8;
Parameters:

```

```

In[ ]:= TRYp = TRYp; (*No heterogeneity, so p not relevant now.*)
TRYf = 99 / 100; (*Starting fraction of resident*)
TRYolder = 13 / 100; (*~ Age 70+ from StatsCan 5022509/38929902 *)
(*https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710000501*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδ0 = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10;
(*Only this fraction of cases seroconvert or boost immunity*)
TRYx = 1 / 5;

```

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

```

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

```

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

```

In[ ]:= TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
TRYβ =  $\frac{\text{TRYδ TRYκ}}{\text{TRYδ} - \text{TRYinf TRYδ} - \text{TRYconvert TRYinf TRYκ}}$ ;

```

$$\frac{\text{TRYβ}}{\text{TRYκ}} // N$$

```

Out[ ]:= 2.08333

```

Variant has a higher transmissibility (set to have the same selection coefficient as for the immune evasive variant):

```

In[ ]:= Flatten[Solve[ $\frac{\beta V - \text{TRYβ}}{\text{TRYβ}} \text{TRYκ} + \text{TRYx} \left( \frac{\text{TRYκ TRYconvert} (\text{TRYβ} - \text{TRYκ})}{\text{TRYβ} (\text{TRYδ} + \text{TRYκ TRYconvert})} \right) \beta V == 0.0833, \beta V]$ ]

```

```

Out[ ]:= {βV → 0.488448}

```

```

In[ ]:= TRYβV = βV /. %;

```

% increase in β:

```

In[ ]:= 100 *  $\frac{\text{TRYβV} - \text{TRYβ}}{\text{TRYβ}}$ 

```

```

Out[ ]:= 17.2276

```

and infects earlier during waning.

Specifically, the mean waning rate (once fixed) increases by 25%:

```

In[ ]:= TRYδ / (1 - x) - TRYδ // Factor

```

$$\text{Out[]} = -\frac{x}{125 (-1 + x)}$$

$$In[] := \frac{TRY\delta + \Delta\delta}{TRY\delta} / . \Delta\delta \rightarrow \frac{TRY\kappa}{1 - TRY\kappa} TRY\delta // N$$

$$Out[] := 1.25$$

while the mean waiting time decreases by 20%:

$$In[] := 1 / \%$$

$$Out[] := 0.8$$

Starting equilibrium would be (r0 includes all of the resistance classes):

$$\left\{ s \rightarrow \frac{\kappa}{\beta}, i \rightarrow \frac{\delta (\beta - \kappa)}{\beta (\delta + \kappa)} \right\}$$

$$In[] := \text{start} = \left\{ s0 \rightarrow \frac{TRY\kappa}{TRY\beta}, i0 \rightarrow \frac{TRY\delta (TRY\beta - TRY\kappa)}{TRY\beta (TRY\delta + TRY\kappa TRYconvert)}, \right. \\ \left. r0 \rightarrow 1 - \frac{TRY\kappa}{TRY\beta} - \frac{TRY\delta (TRY\beta - TRY\kappa)}{TRY\beta (TRY\delta + TRY\kappa TRYconvert)} \right\}$$

$$Out[] := \left\{ s0 \rightarrow \frac{12}{25}, i0 \rightarrow \frac{1}{50}, r0 \rightarrow \frac{1}{2} \right\}$$

[NOTE: For the ease of colouring, the first stage class is the variant.]

$$In[] := \{\text{ages} = 2, \text{stages} = 2\};$$

```

In[ ]:= Clear[solution]
solution[{p_, f_, older_, β_, βV_, δY_, δO_, κ_, q_}, start] :=
  solution[{p, f, older, β, βV, δY, δO, κ, q}, start] =
    Block[{ages = 2, stages = 2},

      dsdt[j_, t_] = (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] +  $\frac{\delta[j]}{\text{TRYx}}$  * rL[j, t] -
        Sum[β[k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t];
      didt[j_, 1, t_] = Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * rL[j, t] +
        Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * s[j, t] - κ[j, 1] * i[j, 1, t];
      didt[j_, 2, t_] =
        Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] - κ[j, 2] * i[j, 2, t];
      drHdt[j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] -  $\frac{\delta[j]}{1 - \text{TRYx}}$  * rH[j, t];
      drLdt[j_, t_] =  $\frac{\delta[j]}{1 - \text{TRYx}}$  * rH[j, t] -
         $\frac{\delta[j]}{\text{TRYx}}$  * rL[j, t] - Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * rL[j, t];
      pars = {β[j_, 1] → βV, β[j_, 2] → β, δ[1] → δY, δ[2] → δO, κ[j_, jj_] → κ};
      frac[1, 1] = (1 - older) (1 - f);
      frac[2, 1] = older (1 - f);
      frac[1, 2] = (1 - older) f;
      frac[2, 2] = older f;
      nvars = Drop[Flatten[Table[{s[j, t],
        Table[i[j, jj, t], {jj, 1, stages}], rH[j, t], rL[j, t]}, {j, 1, ages}]], -1];
      rL[ages, t_] = 1 - Total[nvars];
      neqns = Drop[Flatten[Table[{D[s[j, t], t] == dsdt[j, t],
        Table[D[i[j, jj, t], t] == didt[j, jj, t], {jj, 1, stages}], D[rH[j, t], t] ==
          drHdt[j, t], D[rL[j, t], t] == drLdt[j, t]}, {j, 1, ages}]], -1];
      nstart = Drop[Flatten[Table[{
        Table[i[j, jj, 0] == frac[j, jj] i0, {jj, 1, stages}],
        s[j, 0] == (frac[j, 1] + frac[j, 2]) * s0,
        rH[j, 0] == (frac[j, 1] + frac[j, 2]) (1 - TRYx) r0,
        rL[j, 0] == (frac[j, 1] + frac[j, 2]) TRYx r0}, {j, 1, ages}]], /. start, -1];
      NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
    ]

In[ ]:= all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
Out[ ]:= {{1, 1}, {1, 2}, {2, 1}, {2, 2}}

In[ ]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};

```

```
In[ ]:= colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], ColorData["Pastel", 3 / 4]}
```

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

```
In[ ]:= coltab = Join[{1 -> {0, colours[[1]]}},
  Table[{i -> {i - 1, colours[[i]]}}, {i, 2, Length[all]}]];
  Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
```

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

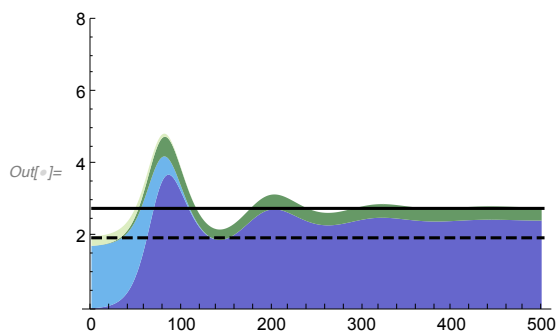
```
( <70,Res <70,Mutant
  70+,Res 70+,Mutant )
```

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYκ, TRYconvert};
```

```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```
In[ ]:= plot1 = Show[
  Plot[Evaluate@Table[ Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> None, Filling -> {{1 -> {0, }}, {2 -> {{1, }},
    {3 -> {{2, }}, {4 -> {{3, }}}}},
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ , {t, 0, maxtime},
    PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}\delta}{1 - \text{TRY}\kappa} (\text{TRY}\beta V - \text{TRY}\kappa)}{\text{TRY}\beta V \left( \frac{\text{TRY}\delta}{1 - \text{TRY}\kappa} + \text{TRY}\kappa \text{TRYconvert} \right)}$ , {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]
```



Mutant fraction change between t=0 and t=50:

```
In[ ]:= 
$$\frac{\text{Sum}[i[j, 1, t], \{j, 1, \text{ages}\}]}{\text{Sum}[i[j, jj, t], \{j, 1, \text{ages}\}, \{jj, 1, \text{stages}\}]}$$
 /. solution[partemp, start] /. t -> 50
```

```
Out[ ]:= {0.384602}
```

```
In[ ]:= Solve[Exp[s 50] == 
$$\left( \frac{p50 / (1 - p50)}{p0 / (1 - p0)} \right) /. p50 \rightarrow \% /. p0 \rightarrow 1 - \text{TRYf}$$
, s][[1]]
```

 **Solve:** Inverse functions are being used by Solve, so some solutions may not be found; use Reduce for complete solution information.

```
Out[ ]:= {s -> 0.0825012}
```

This is consistent with the predicted selection coefficient:

```
In[ ]:= 
$$\frac{\text{TRY}\beta V - \text{TRY}\beta}{\text{TRY}\beta} \text{TRY}\kappa + \text{TRY}\kappa \left( \frac{\text{TRY}\kappa \text{TRYconvert} (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})} \right) \text{TRY}\beta V // N$$

```

```
Out[ ]:= 0.0833
```

New equilibrium:

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

```

```
Out[ ]:= 0.028121
```

% rise in the endemic equilibrium:

```
In[ ]:= 
$$100 * \frac{(\% - \text{TRYinf})}{\text{TRYinf}}$$

```

```
Out[ ]:= 40.6048
```

The following illustrates the relatively minor effect caused by reducing seroconversion (to $q = 80\%$), as long as δ/q is held constant:

```
In[ ]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV,  $\frac{8}{10} \text{TRY}\delta$ ,  $\frac{8}{10} \text{TRY}\delta 0$ , TRYκ,  $\frac{8}{10}}$ ;
```

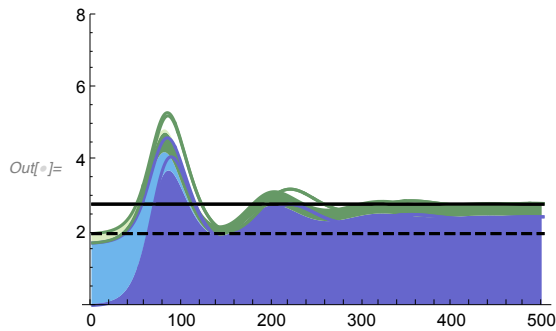
```
In[ ]:= solution[partemp, start];
```

Showing the % of the population infectious:

```

In[ ]:= plot2 = Show[plot1,
  Plot[Evaluate@Table[ Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
    solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
  {t, 0, maxtime}, PlotRange -> {Automatic, {0, maxy}},
  PlotStyle -> {Blue, Blue, Green, Green}],
  Plot[100  $\frac{\text{TRY}\delta (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta (\text{TRY}\delta + \text{TRY}\kappa \text{TRYconvert})}$ ,
  {t, 0, maxtime}, PlotStyle -> {Black, Dashed}],
  Plot[100  $\frac{\frac{\text{TRY}\delta}{1-\text{TRY}\kappa} (\text{TRY}\beta\text{V} - \text{TRY}\kappa)}{\text{TRY}\beta\text{V} \left( \frac{\text{TRY}\delta}{1-\text{TRY}\kappa} + \text{TRY}\kappa \text{TRYconvert} \right)}$ , {t, 0, maxtime}, PlotStyle -> {Black}],
  ImageSize -> 250
]

```



Seroconversion affects the dynamics (curves compared to the previous shaded plot) but not the initial speed of spread of the variant (described by the selection coefficient) or the equilibrium.

```

In[ ]:= Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];

```