Exploring transients around steady state: SIR$_n$ model

Supplementary Material: Endemic does not mean constant as SARS-CoV-2 continues to evolve

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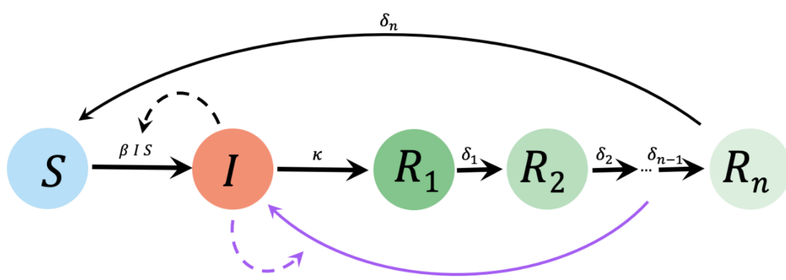
Evolution (2024)

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



Variant evolution (Figures 3, 4, S1, S2, S3)

Figure 3B: persistently 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 behavioural heterogeneity, so p not relevant here.*)
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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

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

Out[∘]= $\left\{\left\{\beta \to -\dfrac{\delta\,\kappa}{-\delta+\text{inf}\ \delta+\text{inf}\ q\ \kappa}\right\}\right\}$

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

In[∘]:= TRYn = 5;

TRYm = 2;

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

In[∘]:= $\dfrac{\text{TRY}\delta + \Delta\delta}{\text{TRY}\delta}\ /.\ \Delta\delta \to \dfrac{\text{TRYm}}{\text{TRYn} - \text{TRYm}}\ \text{TRY}\delta\ //\ \text{N}$

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

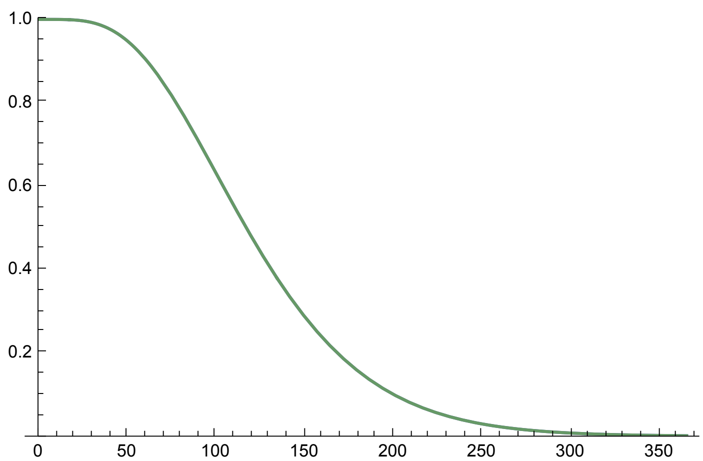
In[∘]:= $$\text{start} = \left\{\text{s0} \to \frac{\text{TRY}\kappa}{\text{TRY}\beta},\ \text{i0} \to \frac{\text{TRY}\delta\ (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta\ (\text{TRY}\delta + \text{TRY}\kappa\ \text{TRYconvert})},\ \text{r0} \to 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta}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

Out[∘]= $\left\{\text{s0} \to \dfrac{12}{25},\ \text{i0} \to \dfrac{1}{50},\ \text{r0} \to \dfrac{1}{2}\right\}$

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 / (TRYδO TRYn)], t]),
  {t, 0, 365}, PlotRange → {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```

Out[∘]=



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_, β_, βV_, δY_, δO_, κ_, q_}, start] :=
 solution[{p, f, older, β, βV, δY, δO, κ, q}, start] =
  Block[{ages = 2, stages = 2, n = TRYn},
   dsdt[j_, t_] =
    (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] + n * δ[j] * r[n, 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}] *
      Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
     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[1, j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] - n * δ[j] * r[1, j, t];
   For[nn = 2, nn ≤ n - TRYm, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] - n * δ[j] * r[nn, j, t];
   ];
   For[nn = n + 1 - TRYm, nn ≤ n, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] -
       Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n * δ[j] * r[nn, 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}],
        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]) 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, TRYδO, TRYκ, TRYconvert};
```

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

Showing the % of the population infectious:

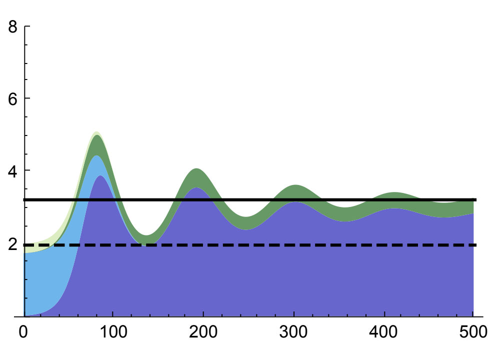
In[∘]:=
```
plot1 = Show[
  Plot[Evaluate@Table[ Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
       solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
   {t, 0, maxtime}, PlotRange → {Automatic, {0, maxy}},
   PlotStyle → None, Filling → {{1 → {0, ■}}, {2 → {{1}, ■}},
     {3 → {{2}, ■}},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

$$\text{Plot}\left[100\,\frac{\text{TRY}\delta\ (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta\ (\text{TRY}\delta + \text{TRY}\kappa\ \text{TRYconvert})},\ \{t, 0, \text{maxtime}\},\right.$$
$$\left.\text{PlotStyle} \to \{\text{Black}, \text{Dashed}\}\right],$$

$$\text{Plot}\left[100\,\frac{\frac{\text{TRYn}}{\text{TRYn}-\text{TRYm}}\ \text{TRY}\delta\ (\text{TRY}\beta\text{V} - \text{TRY}\kappa)}{\text{TRY}\beta\text{V}\ \left(\frac{\text{TRYn}}{\text{TRYn}-\text{TRYm}}\ \text{TRY}\delta + \text{TRY}\kappa\ \text{TRYconvert}\right)},\right.$$
$$\left.\{t, 0, \text{maxtime}\},\ \text{PlotStyle} \to \{\text{Black}\}\right],$$

```
  ImageSize → 250
 ]
```

Out[∘]=



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[∘]= {0.384091}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. 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 → 0.082458}

This is consistent with the predicted selection coefficient:

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

Out[∘]= 0.0833333

New equilibrium:

In[∘]:=
```
(((TRYδ + Δδ) (TRYβV - TRYκ))/(TRYβV ((TRYδ + Δδ) + TRYκ TRYconvert))) /. Δδ -> TRYm/(TRYn - TRYm) TRYδ // N
```

Out[∘]= 0.0325

% rise in the endemic equilibrium:

In[∘]:=
```
100 * (% - TRYinf)/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:

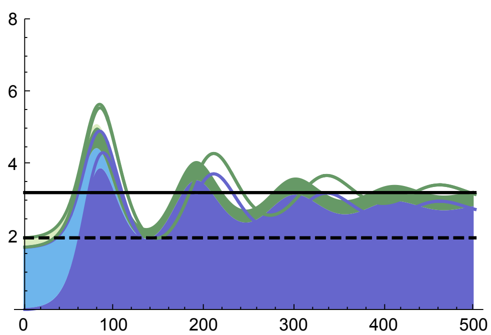
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, 8/10 TRYδ, 8/10 TRYδ0, TRYκ, 8/10};
```

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 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 (TRYn/(TRYn-TRYm) TRYδ (TRYβV - TRYκ))/(TRYβV (TRYn/(TRYn-TRYm) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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 3A: 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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

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

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

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 (40% reduction in mean waning time):

In[•]:=
```
TRYn = 5;
TRYm = 2;
```

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

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

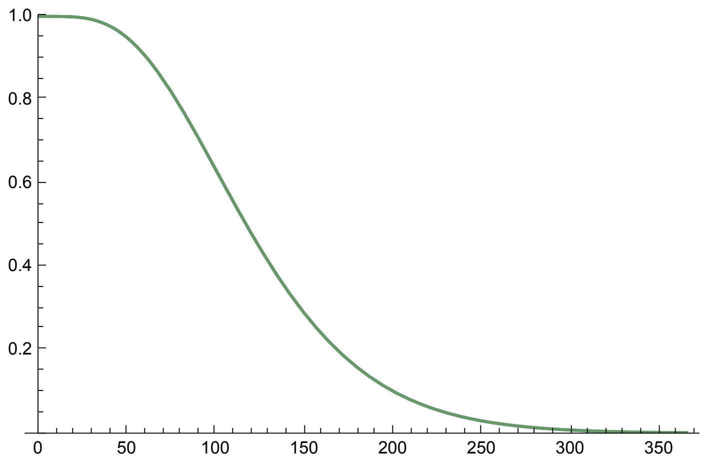
In[•]:= $\text{start} = \left\{s0 \to \frac{\text{TRY}\kappa}{\text{TRY}\beta},\ i0 \to \frac{\text{TRY}\delta\ (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta\ (\text{TRY}\delta + \text{TRY}\kappa\ \text{TRYconvert})},\right.$
$\left. r0 \to 1 - \frac{\text{TRY}\kappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta\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

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

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 / (TRYδO TRYn)], t]),
  {t, 0, 365}, PlotRange → {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```

Out[∘]=



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_, δO_, κ_, q_}, start] :=
 solution[{p, f, older, β, βV, δY, δO, 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.*)
didt[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]) 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     ■
```

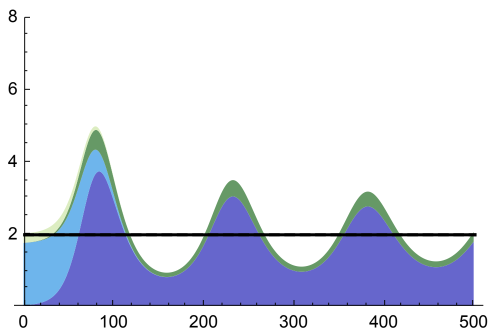
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYϰ, TRYconvert};
```

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, ■}}, {2 → {{1}, ■}},
     {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
  Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYn/TRYn-0) TRYδ (TRYβV - TRYκ))/(TRYβV ((TRYn/TRYn-0) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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

In[∘]:=
```
Sum[i[j, 1, zz, t], {j, 1, ages}, {zz, 1, exposures}] /
   Sum[i[j, jj, zz, t], {j, 1, ages}, {jj, 1, stages}, {zz, 1, exposures}] /.
  solution[partemp, start] /. t → 50
```

Out[∘]= {0.383419}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50))/(p0 / (1 - p0)) /. 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 → 0.0824012}

This is consistent with the predicted selection coefficient:

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

Out[∘]= 0.0833333

New equilibrium:

In[∘]:= $\left(\frac{(\text{TRY}\delta + \Delta\delta)\ (\text{TRY}\beta\text{V} - \text{TRY}\varkappa)}{\text{TRY}\beta\text{V}\ ((\text{TRY}\delta + \Delta\delta) + \text{TRY}\varkappa\ \text{TRYconvert})}\right)\ /.\ \Delta\delta \to \frac{0}{\text{TRYn} - 0}\,\text{TRY}\delta\ //\ \text{N}$

Out[∘]= 0.02

% rise in the endemic equilibrium:

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

Out[∘]= 0.

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

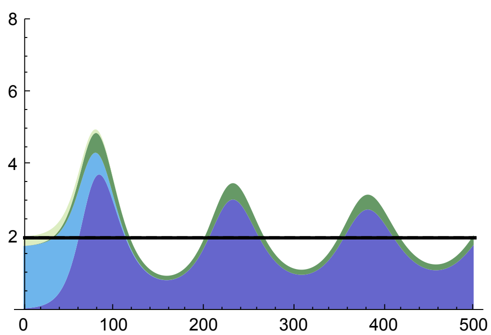
In[∘]:= $\text{partemp} = \left\{\text{TRYp, TRYf, TRYolder, TRY}\beta\text{, TRY}\beta\text{V, }\frac{8}{10}\,\text{TRY}\delta,\ \frac{8}{10}\,\text{TRY}\delta\text{0, TRY}\varkappa,\ \frac{8}{10}\right\};$

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 → {■, ■, ■, ■}],
  Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYn/TRYn-0) TRYδ (TRYβV - TRYκ))/(TRYβV ((TRYn/TRYn-0) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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 4 & 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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

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

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

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

Out[∘]= $\{\beta V \to 0.590208\}$

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):

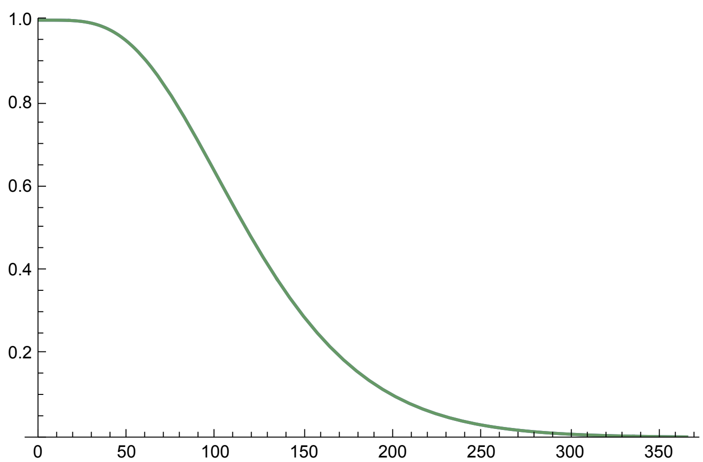
$\left\{s \to \frac{\kappa}{\beta},\ i \to \frac{\delta\ (\beta-\kappa)}{\beta\ (\delta+q\ \kappa)}\right\}$

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

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

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 / (TRYδO TRYn)], t]),
  {t, 0, 365}, PlotRange → {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```

Out[∘]=


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_, β_, βV_, δY_, δO_, κ_, q_}, start] :=
 solution[{p, f, older, β, βV, δY, δO, κ, q}, start] =
  Block[{ages = 2, stages = 2, n = TRYn},
   dsdt[j_, t_] =
    (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] + n * δ[j] * r[n, 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}] *
      Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
     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[1, j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] - n * δ[j] * r[1, j, t];
   For[nn = 2, nn ≤ n - TRYm, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] - n * δ[j] * r[nn, j, t];
   ];
   For[nn = n + 1 - TRYm, nn ≤ n, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] -
       Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n * δ[j] * r[nn, 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}],
        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]) 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	

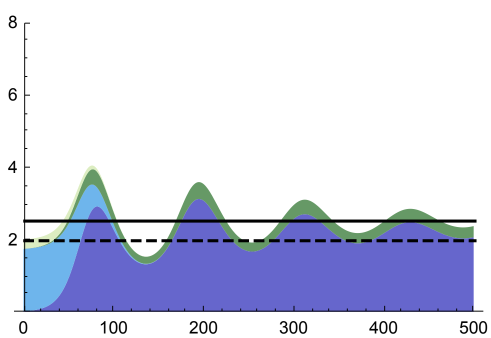
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYκ, TRYconvert};
```

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 (TRYδ (TRYβ - TRYκ)) / (TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYn / (TRYn - TRYm)) TRYδ (TRYβV - TRYκ)) / (TRYβV ((TRYn / (TRYn - TRYm)) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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[∘]= {0.38051}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. 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 → 0.0821547}

This is consistent with the predicted selection coefficient:

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

Out[∘]= 0.0833

New equilibrium:

In[∘]:=
```
(((TRYδ + Δδ) (TRYβV - TRYϰ))/(TRYβV ((TRYδ + Δδ) + TRYϰ TRYconvert))) /. Δδ -> TRYm/(TRYn - TRYm) TRYδ // N
```

Out[∘]= 0.0254283

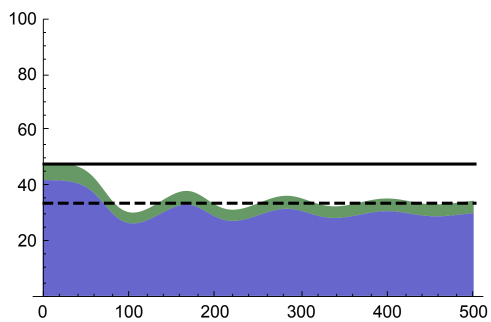
% rise in the endemic equilibrium:

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

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 TRYκ/TRYβ, {t, 0, maxtime}, PlotStyle → {Black}],
 Plot[100 TRYκ/TRYβV, {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
 ImageSize → 250
]
```

Out[•]=


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

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

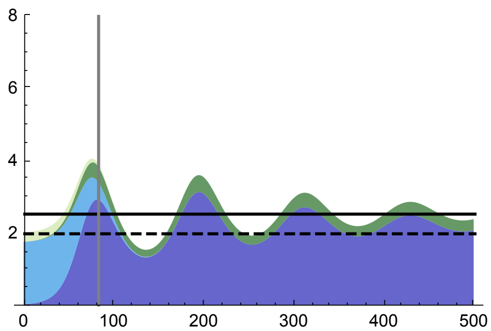
Out[•]= 1.4165

In[•]:=
```
droptime = First[
  Select[Table[Flatten[{t, Sum[100 s[c, t] /. solution[partemp, start], {c, 1, 2}]}],
    {t, 0, maxtime}], #[[2]] < 100 TRYκ/TRYβV &]]
```

Out[•]= {82, 33.842}

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

Out[∘]=



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

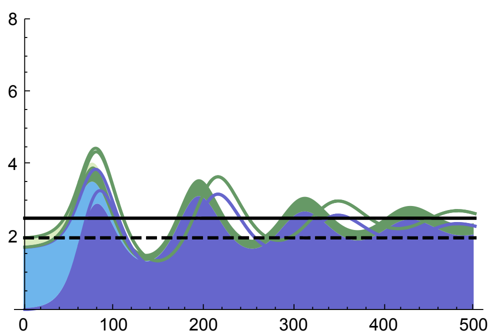
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, 8/10 TRYδ, 8/10 TRYδO, TRYϰ, 8/10};
```

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 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYn/TRYn-0) TRYδ (TRYβV - TRYκ))/(TRYβV ((TRYn/TRYn-0) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```
$i \to \frac{\delta\ (\beta-\kappa)}{\beta\ (\delta+q\ \kappa)}$

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

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

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

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

Out[•]= {βV → 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):
$\left\{s \to \frac{\kappa}{\beta},\ i \to \frac{\delta\ (\beta-\kappa)}{\beta\ (\delta+q\ \kappa)}\right\}$

In[∘]:=

$$\text{start} = \left\{\text{s0} \to \frac{\text{TRY}\varkappa}{\text{TRY}\beta}, \text{i0} \to \frac{\text{TRY}\delta\ (\text{TRY}\beta - \text{TRY}\varkappa)}{\text{TRY}\beta\ (\text{TRY}\delta + \text{TRY}\varkappa\ \text{TRYconvert})}, \text{r0} \to 1 - \frac{\text{TRY}\varkappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta\ (\text{TRY}\beta - \text{TRY}\varkappa)}{\text{TRY}\beta\ (\text{TRY}\delta + \text{TRY}\varkappa\ \text{TRYconvert})}\right\}$$

Out[∘]=

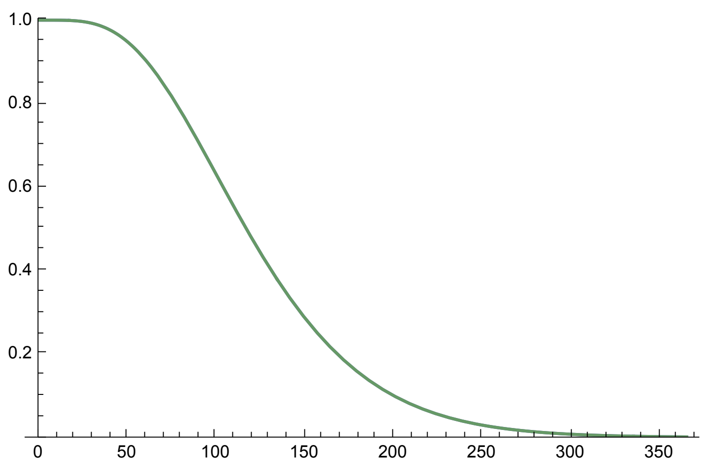
$$\left\{\text{s0} \to \frac{12}{25}, \text{i0} \to \frac{1}{50}, \text{r0} \to \frac{1}{2}\right\}$$

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 / (TRYδO TRYn)], t]),
  {t, 0, 365}, PlotRange → {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```

Out[∘]=



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_, β_, βV_, δY_, δO_, κ_, q_}, start] :=
 solution[{p, f, older, β, βV, δY, δO, κ, q}, start] =
  Block[{ages = 2, stages = 2, n = TRYn},
   dsdt[j_, t_] =
    (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] + n * δ[j] * r[n, 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}] *
      Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
     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[1, j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] - n * δ[j] * r[1, j, t];
   For[nn = 2, nn ≤ n - TRYm, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] - n * δ[j] * r[nn, j, t];
   ];
   For[nn = n + 1 - TRYm, nn ≤ n, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] -
       Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n * δ[j] * r[nn, 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}],
        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]) 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=

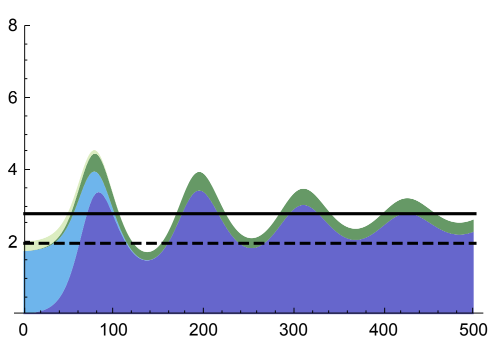
<70,Res	
<70,Mutant	
70+,Res	
70+,Mutant	

In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, 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 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYn/(TRYn-TRYm)) TRYδ (TRYβV - TRYκ))/(TRYβV ((TRYn/(TRYn-TRYm)) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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[∘]= {0.382856}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. 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 → 0.0823535}

This is consistent with the predicted selection coefficient:

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

Out[∘]= 0.0833

New equilibrium:

In[∘]:=
```
(((TRYδ + Δδ) (TRYβV - TRYϰ)) / (TRYβV ((TRYδ + Δδ) + TRYϰ TRYconvert))) /. Δδ -> TRYm / (TRYn - TRYm) TRYδ // N
```

Out[∘]= 0.028121

% rise in the endemic equilibrium:

In[∘]:=
```
100 * (% - TRYinf) / 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:

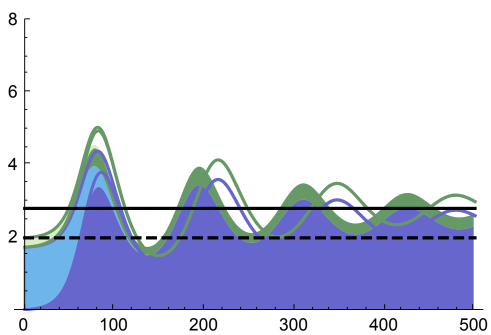
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, 8/10 TRYδ, 8/10 TRYδ0, TRYϰ, 8/10};
```

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 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYn/(TRYn-TRYm)) TRYδ (TRYβV - TRYκ))/(TRYβV ((TRYn/(TRYn-TRYm)) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

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

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

```
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

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

Out[∘]= {βV → 0.363205}

```
In[∘]:= TRYβV = βV /. %;

In[∘]:= TRYβ // N

Out[∘]= 0.416667
```

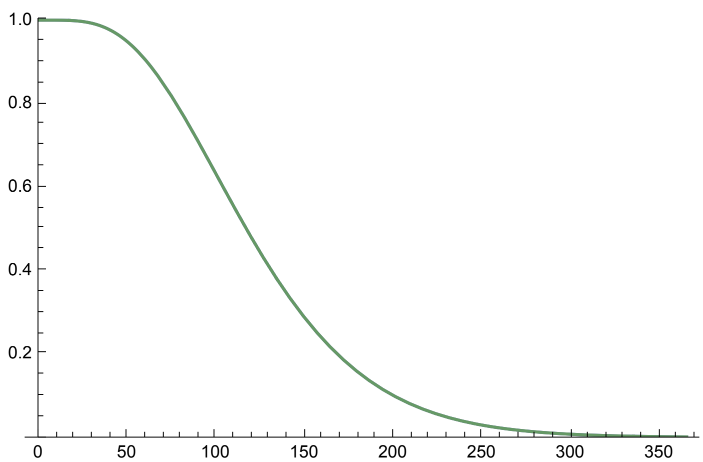
Starting equilibrium would be (r0 includes all of the n resistance classes):
$\left\{s \to \frac{\kappa}{\beta},\ i \to \frac{\delta\,(\beta-\kappa)}{\beta\,(\delta+q\,\kappa)}\right\}$

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

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

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 / (TRYδO TRYn)], t]),
  {t, 0, 365}, PlotRange → {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```

Out[∘]=


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_, δO_, κ_, q_}, start] :=
 solution[{p, f, older, β, βV, δY, δO, 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.*)
didt[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[{
```

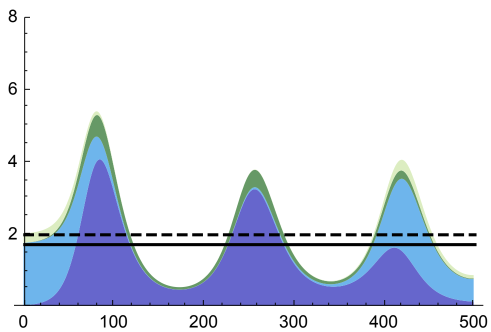
```
          Table[i[j, jj, 1, 0] == 0, {jj, 1, stages}],
          Table[i[j, jj, 2, 0] == frac[j, jj] i0, {jj, 1, stages}],
          s[j, 1, 0] == 0, (*Nobody starts exposed to the variant*)
          s[j, 2, 0] == (frac[j, 1] + frac[j, 2]) * s0,
          Table[r[nn, j, 1, 0] == 0, {nn, 1, n}],
          Table[r[nn, j, 2, 0] == (frac[j, 1] + frac[j, 2]) 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, TRYδO, 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, }}, {2 → {{1}, }},
      {3 → {{2}, }}, {4 → {{3}, }}}],
  Plot[100 (TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime},
    PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYn/TRYn-0) TRYδ (TRYβV - TRYϰ))/(TRYβV ((TRYn/TRYn-0) TRYδ + TRYϰ TRYconvert)),
    {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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

In[∘]:=
```
Sum[i[j, 1, zz, t], {j, 1, ages}, {zz, 1, exposures}] /
   Sum[i[j, jj, zz, t], {j, 1, ages}, {jj, 1, stages}, {zz, 1, exposures}] /.
  solution[partemp, start] /. t → 50
```

Out[∘]= {0.38282}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50))/(p0 / (1 - p0)) /. 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 → 0.0823505}

This is consistent with the predicted selection coefficient:

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

Out[∘]= 0.0833

New equilibrium (if resident fixed):

In[∘]:= $\left(\frac{(\text{TRY}\delta + \Delta\delta)\ (\text{TRY}\beta\text{V} - \text{TRY}\varkappa)}{\text{TRY}\beta\text{V}\ ((\text{TRY}\delta + \Delta\delta) + \text{TRY}\varkappa\ \text{TRYconvert})}\right)$ /. $\Delta\delta$ -> $\frac{0}{\text{TRYn} - 0}\,\text{TRY}\delta$ // N

Out[∘]= 0.0172826

% rise in the endemic equilibrium:

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

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:

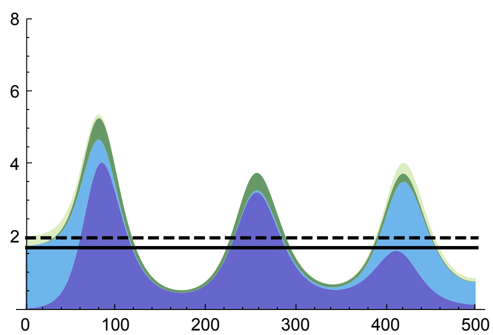
In[∘]:= partemp = $\left\{\text{TRYp, TRYf, TRYolder, TRY}\beta\text{, TRY}\beta\text{V, }\frac{8}{10}\text{TRY}\delta\text{, }\frac{8}{10}\text{TRY}\delta\text{0, TRY}\varkappa\text{, }\frac{8}{10}\right\}$;

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 → {■, ■, ■, ■}],
  Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYn/TRYn-0) TRYδ (TRYβV - TRYκ))/(TRYβV ((TRYn/TRYn-0) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

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

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

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

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

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

Out[•]= 2.08333

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

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

Out[•]= $\{\beta V \to 0.590208\}$

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):

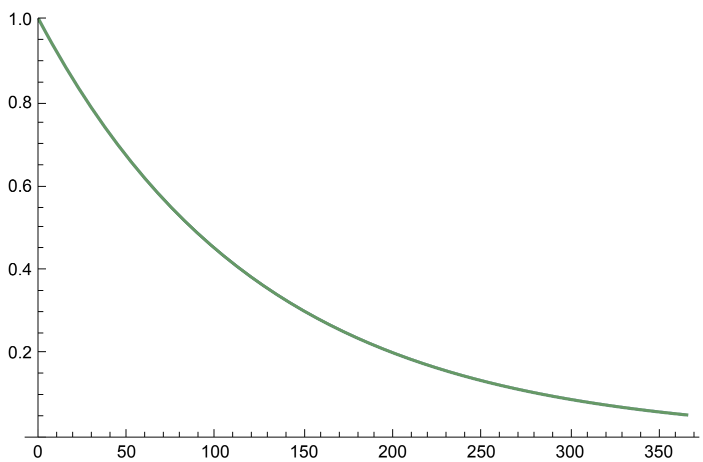
$\left\{s \to \frac{\kappa}{\beta}, i \to \frac{\delta\ (\beta-\kappa)}{\beta\ (\delta+q\ \kappa)}\right\}$

In[∘]:=
```
start = {s0 → TRYϰ/TRYβ, i0 → TRYδ (TRYβ - TRYϰ)/(TRYβ (TRYδ + TRYϰ TRYconvert)),
  r0 → 1 - TRYϰ/TRYβ - TRYδ (TRYβ - TRYϰ)/(TRYβ (TRYδ + TRYϰ TRYconvert))}
```

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

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 / (TRYδO TRYn)], t]),
  {t, 0, 365}, PlotRange → {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```

Out[∘]=


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_, β_, βV_, δY_, δO_, κ_, q_}, start] :=
 solution[{p, f, older, β, βV, δY, δO, κ, q}, start] =
  Block[{ages = 2, stages = 2, n = TRYn},
   dsdt[j_, t_] =
    (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] + n * δ[j] * r[n, 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}] *
      Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
     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[1, j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] - n * δ[j] * r[1, j, t];
   For[nn = 2, nn ≤ n - TRYm, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] - n * δ[j] * r[nn, j, t];
   ];
   For[nn = n + 1 - TRYm, nn ≤ n, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] -
       Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n * δ[j] * r[nn, 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}],
        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]) 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	■

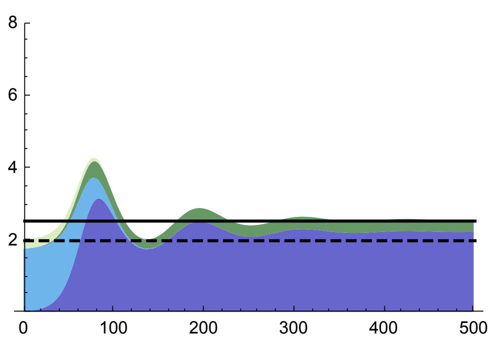
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYκ, TRYconvert};
```

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 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYn/(TRYn-TRYm)) TRYδ (TRYβV - TRYκ))/(TRYβV ((TRYn/(TRYn-TRYm)) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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[ ]= {0.381045}

In[ ]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. 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 + TRYm/TRYn (TRYκ TRYconvert (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)) TRYβV // N
```

Out[ ]= 0.0833

New equilibrium:

In[ ]:=
```
((TRYδ + Δδ) (TRYβV - TRYκ))/(TRYβV ((TRYδ + Δδ) + TRYκ TRYconvert)) /. Δδ -> TRYm/(TRYn - TRYm) TRYδ // N
```

Out[ ]= 0.0254283

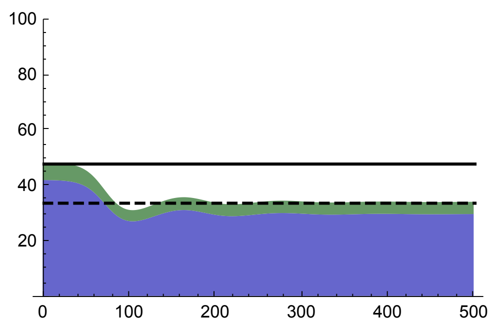
% rise in the endemic equilibrium:

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

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 TRYκ/TRYβ, {t, 0, maxtime}, PlotStyle → {Black}],
 Plot[100 TRYκ/TRYβV, {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
 ImageSize → 250
]
```

Out[∘]=


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

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

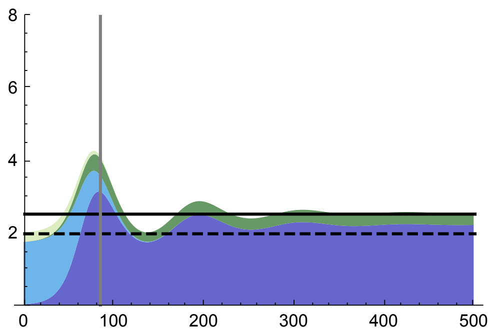
Out[∘]= 1.4165

In[∘]:=
```
droptime = First[
  Select[Table[Flatten[{t, Sum[100 s[c, t] /. solution[partemp, start], {c, 1, 2}]}],
    {t, 0, maxtime}], #[[2]] < 100 TRYκ/TRYβV &]]
```

Out[∘]= {84, 33.7945}

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

Out[∘]=



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

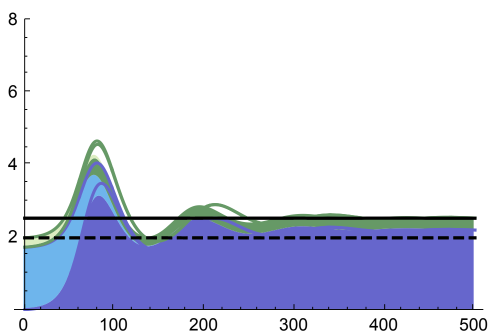
In[∘]:= partemp = $\left\{\text{TRYp, TRYf, TRYolder, TRY}\beta\text{, TRY}\beta\text{V, }\frac{8}{10}\text{TRY}\delta\text{, }\frac{8}{10}\text{TRY}\delta\text{O, TRY}\varkappa\text{, }\frac{8}{10}\right\}$;

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 → {■, ■, ■, ■}],
   Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)),
    {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
   Plot[100 ((TRYn/TRYn-0) TRYδ (TRYβV - TRYκ))/(TRYβV ((TRYn/TRYn-0) TRYδ + TRYκ TRYconvert)),
    {t, 0, maxtime}, PlotStyle → {Black}],
   ImageSize → 250
  ]
```

Out[∘]=



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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```
$i \to \frac{\delta\ (\beta-\kappa)}{\beta\ (\delta+q\ \kappa)}$

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

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

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

Out[•]= $\{\beta V \to 0.590208\}$

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;
```

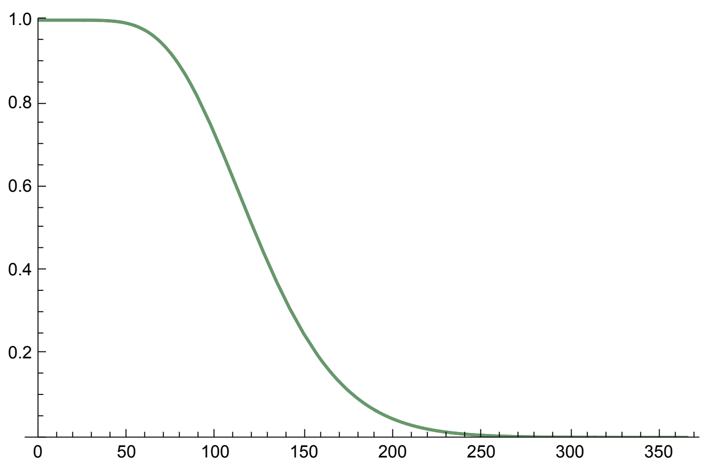
Starting equilibrium would be (r0 includes all of the n resistance classes):
$\left\{s \to \frac{\kappa}{\beta},\ i \to \frac{\delta\ (\beta-\kappa)}{\beta\ (\delta+q\ \kappa)}\right\}$

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

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

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 / (TRYδO TRYn)], t]),
  {t, 0, 365}, PlotRange → {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```

Out[∘]=


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_, β_, βV_, δY_, δO_, κ_, q_}, start] :=
 solution[{p, f, older, β, βV, δY, δO, κ, q}, start] =
  Block[{ages = 2, stages = 2, n = TRYn},
   dsdt[j_, t_] =
    (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] + n * δ[j] * r[n, 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}] *
      Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
     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[1, j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] - n * δ[j] * r[1, j, t];
   For[nn = 2, nn ≤ n - TRYm, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] - n * δ[j] * r[nn, j, t];
   ];
   For[nn = n + 1 - TRYm, nn ≤ n, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] -
       Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n * δ[j] * r[nn, 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}],
        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]) 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, TRYδO, 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}, ■}}}],
```

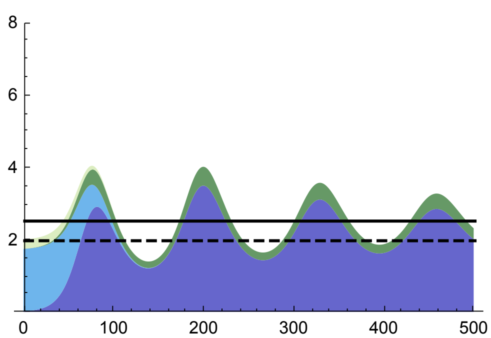
$$\text{Plot}\left[100\,\frac{\text{TRY}\delta\ (\text{TRY}\beta - \text{TRY}\varkappa)}{\text{TRY}\beta\ (\text{TRY}\delta + \text{TRY}\varkappa\ \text{TRYconvert})}, \{t, 0, \text{maxtime}\},\right.$$

```
   PlotStyle → {Black, Dashed}],
```

$$\text{Plot}\left[100\,\frac{\frac{\text{TRYn}}{\text{TRYn}-\text{TRYm}}\ \text{TRY}\delta\ (\text{TRY}\beta\text{V} - \text{TRY}\varkappa)}{\text{TRY}\beta\text{V}\left(\frac{\text{TRYn}}{\text{TRYn}-\text{TRYm}}\ \text{TRY}\delta + \text{TRY}\varkappa\ \text{TRYconvert}\right)},\right.$$

```
   {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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[•]= {0.380508}

In[•]:=
```
Solve[Exp[s 50] == (p50 / (1 - p50) / (p0 / (1 - p0)) /. 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 → 0.0821546}

This is consistent with the predicted selection coefficient:

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

Out[•]= 0.0833

New equilibrium:

In[•]:=
```
((TRYδ + Δδ) (TRYβV - TRYϰ) / (TRYβV ((TRYδ + Δδ) + TRYϰ TRYconvert))) /. Δδ -> TRYm/(TRYn - TRYm) TRYδ // N
```

Out[•]= 0.0254283

% rise in the endemic equilibrium:

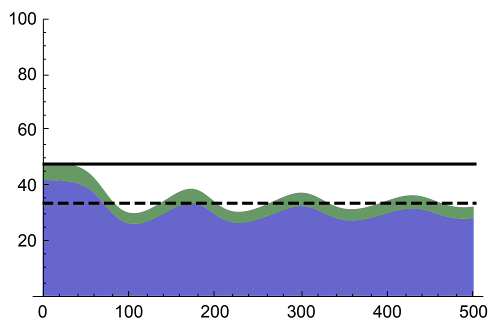
In[•]:=
```
100 * (% - TRYinf)/TRYinf
```

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 TRYκ/TRYβ, {t, 0, maxtime}, PlotStyle → {Black}],
 Plot[100 TRYκ/TRYβV, {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
 ImageSize → 250
]
```

Out[∘]=



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

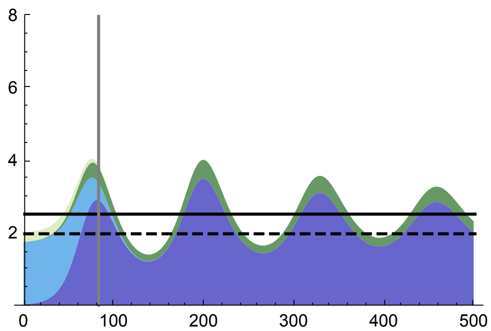
In[∘]:= $\left(1 + \frac{(\text{TRY}\beta\text{V} - \text{TRY}\beta)}{\text{TRY}\beta}\right)$

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 TRYκ/TRYβV &]]
```

Out[∘]= {82, 33.8}

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

Out[∘]=


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

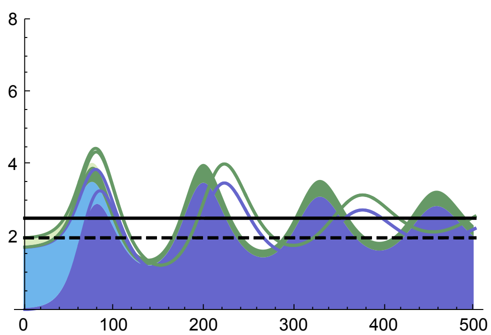
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, 8/10 TRYδ, 8/10 TRYδO, TRYϰ, 8/10};
```

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 (TRYδ (TRYβ - TRYκ)) / (TRYβ (TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYn/TRYn-0) TRYδ (TRYβV - TRYκ)) / (TRYβV ((TRYn/TRYn-0) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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 3B: 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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

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

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

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

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

$\frac{\text{TRY}\beta}{\text{TRY}\kappa}$ // 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%:

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

Out[•]= 1.66667

while the mean waiting time decreases by 40%:

In[•]:= `1 / %`

Out[•]= 0.6

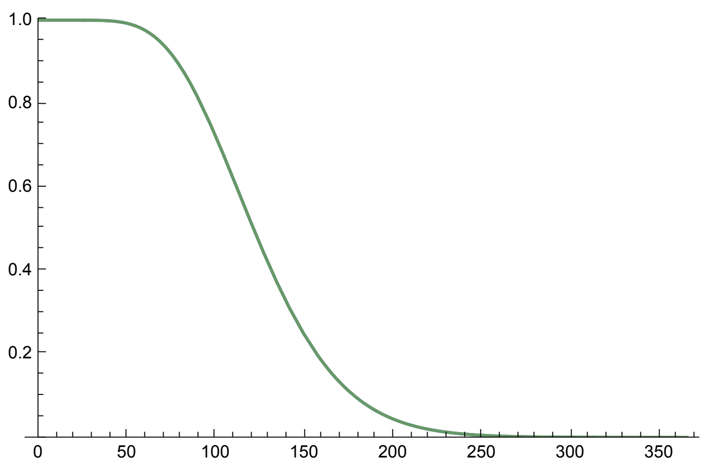
Starting equilibrium would be (r0 includes all of the n resistance classes):
$\left\{s \to \frac{\kappa}{\beta},\ i \to \frac{\delta\ (\beta-\kappa)}{\beta\ (\delta+q\ \kappa)}\right\}$

In[∘]:=
```
start = {s0 → TRYϰ/TRYβ, i0 → TRYδ (TRYβ - TRYϰ)/(TRYβ (TRYδ + TRYϰ TRYconvert)),
  r0 → 1 - TRYϰ/TRYβ - TRYδ (TRYβ - TRYϰ)/(TRYβ (TRYδ + TRYϰ TRYconvert))}
```

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

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]]
]
```

Out[∘]=


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_, β_, βV_, δY_, δO_, κ_, q_}, start] :=
 solution[{p, f, older, β, βV, δY, δO, κ, q}, start] =
  Block[{ages = 2, stages = 2, n = TRYn},
   dsdt[j_, t_] =
    (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] + n * δ[j] * r[n, 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}] *
      Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
     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[1, j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] - n * δ[j] * r[1, j, t];
   For[nn = 2, nn ≤ n - TRYm, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] - n * δ[j] * r[nn, j, t];
   ];
   For[nn = n + 1 - TRYm, nn ≤ n, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] -
       Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n * δ[j] * r[nn, 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}],
        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]) 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, TRYδO, TRYκ, TRYconvert};
```

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

Showing the % of the population infectious:

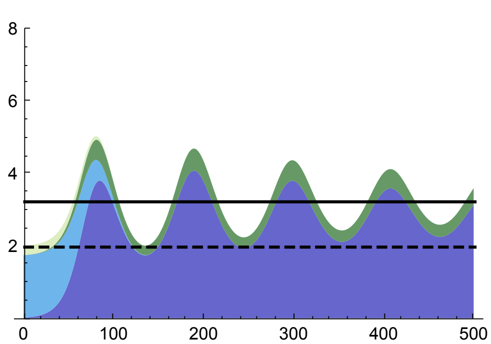
In[∘]:=
```
plot1 = Show[
  Plot[Evaluate@Table[ Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
       solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
   {t, 0, maxtime}, PlotRange → {Automatic, {0, maxy}},
   PlotStyle → None, Filling → {{1 → {0, ■}}, {2 → {{1}, ■}},
     {3 → {{2}, ■}},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

$$\text{Plot}\left[100\,\frac{\text{TRY}\delta\ (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta\ (\text{TRY}\delta + \text{TRY}\kappa\ \text{TRYconvert})},\ \{t, 0, \text{maxtime}\},\ \text{PlotStyle} \to \{\text{Black}, \text{Dashed}\}\right],$$

$$\text{Plot}\left[100\,\frac{\frac{\text{TRYn}}{\text{TRYn}-\text{TRYm}}\ \text{TRY}\delta\ (\text{TRY}\beta\text{V} - \text{TRY}\kappa)}{\text{TRY}\beta\text{V}\left(\frac{\text{TRYn}}{\text{TRYn}-\text{TRYm}}\ \text{TRY}\delta + \text{TRY}\kappa\ \text{TRYconvert}\right)},\ \{t, 0, \text{maxtime}\},\ \text{PlotStyle} \to \{\text{Black}\}\right],$$

```
  ImageSize → 250
 ]
```

Out[∘]=



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[•]= {0.383891}
```

```
In[•]:= Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. 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 → 0.0824411}
```

This is consistent with the predicted selection coefficient:

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

```
Out[•]= 0.0833333
```

New equilibrium:

```
In[•]:= (((TRYδ + Δδ) (TRYβV - TRYϰ))/(TRYβV ((TRYδ + Δδ) + TRYϰ TRYconvert))) /. Δδ -> TRYm/(TRYn - TRYm) TRYδ // N
```

```
Out[•]= 0.0325
```

% rise in the endemic equilibrium:

```
In[•]:= 100 * (% - TRYinf)/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:

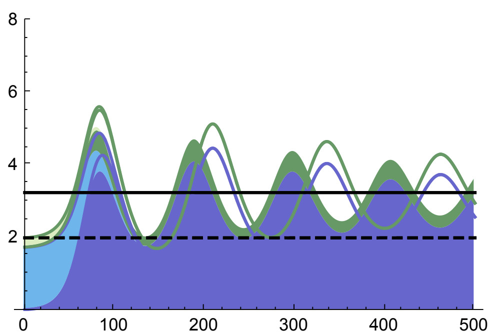
```
In[•]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, 8/10 TRYδ, 8/10 TRYδ0, TRYϰ, 8/10};
```

```
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 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 (TRYn/(TRYn-TRYm) TRYδ (TRYβV - TRYκ))/(TRYβV (TRYn/(TRYn-TRYm) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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 S4A: Multiple variants, first more transmissible then persistently evasive (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*)
TRYfnew = 1 / 1000;(*Starting fraction among variants of the second variant*)
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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```
$i \to \frac{\delta\ (\beta-\kappa)}{\beta\ (\delta+q\ \kappa)}$

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

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

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

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

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

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 = 5;
TRYm = 0;
```

Second variant has the same transmissibility as the first variant

In[∘]:= TRYβVnew = TRYβV;

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

In[∘]:=
```
TRYm = 2;
```

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

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

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

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

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

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 last variant, the second the initial variant, and the third stage class is the resident.]

In[∘]:=
```
{ages = 2, stages = 3, n = TRYn};
```

In[∘]:=
```
Clear[solution]
solution[{p_, f_, fnew_, older_, β_, βV_, βVnew_, δY_, δO_, κ_, q_}, start] :=
 solution[{p, f, fnew, older, β, βV, βVnew, δY, δO, κ, q}, start] =
  Block[{ages = 2, stages = 3, n = TRYn},
   dsdt[j_, t_] =
    (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] + n * δ[j] * r[n, 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}] *
      Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
     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];
   didt[j_, 3, t_] = Sum[β[k, 3] * i[k, 3, t], {k, 1, ages}] * s[j, t] -
     κ[j, 3] * i[j, 3, t];
   drdt[1, j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] - n * δ[j] * r[1, j, t];
```

```
    For[nn = 2, nn ≤ n - TRYm, nn++,
     drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] - n * δ[j] * r[nn, j, t];
    ];
    For[nn = n + 1 - TRYm, nn ≤ n, nn++,
     drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] -
        Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n * δ[j] * r[nn, j, t];
    ];
    pars = {β[j_, 1] → βVnew, β[j_, 2] → βV,
      β[j_, 3] → β, δ[1] → δY, δ[2] → δO, κ[j_, jj_] → κ};
    frac[1, 1] = (1 - older) (1 - f) fnew;
    frac[2, 1] = older (1 - f) fnew;
    frac[1, 2] = (1 - older) (1 - f) (1 - fnew);
    frac[2, 2] = older (1 - f) (1 - fnew);
    frac[1, 3] = (1 - older) f;
    frac[2, 3] = 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] == Sum[frac[j, jj], {jj, 1, stages}] * s0,
          Table[r[nn, j, 0] == Sum[frac[j, jj], {jj, 1, stages}] 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}, {1, 3}, {2, 1}, {2, 2}, {2, 3}}`

In[◦]:=
```
labels = {"<70,Res", "<70,Mutant1",
   "<70,Mutant2", "70+,Res", "70+,Mutant1", "70+,Mutant2"};
```

In[◦]:=
```
colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.7, 0.9, 0.5], RGBColor[0.4, 0.6, 0.4],
  ColorData["Pastel", 3 / 4], RGBColor[0.86, 0.93, 0.76, 0.5]}
```

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,Mutant1
  <70,Mutant2
  70+,Res
  70+,Mutant1
  70+,Mutant2 )
```

In[∘]:=
```
partemp = {TRYp, TRYf, TRYfnew, TRYolder,
    TRYβ, TRYβV, TRYβVnew, TRYδ, TRYδO, TRYϰ, TRYconvert};
```

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

Showing the % of the population infectious:

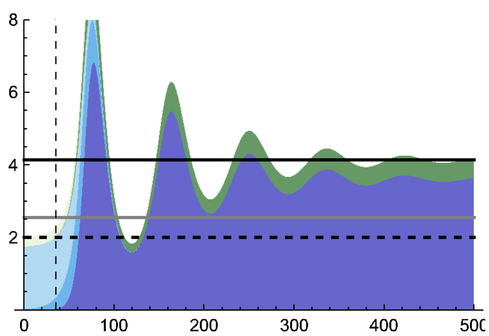
With these parameters, there are 35 days between when the two variants represent 1% of the infections (the starting point for the first variant):

In[∘]:=
```
timeorig1 = t /. FindRoot[
   (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}] /. solution[partemp, start]) ==
    0.01, {t, 1, 5}]
```

Out[∘]= 35.2168

In[∘]:=
```
plotmult1 = 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}, }}, {5 → {{4}, }}, {6 → {{5}, }}}],
  Plot[100 (TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 (TRYδ (TRYβV - TRYϰ))/(TRYβV (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime}, PlotStyle → {Gray}],
  Plot[100 (TRYn/(TRYn-TRYm) TRYδ (TRYβV - TRYϰ))/(TRYβV (TRYn/(TRYn-TRYm) TRYδ + TRYϰ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ListPlot[{{timeorig1, 0}, {timeorig1, maxy}}, Joined → True,
   PlotStyle → {{Black, Thin, Dashed}}],
  ImageSize → 250
 ]
```

Out[∘]=



Comparing selection relative to each variant on its own and relative to the selection for the combination compared to the original resident strain:

In[∘]:=
```
eachsel = (TRYβV - TRYβ)/TRYβ TRYϰ /. start // N
maxsel = (TRYβV - TRYβ)/TRYβ TRYϰ + TRYm r0/TRYn TRYβV /. start // N
```

Out[∘]= 0.0833

Out[∘]= 0.201342

Note that in this case the second immune evasive variant has a higher selection coefficient relative to the first variant because transmission is higher after the first has spread:

In[•]:=
```
expsel = TRYm r0/TRYn TRYβV /. start // N
```

Out[•]= 0.118042

Selection estimated from the change in new variant relative to the previous variant (only) for the first 50 generations after the second variant reaches 1% of infections:

In[•]:=
```
Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /. t → timeorig1
Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /.
 t → timeorig1 + 50
```

Out[•]= {0.0602677}

Out[•]= {0.912043}

In[•]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. p50 → % /. p0 → %%), 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 → 0.101713}

This is close to the expected selection of the second variant, but selection is more variable over time because of the non-equilibrium dynamics.

Estimating the time & strength of selection at the midpoint of spread (frequency of 50% among all variants):

In[•]:=
```
time1 = t /. FindRoot[
  (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}] /. solution[partemp, start]) == 0.5,
  {t, 10, 50}]
```

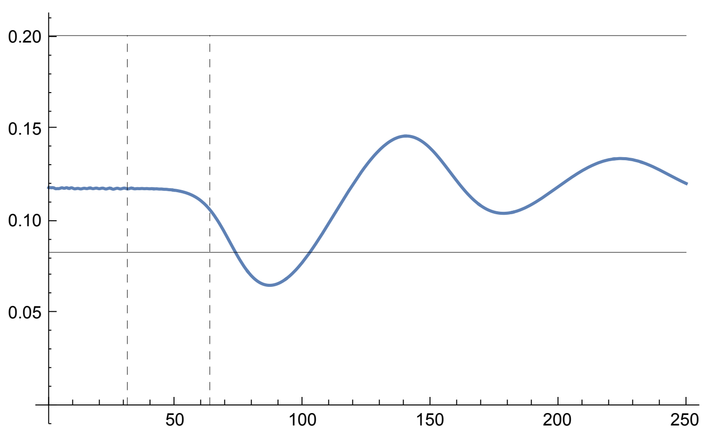
Out[•]= 63.1541

Strength of selection at the midpoint for the new variant versus the previous variant (only):

In[•]:=
```
(Log[(pnew / (1 - pnew))/(pold / (1 - pold))] /.
    pnew -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /.
       t → t + 1) /. pold -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /.
      solution[partemp, start])) /. t → time1
```

Out[•]= {{0.106543}}

In[•]:=
```
Show[Plot[Evaluate@
    (Log[(pnew / (1 - pnew))/(pold / (1 - pold))] /. pnew -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /.
          solution[partemp, start] /. t → t + 1) /.
      pold -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start])),
   {t, 0, maxtime / 2}],
  Plot[{eachsel, maxsel}, {t, 0, maxtime / 2}, PlotStyle → {{Black, Thin}}],
  ListPlot[{{timeorig, 0}, {timeorig, maxsel}},
   Joined → True, PlotStyle → {{Black, Thin, Dashed}}],
  ListPlot[{{time1, 0}, {time1, maxsel}}, Joined → True,
   PlotStyle → {{Black, Thin, Dashed}}],
  PlotRange → {Automatic, {0, maxsel}}, AxesOrigin → {0, 0}
 ]
```

Out[•]=


Increasing the gap between variants (~63 days)

In[•]:=
```
TRYfnew = 1 / 100 000;(*Starting fraction among variants of the second variant*)
```

In[∘]:=
```
partemp = {TRYp, TRYf, TRYfnew, TRYolder,
   TRYβ, TRYβV, TRYβVnew, TRYδ, TRYδO, TRYϰ, TRYconvert};
```

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

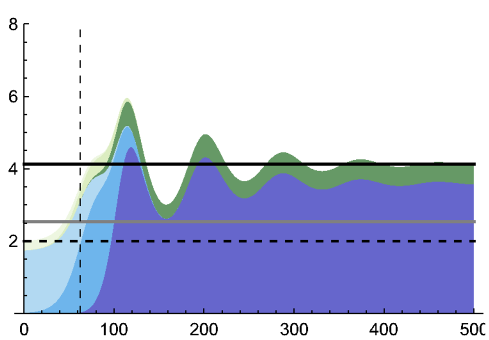
With these parameters, there are 63 days between these two variants:

In[∘]:=
```
timeorig2 = t /. FindRoot[
  (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}] /. solution[partemp, start]) ==
   0.01, {t, 1, 5}]
```

Out[∘]= 62.6272

In[∘]:=
```
plotmult2 = 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}, ■}}, {5 → {{4}, ■}}, {6 → {{5}, ■}}}],
  Plot[100 (TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 (TRYδ (TRYβV - TRYϰ))/(TRYβV (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime}, PlotStyle → {Gray}],
  Plot[100 (TRYn/(TRYn-TRYm) TRYδ (TRYβV - TRYϰ))/(TRYβV (TRYn/(TRYn-TRYm) TRYδ + TRYϰ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ListPlot[{{timeorig2, 0}, {timeorig2, maxy}}, Joined → True,
   PlotStyle → {{Black, Thin, Dashed}}],
  ImageSize → 250
 ]
```

Out[∘]=



Selection estimated from the change in new variant relative to the previous variant (only) for the first 50 generations after the second variant reaches 1% of infections:

```
In[∘]:= Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /. t → timeorig2
        Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /.
         t → timeorig2 + 50
Out[∘]= {0.0161737}
Out[∘]= {0.841588}
```

```
In[∘]:= Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. p50 → % /. p0 → %%), 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 → 0.115563}
```

This is close to the expected selection of the second variant, but selection is more variable over time because of the non-equilibrium dynamics.

Estimating the time & strength of selection at the midpoint of spread (frequency of 50% among all variants):

```
In[∘]:= time2 = t /. FindRoot[
         (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}] /. solution[partemp, start]) == 0.5,
         {t, 10, 50}]
```

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

General: Further output of InterpolatingFunction::dmval will be suppressed during this calculation.

```
Out[∘]= 97.7799
```

Strength of selection at the midpoint for the new variant versus the previous variant (only):

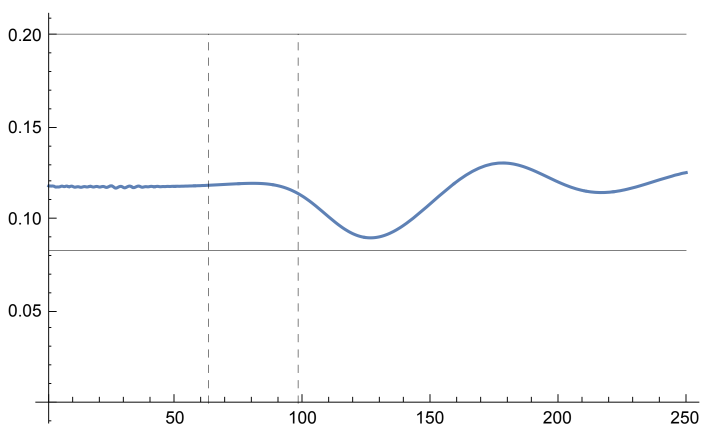
In[∘]:=
```
(Log[(pnew / (1 - pnew))/(pold / (1 - pold))] /.
    pnew -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /.
        t → t + 1) /. pold -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /.
       solution[partemp, start])) /. t → time2
```

Out[∘]= {{0.114405}}

Strength of selection at the midpoint for the new variant versus the previous variant (only):

In[∘]:=
```
Show[Plot[Evaluate@
    (Log[(pnew / (1 - pnew))/(pold / (1 - pold))] /. pnew -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /.
          solution[partemp, start] /. t → t + 1) /.
       pold -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start])),
   {t, 0, maxtime / 2}],
  Plot[{eachsel, maxsel}, {t, 0, maxtime / 2}, PlotStyle → {{Black, Thin}}],
  ListPlot[{{timeorig2, 0}, {timeorig2, maxsel}},
   Joined → True, PlotStyle → {{Black, Thin, Dashed}}],
  ListPlot[{{time2, 0}, {time2, maxsel}}, Joined → True,
   PlotStyle → {{Black, Thin, Dashed}}],
  PlotRange → {Automatic, {0, maxsel}}, AxesOrigin → {0, 0}
 ]
```

Out[∘]=



Increasing the gap between variants (~97 days)

In[∘]:=
```
TRYfnew = 1 / 10 000 000; (*Starting fraction among variants of the second variant*)
```

In[∘]:=
```
partemp = {TRYp, TRYf, TRYfnew, TRYolder,
    TRYβ, TRYβV, TRYβVnew, TRYδ, TRYδO, TRYκ, TRYconvert};
```

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

With these parameters, there are 97 days between these two variants:

In[∘]:=
```
timeorig3 = t /. FindRoot[
   (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}] /. solution[partemp, start]) ==
   0.01, {t, 10, 50}]
```

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

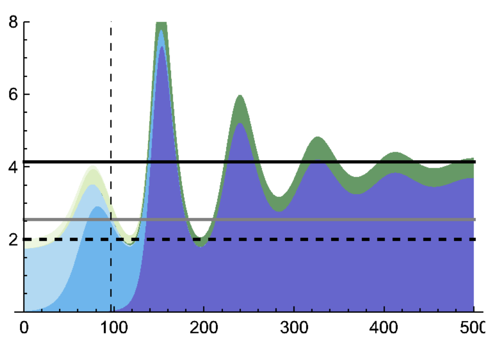
InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

General: Further output of InterpolatingFunction::dmval will be suppressed during this calculation.

Out[∘]= 96.8657

In[∘]:=
```
plotmult3 = 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}, ■}}, {5 → {{4}, ■}}, {6 → {{5}, ■}}}],
  Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 (TRYδ (TRYβV - TRYκ))/(TRYβV (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime}, PlotStyle → {Gray}],
  Plot[100 ((TRYn/(TRYn-TRYm)) TRYδ (TRYβV - TRYκ))/(TRYβV ((TRYn/(TRYn-TRYm)) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ListPlot[{{timeorig3, 0}, {timeorig3, maxy}}, Joined → True,
   PlotStyle → {{Black, Thin, Dashed}}],
  ImageSize → 250
 ]
```

Out[∘]=



Selection estimated from the change in new variant relative to the previous variant (only) for the first 50 generations after the second variant reaches 1% of infections:

In[∘]:=
```
Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /. t → timeorig3
Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /.
 t → timeorig3 + 50
```

Out[∘]= {0.0107699}

Out[∘]= {0.900221}

In[∘]:=
```
Solve[Exp[s 50] == (p50 / (1 - p50))/(p0 / (1 - p0)) /. p50 → % /. p0 → %%), 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 → 0.134397}
```

This is close to the expected selection of the second variant, but selection is more variable over time because of the non-equilibrium dynamics.

Estimating the time & strength of selection at the midpoint of spread (frequency of 50% among all variants):

In[∘]:=
```
time3 = t /. FindRoot[
  (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}] /. solution[partemp, start]) == 0.5,
  {t, 10, 50}]
```

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

General: Further output of InterpolatingFunction::dmval will be suppressed during this calculation.

Out[∘]=
```
129.979
```

Strength of selection at the midpoint for the new variant versus the previous variant (only):

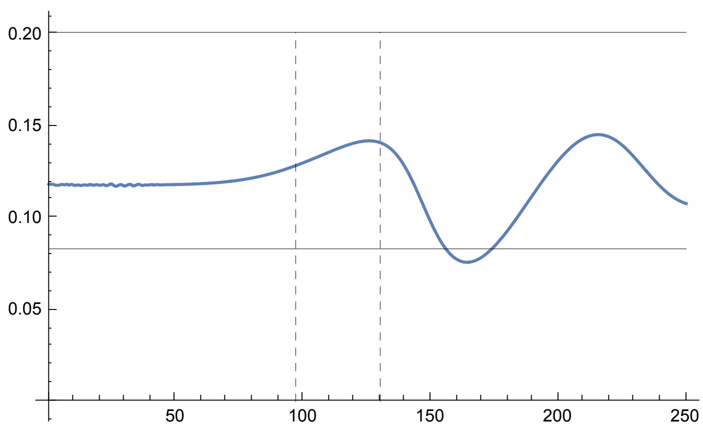
In[∘]:=
```
(Log[(pnew / (1 - pnew)) / (pold / (1 - pold))] /.
    pnew -> (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /.
      t → t + 1) /. pold -> (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /.
      solution[partemp, start])) /. t → time3
```

Out[∘]=
```
{{0.141205}}
```

This selection coefficient is stronger than expected (0.0833) when it spreads at this point.

In[∘]:=
```
Show[Plot[Evaluate@
    (Log[(pnew / (1 - pnew)) / (pold / (1 - pold))] /. pnew -> (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /.
            solution[partemp, start] /. t → t + 1) /.
        pold -> (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start])),
   {t, 0, maxtime / 2}],
  Plot[{eachsel, maxsel}, {t, 0, maxtime / 2}, PlotStyle → {{Black, Thin}}],
  ListPlot[{{timeorig3, 0}, {timeorig3, maxsel}}, Joined → True,
   PlotStyle → {{Black, Thin, Dashed}}], ListPlot[{{time3, 0}, {time3, maxsel}},
   Joined → True, PlotStyle → {{Black, Thin, Dashed}}],
  PlotRange → {Automatic, {0, maxsel}}, AxesOrigin → {0, 0}
]
```

Out[∘]=



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

Figure S4B: Multiple variants, first persistently evasive then 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*)
TRYfnew = 1 / 1000;(*Starting fraction among variants of the second variant*)
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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

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

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

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

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

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

Out[•]= 2.08333

First variant has the same transmissibility as the resident

```
In[•]:= TRYβV = TRYβ;
```

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

```
In[•]:= TRYn = 5;
TRYm = 2;
```

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

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

Out[•]= 1.66667

while the mean waiting time decreases by 40%:

```
In[•]:= 1 / %
Out[•]= 0.6
```

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

In[•]:=
```
Flatten[Solve[(βV - TRYβ)/TRYβ TRYϰ == 0.0833, βV]]
```
Out[•]=
```
{βV → 0.590208}
```
In[•]:=
```
TRYβVnew = βV /. %;
```
% increase in β:

In[•]:=
```
100 * (TRYβVnew - TRYβ)/TRYβ
```
Out[•]=
```
41.65
```
and keeps the immune evasive properties of the first variant.

Starting equilibrium would be (r0 includes all of the n resistance classes):
$\left\{s \to \frac{\kappa}{\beta},\ i \to \frac{\delta\,(\beta-\kappa)}{\beta\,(\delta+q\,\kappa)}\right\}$

In[•]:=
```
start = {s0 → TRYϰ/TRYβ, i0 → TRYδ (TRYβ - TRYϰ)/(TRYβ (TRYδ + TRYϰ TRYconvert)),
   r0 → 1 - TRYϰ/TRYβ - TRYδ (TRYβ - TRYϰ)/(TRYβ (TRYδ + TRYϰ TRYconvert))}
```
Out[•]=
```
{s0 → 12/25, i0 → 1/50, r0 → 1/2}
```
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 last variant, the second the initial variant, and the third stage class is the resident.]

In[•]:=
```
{ages = 2, stages = 3, n = TRYn};
```
In[•]:=
```
Clear[solution]
solution[{p_, f_, fnew_, older_, β_, βV_, βVnew_, δY_, δO_, ϰ_, q_}, start] :=
 solution[{p, f, fnew, older, β, βV, βVnew, δY, δO, ϰ, q}, start] =
  Block[{ages = 2, stages = 3, n = TRYn},
   dsdt[j_, t_] =
    (1 - q) * Sum[ϰ[j, jj] * i[j, jj, t], {jj, 1, stages}] + n * δ[j] * r[n, 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}] *
      Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
     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}] *
      Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
     Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] * s[j, t] - ϰ[j, 2] * i[j, 2, t];
   didt[j_, 3, t_] = Sum[β[k, 3] * i[k, 3, t], {k, 1, ages}] * s[j, t] -
     ϰ[j, 3] * i[j, 3, t];
   drdt[1, j_, t_] = q * Sum[ϰ[j, jj] * i[j, jj, t], {jj, 1, stages}] - n * δ[j] * r[1, j, t];
```

```
  For[nn = 2, nn ≤ n - TRYm, nn++,
   drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] - n * δ[j] * r[nn, j, t];
  ];
  For[nn = n + 1 - TRYm, nn ≤ n, nn++,
   drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] -
      Sum[β[k, 1] * i[k, 1, t] + β[k, 2] * i[k, 2, t], {k, 1, ages}] * r[nn, j, t] -
      n * δ[j] * r[nn, j, t];
  ];
  pars = {β[j_, 1] → βVnew, β[j_, 2] → βV,
    β[j_, 3] → β, δ[1] → δY, δ[2] → δO, κ[j_, jj_] → κ};
  frac[1, 1] = (1 - older) (1 - f) fnew;
  frac[2, 1] = older (1 - f) fnew;
  frac[1, 2] = (1 - older) (1 - f) (1 - fnew);
  frac[2, 2] = older (1 - f) (1 - fnew);
  frac[1, 3] = (1 - older) f;
  frac[2, 3] = 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] == Sum[frac[j, jj], {jj, 1, stages}] * s0,
         Table[r[nn, j, 0] == Sum[frac[j, jj], {jj, 1, stages}] 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}, {1, 3}, {2, 1}, {2, 2}, {2, 3}}
```

In[∘]:=
```
labels = {"<70,Res", "<70,Mutant1",
   "<70,Mutant2", "70+,Res", "70+,Mutant1", "70+,Mutant2"};
```

In[∘]:=
```
colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.7, 0.9, 0.5], RGBColor[0.4, 0.6, 0.4],
  ColorData["Pastel", 3 / 4], RGBColor[0.86, 0.93, 0.76, 0.5]}
```

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,Mutant1	■
<70,Mutant2	■
70+,Res	■
70+,Mutant1	■
70+,Mutant2	■

In[∘]:=
```
partemp = {TRYp, TRYf, TRYfnew, TRYolder,
   TRYβ, TRYβV, TRYβVnew, TRYδ, TRYδO, TRYκ, TRYconvert};
```

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

Showing the % of the population infectious:

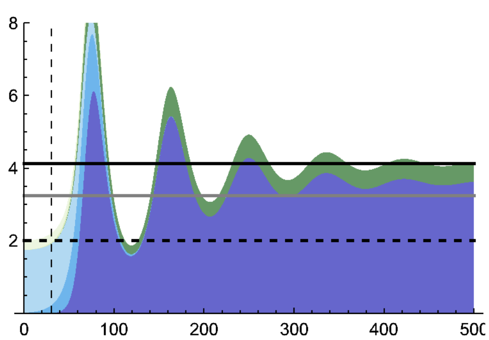
With these parameters, there are 35 days between when the two variants represent 1% of the infections (the starting point for the first variant):

In[∘]:=
```
timeorig1 = t /. FindRoot[
   (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}] /. solution[partemp, start]) ==
    0.01, {t, 1, 5}]
```

Out[∘]= 35.29

In[∘]:=
```
plotmult1 = 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}, ■}}, {5 → {{4}, ■}}, {6 → {{5}, ■}}}],
  Plot[100 (TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYn/(TRYn-TRYm)) TRYδ (TRYβV - TRYϰ))/(TRYβV ((TRYn/(TRYn-TRYm)) TRYδ + TRYϰ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Gray}],
  Plot[100 ((TRYn/(TRYn-TRYm)) TRYδ (TRYβVnew - TRYϰ))/(TRYβVnew ((TRYn/(TRYn-TRYm)) TRYδ + TRYϰ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ListPlot[{{timeorig, 0}, {timeorig, maxy}}, Joined → True,
   PlotStyle → {{Black, Thin, Dashed}}],
  ImageSize → 250
 ]
```

Out[∘]=



Comparing selection relative to each variant on its own and relative to the selection for the combination compared to the original resident strain:

In[∘]:=

$$\text{eachsel} = \text{TRYm}\,\frac{\text{r0}}{\text{TRYn}}\,\text{TRY}\beta \;/.\; \text{start} \;//\; \text{N}$$

$$\text{maxsel} = \frac{\text{TRY}\beta\text{Vnew} - \text{TRY}\beta\text{V}}{\text{TRY}\beta\text{V}}\,\text{TRY}\varkappa + \text{TRYm}\,\frac{\text{r0}}{\text{TRYn}}\,\text{TRY}\beta \;/.\; \text{start} \;//\; \text{N}$$

Out[∘]= 0.0833333

Out[∘]= 0.166633

In this case the second immune evasive variant has the same selection coefficient relative to the first variant because the number of recovered classes does not affect selection on a more transmissible variant:

In[∘]:=
```
expsel = (TRYβVnew - TRYβV)/TRYβV TRYϰ // N
```

Out[∘]= 0.0833

Selection estimated from the change in new variant relative to the previous variant (only) for the first 50 generations after the second variant reaches 1% of infections:

In[∘]:=
```
Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /. t → timeorig1
Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /.
 t → timeorig1 + 50
```

Out[∘]= {0.0598229}

Out[∘]= {0.859938}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. p50 → % /. p0 → %%), 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 → 0.0913892}

This is close to the expected selection of the second variant, but selection is more variable over time because of the non-equilibrium dynamics.

Estimating the time & strength of selection at the midpoint of spread (frequency of 50% among all variants):

In[∘]:=
```
time1 = t /. FindRoot[
   (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}] /. solution[partemp, start]) == 0.5,
   {t, 10, 50}]
```

Out[∘]= 64.5643

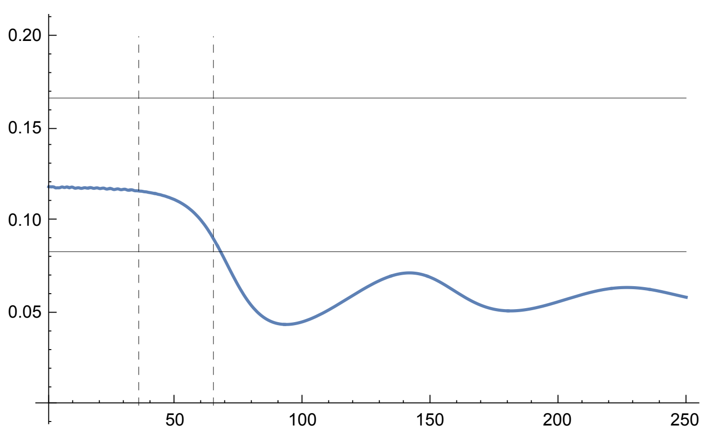
Strength of selection at the midpoint for the new variant versus the previous variant (only):

In[•]:=
```
(Log[(pnew / (1 - pnew)) / (pold / (1 - pold))] /.
    pnew -> (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /.
        t → t + 1) /. pold -> (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /.
       solution[partemp, start])) /. t → time1
```

Out[•]= {{0.0904554}}

This selection coefficient is weaker than expected (0.0833) when it spreads at this point, as the previous immune evasive variant has depleted the pool of susceptible individuals (not just S but m of the R classes).

In[•]:=
```
Show[Plot[Evaluate@
   (Log[(pnew / (1 - pnew)) / (pold / (1 - pold))] /. pnew -> (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /.
          solution[partemp, start] /. t → t + 1) /.
     pold -> (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start])),
  {t, 0, maxtime / 2}],
 Plot[{eachsel, maxsel}, {t, 0, maxtime / 2}, PlotStyle → {{Black, Thin}}],
 ListPlot[{{timeorig1, 0}, {timeorig1, 0.2}},
  Joined → True, PlotStyle → {{Black, Thin, Dashed}}],
 ListPlot[{{time1, 0}, {time1, 0.2}}, Joined → True,
  PlotStyle → {{Black, Thin, Dashed}}],
 PlotRange → {Automatic, {0, 0.2}}, AxesOrigin → {0, 0}
]
```

Out[•]=


Increasing the gap between variants (~63 days)

In[∘]:=
```
TRYfnew = 1 / 90 000;(*Starting fraction among variants of the second variant*)
```

In[∘]:=
```
partemp = {TRYp, TRYf, TRYfnew, TRYolder,
    TRYβ, TRYβV, TRYβVnew, TRYδ, TRYδO, TRYκ, TRYconvert};
```

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

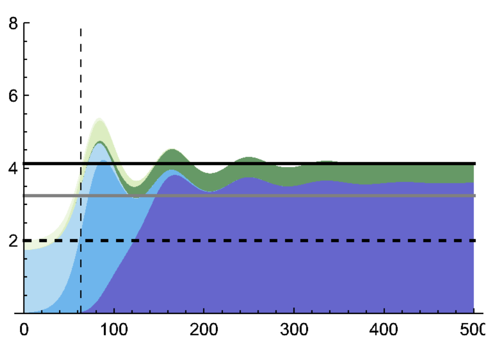
With these parameters, there are 63 days between these two variants:

In[∘]:=
```
timeorig2 = t /. FindRoot[
   (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}] /. solution[partemp, start]) ==
   0.01, {t, 1, 5}]
```

Out[∘]=
```
63.0988
```

In[∘]:=
```
plotmult2 = 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}, }}, {5 → {{4}, }}, {6 → {{5}, }}}],
  Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 (TRYn/(TRYn-TRYm) TRYδ (TRYβV - TRYκ))/(TRYβV (TRYn/(TRYn-TRYm) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Gray}],
  Plot[100 (TRYn/(TRYn-TRYm) TRYδ (TRYβVnew - TRYκ))/(TRYβVnew (TRYn/(TRYn-TRYm) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ListPlot[{{timeorig2, 0}, {timeorig2, maxy}}, Joined → True,
   PlotStyle → {{Black, Thin, Dashed}}],
  ImageSize → 250
 ]
```

Out[∘]=



Selection estimated from the change in new variant relative to the previous variant (only) for the first 50 generations after the second variant reaches 1% of infections:

In[∘]:=
```
Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /. t → timeorig2
Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /.
 t → timeorig2 + 50
```

Out[∘]= {0.0157182}

Out[∘]= {0.482923}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. p50 → % /. p0 → %%), 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 → 0.0813752}

This is close to the expected selection of the second variant, but selection is more variable over time because of the non-equilibrium dynamics.

Estimating the time & strength of selection at the midpoint of spread (frequency of 50% among all variants):

In[∘]:=
```
time2 = t /. FindRoot[
  (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}] /. solution[partemp, start]) == 0.5,
  {t, 10, 50}]
```

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

General: Further output of InterpolatingFunction::dmval will be suppressed during this calculation.

Out[∘]= 114.453

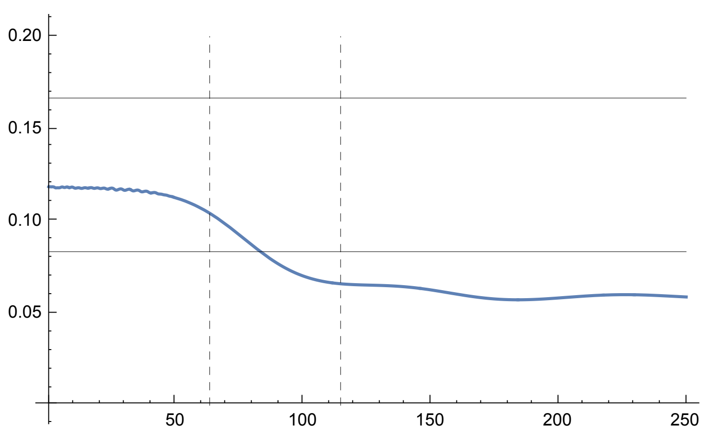
Strength of selection at the midpoint for the new variant versus the previous variant (only):

In[∘]:=
```
(Log[(pnew / (1 - pnew))/(pold / (1 - pold))] /.
    pnew -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /.
       t → t + 1) /. pold -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /.
      solution[partemp, start])) /. t → time2
```

Out[∘]= {{0.0659235}}

This selection coefficient is weaker than expected (0.0833) when it spreads at this point, as the previous immune evasive variant has depleted the pool of susceptible individuals (not just S but m of the R classes).

In[∘]:=
```
Show[Plot[Evaluate@
   (Log[(pnew / (1 - pnew))/(pold / (1 - pold))] /. pnew -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /.
          solution[partemp, start] /. t → t + 1) /.
     pold -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start])),
  {t, 0, maxtime / 2}],
 Plot[{eachsel, maxsel}, {t, 0, maxtime / 2}, PlotStyle → {{Black, Thin}}],
 ListPlot[{{timeorig2, 0}, {timeorig2, 0.2}},
  Joined → True, PlotStyle → {{Black, Thin, Dashed}}],
 ListPlot[{{time2, 0}, {time2, 0.2}}, Joined → True,
  PlotStyle → {{Black, Thin, Dashed}}],
 PlotRange → {Automatic, {0, 0.2}}, AxesOrigin → {0, 0}
]
```

Out[∘]=


Increasing the gap between variants (~97 days)

```
In[∘]:= TRYfnew = 1 / 2 800 000;(*Starting fraction among variants of the second variant*)
```

```
In[∘]:= partemp = {TRYp, TRYf, TRYfnew, TRYolder,
    TRYβ, TRYβV, TRYβVnew, TRYδ, TRYδO, TRYκ, TRYconvert};
```

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

With these parameters, there are 97 days between these two variants:

```
In[∘]:= timeorig3 = t /. FindRoot[
    (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}] /. solution[partemp, start]) ==
    0.01, {t, 10, 50}]
```

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

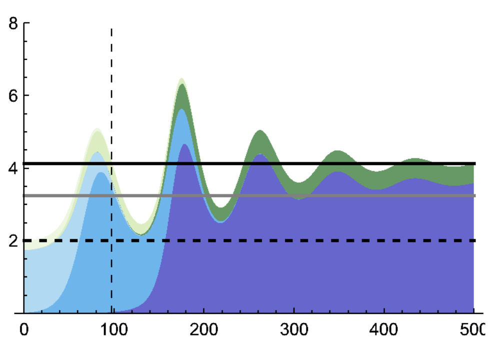
InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

General: Further output of InterpolatingFunction::dmval will be suppressed during this calculation.

```
Out[∘]= 97.2746
```

In[∘]:=
```
plotmult3 = 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}, }}, {5 → {{4}, }}, {6 → {{5}, }}}],
  Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYn/(TRYn-TRYm)) TRYδ (TRYβV - TRYκ))/(TRYβV ((TRYn/(TRYn-TRYm)) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Gray}],
  Plot[100 ((TRYn/(TRYn-TRYm)) TRYδ (TRYβVnew - TRYκ))/(TRYβVnew ((TRYn/(TRYn-TRYm)) TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ListPlot[{{timeorig3, 0}, {timeorig3, maxy}}, Joined → True,
   PlotStyle → {{Black, Thin, Dashed}}],
  ImageSize → 250
 ]
```

Out[∘]=



Selection estimated from the change in new variant relative to the previous variant (only) for the first 50 generations after the second variant reaches 1% of infections:

In[∘]:=
```
Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /. t → timeorig3
Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /.
  t → timeorig3 + 50
```

Out[∘]= {0.0105907}

Out[∘]= {0.34365}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. p50 → % /. p0 → %%), 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 → 0.0778013}

This is close to the expected selection of the second variant, but selection is more variable over time because of the non-equilibrium dynamics.

Estimating the time & strength of selection at the midpoint of spread (frequency of 50% among all variants):

In[∘]:=
```
time3 = t /. FindRoot[
   (Sum[i[j, 1, t], {j, 1, ages}] / Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, stages}] /. solution[partemp, start]) == 0.5,
   {t, 10, 50}]
```

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

InterpolatingFunction: Input value {560.} lies outside the range of data in the interpolating function. Extrapolation will be used.

General: Further output of InterpolatingFunction::dmval will be suppressed during this calculation.

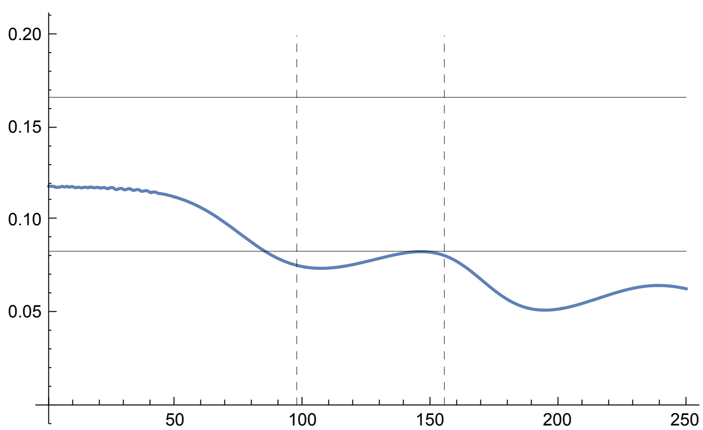
Out[∘]= 155.129

Strength of selection at the midpoint for the new variant versus the previous variant (only):

In[•]:=
```
(Log[(pnew / (1 - pnew))/(pold / (1 - pold))] /.
    pnew -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start] /.
        t → t + 1) /. pold -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /.
       solution[partemp, start])) /. t → time3
```

Out[•]= {{0.0810277}}

In[•]:=
```
Show[Plot[Evaluate@
    (Log[(pnew / (1 - pnew))/(pold / (1 - pold))] /. pnew -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /.
          solution[partemp, start] /. t → t + 1) /.
      pold -> (Sum[i[j, 1, t], {j, 1, ages}]/Sum[i[j, jj, t], {j, 1, ages}, {jj, 1, 2}] /. solution[partemp, start])),
   {t, 0, maxtime / 2}],
  Plot[{eachsel, maxsel}, {t, 0, maxtime / 2}, PlotStyle → {{Black, Thin}}],
  ListPlot[{{timeorig3, 0}, {timeorig3, 0.2}},
   Joined → True, PlotStyle → {{Black, Thin, Dashed}}],
  ListPlot[{{time3, 0}, {time3, 0.2}}, Joined → True,
   PlotStyle → {{Black, Thin, Dashed}}],
  PlotRange → {Automatic, {0, 0.2}}, AxesOrigin → {0, 0}
 ]
```

Out[•]=


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

Vaccines (Figure 6)

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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

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

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

Incidence is expected to decline by:

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

Out[∘]= {0.000576946, 0.0083612}

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

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

Out[∘]= 2.08333

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

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

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

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

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

In[◦]:=
```
Clear[solution]
solution[{p_, f_, older_, β_, βV_, δY_, δO_, vY_, vO_, ϰ_, q_}, start] :=
 solution[{p, f, older, β, βV, δY, δO, vY, vO, ϰ, q}, start] =
  Block[{ages = 2, stages = 2, n = TRYn},
   dsdt[j_, t_] =
    (1 - q) * Sum[ϰ[j, jj] * i[j, jj, t], {jj, 1, stages}] + n * δ[j] * r[n, j, t] -
     Sum[β[k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t] - q * v[j];
   didt[j_, 1, t_] = Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] *
      Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
     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[1, j_, t_] = q * v[j] + q * Sum[ϰ[j, jj] * i[j, jj, t], {jj, 1, stages}] -
     n * δ[j] * r[1, j, t];
   For[nn = 2, nn ≤ n - TRYm, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] - n * δ[j] * r[nn, j, t];
   ];
   For[nn = n + 1 - TRYm, nn ≤ n, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] -
       Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n * δ[j] * r[nn, j, t];
   ];
   pars = {β[j_, 1] → βV, β[j_, 2] → β,
     δ[1] → δY, δ[2] → δO, ϰ[j_, jj_] → ϰ, v[1] → vY, v[2] → vO};
   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]) 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
```

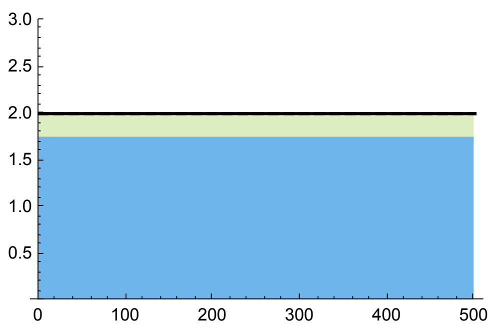
CASE: No vaccinations

```
In[∘]:= TRYvY = (1 - TRYolder) * 0; (*Fraction of susceptibles getting vaccinated per day*)
        TRYvO = TRYolder * 0;
        (*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, ■}}, {2 → {{1}, ■}}, {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
 Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
  PlotStyle → {Black, Dashed}],
 Plot[100 ((TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)) - (TRYvY + TRYvO)/(TRYδ + TRYκ TRYconvert)),
  {t, 0, maxtime}, PlotStyle → {Black}],
 ImageSize → 250
]
```

Out[∘]=



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

In[∘]:=
```
{{Mean[
    Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start], {t, 1, 10}]]],
   Mean[Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]},
  {Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, 1, 10}]]],
   Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]}} // MatrixForm
```

Out[∘]//MatrixForm=

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

CASE: Low vaccination rate

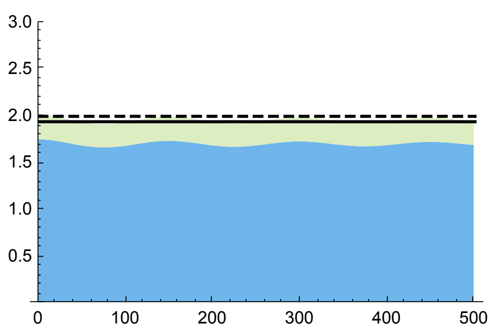
In[∘]:=
```
TRYvY = (1 - TRYolder) TRYvLOW;
(*Fraction of younger susceptibles getting vaccinated per day*)
TRYvO = TRYolder TRYvLOW;
(*Fraction of older susceptibles getting vaccinated per day*)
```

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, ■}}, {2 → {{1}, ■}}, {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
 Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
  PlotStyle → {Black, Dashed}],
 Plot[100 ((TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)) - (TRYvY + TRYvO)/(TRYδ + TRYκ TRYconvert)),
  {t, 0, maxtime}, PlotStyle → {Black}],
 ImageSize → 250
]
```

Out[∘]=


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

In[∘]:=
```
{{Mean[
    Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start], {t, 1, 10}]]],
   Mean[Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]},
  {Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, 1, 10}]]],
   Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]}} // MatrixForm
```

Out[∘]//MatrixForm=

$$\begin{pmatrix} 0.0199813 & 0.0193475 \\ 0.0199813 & 0.0193475 \end{pmatrix}$$

In[∘]:=
```
Transpose[%][[2]] / Transpose[%][[1]] - 1
```

Out[∘]=
```
{-0.0317231, -0.0317229}
```

CASE: High vaccination rate

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

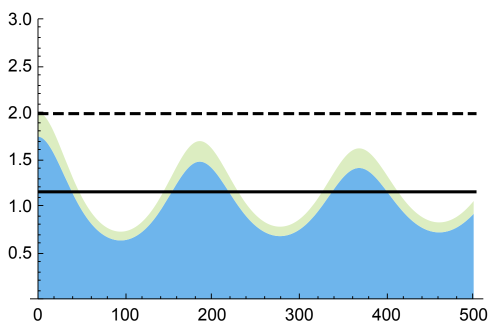
In[∘]:=
```
partemp =
  {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYvY, TRYvO, TRYϰ, TRYconvert};
```

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, ■}}, {2 → {{1}, ■}}, {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
 Plot[100 (TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime},
  PlotStyle → {Black, Dashed}],
 Plot[100 ((TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)) - (TRYvY + TRYv0)/(TRYδ + TRYϰ TRYconvert)),
  {t, 0, maxtime}, PlotStyle → {Black}],
 ImageSize → 250
]
```

Out[∘]=



In[∘]:=
```
{neweq, oldeq} /. oldeq -> (TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)) /.
  neweq -> ((TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)) - (TRYvY + TRYv0)/(TRYδ + TRYϰ TRYconvert)) // N
```

Out[∘]= {0.0116388, 0.02}

In[∘]:=
```
100 (neweq - oldeq)/oldeq /. oldeq -> (TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)) /.
  neweq -> ((TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)) - (TRYvY + TRYv0)/(TRYδ + TRYϰ TRYconvert)) // 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[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start], {t, 1, 10}]]],
   Mean[Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]},
  {Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, 1, 10}]]],
   Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]}} // MatrixForm
```

Out[∘]//MatrixForm=

$$\begin{pmatrix} 0.0197325 & 0.0100449 \\ 0.0197325 & 0.0100449 \end{pmatrix}$$

In[∘]:=
```
Transpose[%][[2]] / Transpose[%][[1]] - 1
```

Out[∘]= {-0.490945, -0.490945}

CASE: High vaccination rate only in older individuals

In[∘]:=
```
TRYvY = 0; (*Fraction of susceptibles getting vaccinated per day*)
TRYvO = TRYolder TRYvHIGH;
(*Fraction of older susceptibles getting vaccinated per day*)
```

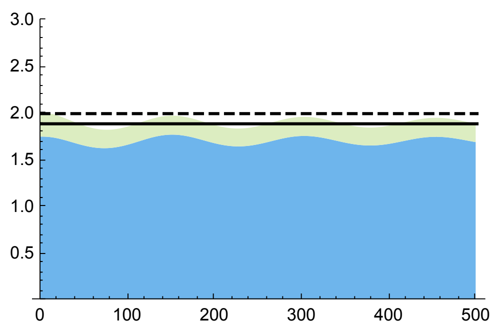
In[∘]:=
```
partemp =
  {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYvY, TRYvO, TRYκ, TRYconvert};
```

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, ■}}, {2 → {{1}, ■}}, {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
 Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
  PlotStyle → {Black, Dashed}],
 Plot[100 ((TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)) - (TRYvY + TRYvO)/(TRYδ + TRYκ TRYconvert)),
  {t, 0, maxtime}, PlotStyle → {Black}],
 ImageSize → 250
]
```

Out[∘]=



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[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start], {t, 1, 10}]]],
   Mean[Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]},
  {Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, 1, 10}]]],
   Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]}} // MatrixForm
```

Out[∘]//MatrixForm=

$$\begin{pmatrix} 0.0199874 & 0.019412 \\ 0.0198141 & 0.015192 \end{pmatrix}$$

In[∘]:=
```
Transpose[%][[2]] / Transpose[%][[1]] - 1
```

Out[∘]= {-0.028788, -0.233273}

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

$$\begin{pmatrix} 0.0199874 & 0.019465 \\ 0.0198141 & 0.0152335 \end{pmatrix}$$

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];

Figure 6alt: Change in vaccinations [Per capita vaccination of susceptibles]

No substantive effect if the total daily rate of vaccinations is held constant.

Compared to the previous section, we now model vaccines per capita, assuming still that susceptibles (only) are targeted. We adjust the vaccination rates by the expected fraction of susceptible individuals to obtain the same rate of vaccination overall:

In[∘]:=
```
TRYvLOW = (1 / 8333)/(TRYκ/TRYβ); (* 0.00012 vaccinations per person per day*)

TRYvHIGH = (1 / 575)/(TRYκ/TRYβ); (* 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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

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

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

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

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):

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

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

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

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

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

In[•]:=
```
Clear[solution]
solution[{p_, f_, older_, β_, βV_, δY_, δO_, vY_, vO_, ϰ_, q_}, start] :=
 solution[{p, f, older, β, βV, δY, δO, vY, vO, ϰ, q}, start] =
  Block[{ages = 2, stages = 2, n = TRYn},
   dsdt[j_, t_] =
    (1 - q) * Sum[ϰ[j, jj] * i[j, jj, t], {jj, 1, stages}] + n * δ[j] * r[n, j, t] -
     Sum[β[k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t] -
     q * v[j] * s[j, t];
   didt[j_, 1, t_] = Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] *
      Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] +
     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[1, j_, t_] = q * v[j] * s[j, t] + q * Sum[ϰ[j, jj] * i[j, jj, t], {jj, 1, stages}] -
     n * δ[j] * r[1, j, t];
   For[nn = 2, nn ≤ n - TRYm, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] - n * δ[j] * r[nn, j, t];
   ];
   For[nn = n + 1 - TRYm, nn ≤ n, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] -
       Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] - n * δ[j] * r[nn, j, t];
   ];
   pars = {β[j_, 1] → βV, β[j_, 2] → β,
     δ[1] → δY, δ[2] → δO, ϰ[j_, jj_] → ϰ, v[1] → vY, v[2] → vO};
   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]) 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 )
```

CASE: No vaccinations

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

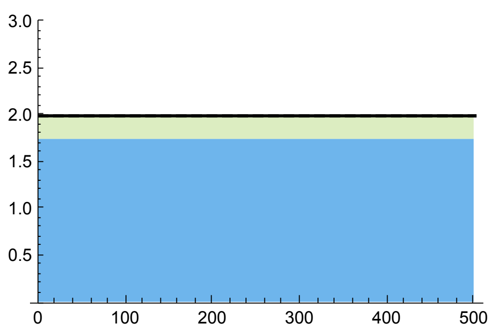
In[∘]:=
```
partemp =
  {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYvY, TRYvO, TRYκ, TRYconvert};
```

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, ■}}, {2 → {{1}, ■}}, {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
  Plot[100 (TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)) -
      (((1 - TRYolder) TRYvY + TRYolder TRYvO) TRYϰ TRYconvert)/(TRYβ (TRYδ + TRYϰ TRYconvert))),
   {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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

In[∘]:=
```
{{Mean[
    Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start], {t, 1, 10}]]],
   Mean[Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]},
  {Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, 1, 10}]]],
   Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]}} // MatrixForm
```

Out[∘]//MatrixForm=

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

CASE: Low vaccination rate

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

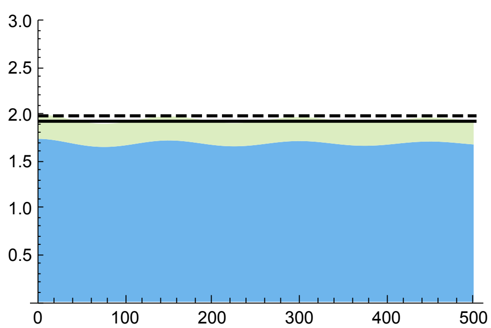
In[∘]:=
```
partemp =
  {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYvY, TRYvO, TRYϰ, TRYconvert};
```

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, ■}}, {2 → {{1}, ■}}, {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
 Plot[100 (TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime},
  PlotStyle → {Black, Dashed}],
 Plot[100 ((TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)) -
     (((1 - TRYolder) TRYvY + TRYolder TRYvO) TRYϰ TRYconvert)/(TRYβ (TRYδ + TRYϰ TRYconvert))),
  {t, 0, maxtime}, PlotStyle → {Black}],
 ImageSize → 250
]
```

Out[∘]=



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

In[∘]:=
```
{{Mean[
    Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start], {t, 1, 10}]]],
   Mean[Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]},
  {Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, 1, 10}]]],
   Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]}} // MatrixForm
```

Out[∘]//MatrixForm=

$$\begin{pmatrix} 0.0199814 & 0.0193522 \\ 0.0199814 & 0.0193523 \end{pmatrix}$$

CASE: High vaccination rate

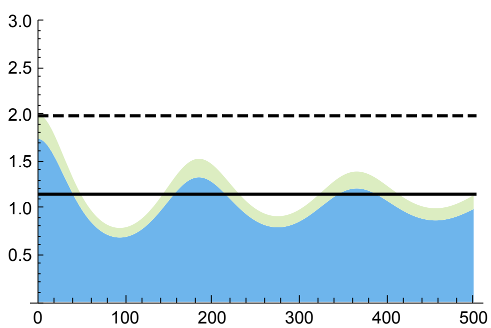
In[∘]:=
```
TRYvY = TRYvHIGH; (*Fraction of susceptibles getting vaccinated per day*)
TRYvO = TRYvHIGH; (*Fraction of older susceptibles getting vaccinated per day*)
```

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, ■}}, {2 → {{1}, ■}}, {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
 Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
  PlotStyle → {Black, Dashed}],
 Plot[100 ((TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)) -
     (((1 - TRYolder) TRYvY + TRYolder TRYv0) TRYκ TRYconvert)/(TRYβ (TRYδ + TRYκ TRYconvert))),
  {t, 0, maxtime}, PlotStyle → {Black}],
 ImageSize → 250
]
```

Out[∘]=


In[∘]:=
```
{neweq, oldeq} /. oldeq -> (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)) /.
  neweq -> ((TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)) -
     (((1 - TRYolder) TRYvY + TRYolder TRYv0) TRYκ TRYconvert)/(TRYβ (TRYδ + TRYκ TRYconvert))) // N
```

Out[∘]= {0.0116388, 0.02}

In[∘]:=
```
100 (neweq - oldeq)/oldeq /. oldeq -> TRYδ (TRYβ - TRYϰ)/(TRYβ (TRYδ + TRYϰ TRYconvert)) /.
  neweq -> (TRYδ (TRYβ - TRYϰ)/(TRYβ (TRYδ + TRYϰ TRYconvert)) -
     ((1 - TRYolder) TRYvY + TRYolder TRYvO) TRYϰ TRYconvert/(TRYβ (TRYδ + TRYϰ TRYconvert))) // 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[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start], {t, 1, 10}]]],
   Mean[Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]},
  {Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, 1, 10}]]],
   Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]}} // MatrixForm
```

Out[∘]//MatrixForm=

$$\begin{pmatrix} 0.0197349 & 0.0111482 \\ 0.0197349 & 0.0111482 \end{pmatrix}$$

In[∘]:=
```
Transpose[%][[2]] / Transpose[%][[1]] - 1
```

Out[∘]= {-0.435103, -0.435103}

CASE: High vaccination rate only in older individuals

In[∘]:=
```
TRYvY = 0; (*Fraction of susceptibles getting vaccinated per day*)
TRYvO = TRYvHIGH; (*Fraction of older susceptibles getting vaccinated per day*)
```

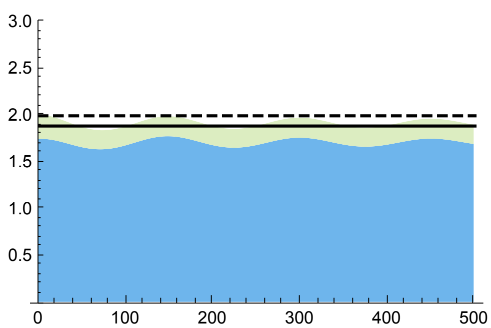
In[∘]:=
```
partemp =
  {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYvY, TRYvO, TRYϰ, TRYconvert};
```

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, ■}}, {2 → {{1}, ■}}, {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
 Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
  PlotStyle → {Black, Dashed}],
 Plot[100 ((TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)) -
     (((1 - TRYolder) TRYvY + TRYolder TRYvO) TRYκ TRYconvert)/(TRYβ (TRYδ + TRYκ TRYconvert))),
  {t, 0, maxtime}, PlotStyle → {Black}],
 ImageSize → 250
]
```

Out[∘]=



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[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start], {t, 1, 10}]]],
   Mean[Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]},
  {Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, 1, 10}]]],
   Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]}} // MatrixForm
```

Out[∘]//MatrixForm=

$$\begin{pmatrix} 0.0199875 & 0.0194449 \\ 0.0198159 & 0.0159056 \end{pmatrix}$$

In[∘]:=
```
Transpose[%][[2]] / Transpose[%][[1]] - 1
```

Out[∘]=
```
{-0.0271452, -0.197335}
```

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

Figure 6alt: Change in vaccinations [Per capita vaccination of all individuals]

Slightly less effective (vaccines not focused solely on those most susceptible)
[NOTE: Dashed curves are not the equilibrium for this model but for the previous case, illustrating the impact of vaccinating everybody.]

Compared to the previous section, we now model vaccines per capita, assuming that all individuals are targetted, with the same total vaccination rate:

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

In[∘]:=
```
maxtime = 5000;
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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

In[∘]:=
```
Solve[δ (β - κ) / (β (δ + q κ)) == inf, β]
```

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

In[∘]:=
```
TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
TRYβ = TRYδ TRYκ / (TRYδ - TRYinf TRYδ - TRYconvert TRYinf TRYκ);

TRYβ / TRYκ // 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):
$\left\{\text{s} \to \frac{\kappa}{\beta},\ \text{i} \to \frac{\delta\ (\beta-\kappa)}{\beta\ (\delta+q\ \kappa)}\right\}$

In[∘]:=
```
start = {s0 → TRYκ / TRYβ, i0 → TRYδ (TRYβ - TRYκ) / (TRYβ (TRYδ + TRYκ TRYconvert)),
   r0 → 1 - TRYκ / TRYβ - TRYδ (TRYβ - TRYκ) / (TRYβ (TRYδ + TRYκ TRYconvert))}
```

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

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

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

In[∘]:=
```
Clear[solution]
solution[{p_, f_, older_, β_, βV_, δY_, δO_, vY_, vO_, ϰ_, q_}, start] :=
 solution[{p, f, older, β, βV, δY, δO, vY, vO, ϰ, q}, start] =
  Block[{ages = 2, stages = 2, n = TRYn},
   dsdt[j_, t_] =
    (1 - q) * Sum[(ϰ[j, jj] + v[j]) * i[j, jj, t], {jj, 1, stages}] + n * δ[j] * r[n, j, t] -
     Sum[β[k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, t] -
     q * v[j] * s[j, t];
   didt[j_, 1, t_] = Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] *
      Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] + Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] *
      s[j, t] - ϰ[j, 1] * i[j, 1, t] - v[j] * 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] - v[j] * i[j, 2, t];
   drdt[1, j_, t_] = q * v[j] * s[j, t] +
     q * Sum[(ϰ[j, jj] + v[j]) * i[j, jj, t], {jj, 1, stages}] - n * δ[j] * r[1, j, t] +
         Sum[v[j] * r[nn, j, t], {nn, 2, n}];
   For[nn = 2, nn ≤ n - TRYm, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] - n * δ[j] * r[nn, j, t] - v[j] * r[nn, j, t];
   ];
   For[nn = n + 1 - TRYm, nn ≤ n, nn++,
    drdt[nn, j_, t_] = n * δ[j] * r[nn - 1, j, t] - Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] *
        r[nn, j, t] - n * δ[j] * r[nn, j, t] - v[j] * r[nn, j, t];
   ];
   pars = {β[j_, 1] → βV, β[j_, 2] → β,
     δ[1] → δY, δ[2] → δO, ϰ[j_, jj_] → ϰ, v[1] → vY, v[2] → vO};
   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]) r0/n, {nn, 1, n}]}, {j, 1, ages}]] /. start, -1];
   NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
  ]
```

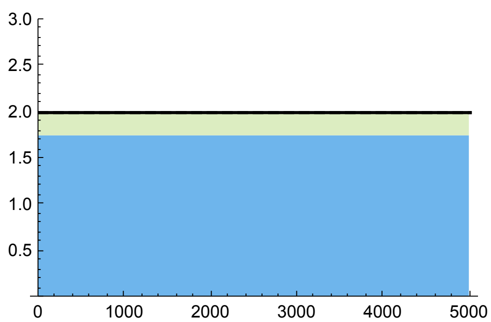
In[∘]:=
```
all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
```
Out[∘]=
```
{{1, 1}, {1, 2}, {2, 1}, {2, 2}}
```
In[∘]:=
```
labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};
```
In[∘]:=
```
colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
  RGBColor[0.4, 0.6, 0.4], 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
```

CASE: No vaccinations

In[∘]:=
```
TRYvY = 0; (*Fraction of susceptibles getting vaccinated per day*)
TRYvO = 0; (*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, ■}}, {2 → {{1}, ■}}, {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
 Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
  PlotStyle → {Black, Dashed}],
 Plot[100 ((TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)) - ((1 - TRYolder) TRYvY + TRYolder TRYv0)/(TRYδ + TRYκ TRYconvert)),
  {t, 0, maxtime}, PlotStyle → {Black}],
 ImageSize → 250
]
```

Out[∘]=



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

In[∘]:=
```
{{Mean[
    Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start], {t, 1, 10}]]],
   Mean[Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]},
  {Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, 1, 10}]]],
   Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]}} // MatrixForm
```

Out[∘]//MatrixForm=

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

CASE: Low vaccination rate

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

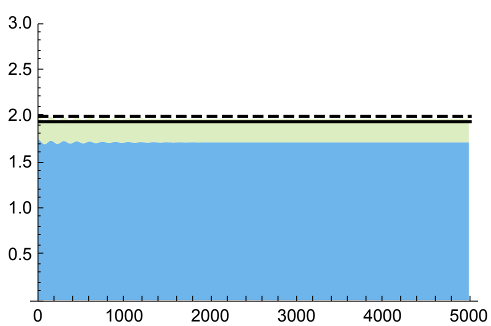
```
In[*]:= partemp =
          {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYvY, TRYvO, TRYκ, TRYconvert};
```

```
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, ■}}, {2 → {{1}, ■}}, {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
         Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
          PlotStyle → {Black, Dashed}],
         Plot[100 ((TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)) - ((1 - TRYolder) TRYvY + TRYolder TRYvO)/(TRYδ + TRYκ TRYconvert)),
          {t, 0, maxtime}, PlotStyle → {Black}],
         ImageSize → 250
        ]
```

Out[*]=



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

In[∘]:=
```
{{Mean[
    Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start], {t, 1, 10}]]],
   Mean[Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]},
  {Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, 1, 10}]]],
   Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]}} // MatrixForm
```

Out[∘]//MatrixForm=

$$\begin{pmatrix} 0.0199779 & 0.0195853 \\ 0.0199779 & 0.0195853 \end{pmatrix}$$

CASE: High vaccination rate

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

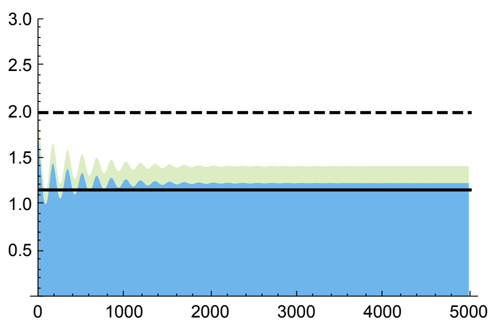
In[∘]:=
```
partemp =
  {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYvY, TRYvO, TRYϰ, TRYconvert};
```

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, ■}}, {2 → {{1}, ■}}, {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
 Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
  PlotStyle → {Black, Dashed}],
 Plot[100 ((TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)) - ((1 - TRYolder) TRYvY + TRYolder TRYv0)/(TRYδ + TRYκ TRYconvert)),
  {t, 0, maxtime}, PlotStyle → {Black}],
 ImageSize → 250
]
```

Out[∘]=



NOTE: Dashed line above is for the previous case, where vaccinations were focused on the susceptibles. Vaccinating the recovered class as well is slightly less effective as expected.

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

In[∘]:=
```
{{Mean[
    Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start], {t, 1, 10}]]],
   Mean[Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]},
  {Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, 1, 10}]]],
   Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]}} // MatrixForm
```

Out[∘]//MatrixForm=

$$\begin{pmatrix} 0.019683 & 0.0140665 \\ 0.019683 & 0.0140665 \end{pmatrix}$$

In[∘]:=
```
Transpose[%][[2]] / Transpose[%][[1]] - 1
```

Out[∘]= {-0.285346, -0.285346}

CASE: High vaccination rate only in older individuals

In[∘]:=
```
TRYvY = 0; (*Fraction of susceptibles getting vaccinated per day*)
TRYvO = TRYvHIGH; (*Fraction of older susceptibles getting vaccinated per day*)
```

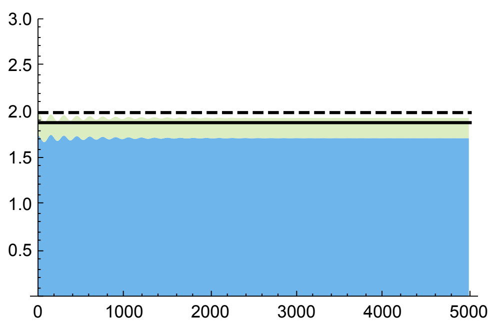
In[∘]:=
```
partemp =
  {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYvY, TRYvO, TRYϰ, TRYconvert};
```

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, ■}}, {2 → {{1}, ■}}, {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
 Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
  PlotStyle → {Black, Dashed}],
 Plot[100 ((TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)) - ((1 - TRYolder) TRYvY + TRYolder TRYv0)/(TRYδ + TRYκ TRYconvert)),
  {t, 0, maxtime}, PlotStyle → {Black}],
 ImageSize → 250
]
```

Out[◦]=



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[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start], {t, 1, 10}]]],
   Mean[Flatten[Table[(i[1, 1, t] + i[1, 2, t])/(1 - TRYolder) /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]},
  {Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, 1, 10}]]],
   Mean[Flatten[Table[(i[2, 1, t] + i[2, 2, t])/TRYolder /. solution[partemp, start],
      {t, maxtime - 9, maxtime}]]]}} // MatrixForm
```

Out[∘]//MatrixForm=

$$\begin{pmatrix} 0.0199832 & 0.0196437 \\ 0.0197933 & 0.0167817 \end{pmatrix}$$

In[∘]:=
```
Transpose[%][[2]] / Transpose[%][[1]] - 1
```

Out[∘]= {-0.0169873, -0.152151}

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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

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

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

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

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

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

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):

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

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

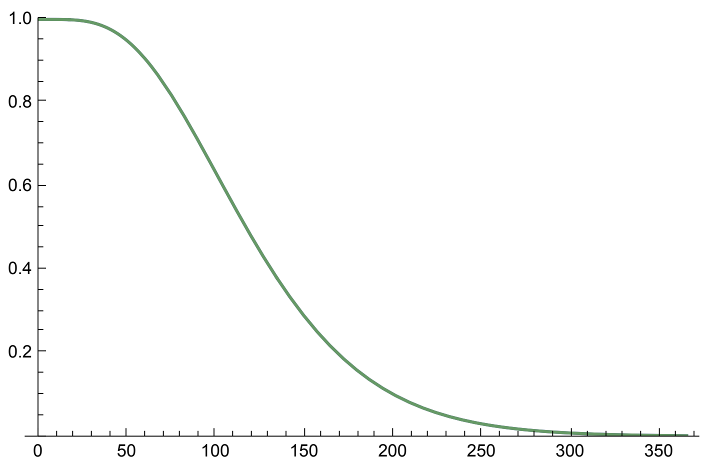
Out[]= $\left\{s0 \to \frac{12}{25}, i0 \to \frac{1}{50}, r0 \to \frac{1}{2}\right\}$

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 / (TRYδO n)], t]),
  {t, 0, 365}, PlotRange → {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```

Out[•]=



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_, β_, δY_, δO_, κ_, q_}, start] :=
 solution[{p, f, older, β, δY, δO, κ, q}, start] =
  Block[{ages = 2, stages = 2, n = 5},
   dsdt[j_, jj_, t_] = (1 - q) * κ[j, jj] * i[j, jj, t] + n * δ[j, jj] * r[n, j, jj, t] - Sum[
       m[jj, kk] × β[jj, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * s[j, jj, t] ;
   didt[j_, jj_, t_] = Sum[m[jj, kk] × β[jj, kk] * i[k, kk, t], {k, 1, ages},
       {kk, 1, stages}] * s[j, jj, t] - κ[j, jj] * i[j, jj, t];
   drdt[1, j_, jj_, t_] = q * κ[j, jj] * i[j, jj, t] - n * δ[j, jj] * r[1, j, jj, t];
   For[nn = 2, nn ≤ n, nn++,
    drdt[nn, j_, jj_, t_] =
      n * δ[j, jj] * r[nn - 1, j, jj, t] - n * δ[j, jj] * r[nn, j, jj, t];
   ];
   pars = {m[jj_, kk_] → (1 - p)^(jj+kk-2),
     β[j_, k_] → β, δ[1, jj_] → δY, δ[2, jj_] → 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, 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] 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[∘]:=

$$\text{neweq}[\{p\_, f\_, \text{older}\_, \beta\_, \delta Y\_, \delta O\_, \varkappa\_, q\_\}] = \frac{1}{2\,(-1+p)^2\,\beta\,(\delta + q\,\varkappa)}\,\delta\Big((1+f\,(-2+p))\,(-1+p)\,p\,\beta - (2+(-2+p)\,p)\,\varkappa + 2\sqrt{4\,(-1+f)\,(-1+p)\,p\,\beta\,\varkappa + ((-1+p)\,(-1+f\,p)\,\beta - p\,\varkappa)^2} - p\sqrt{4\,(-1+f)\,(-1+p)\,p\,\beta\,\varkappa + ((-1+p)\,(-1+f\,p)\,\beta - p\,\varkappa)^2}\Big)\;/.\;\delta \to \delta Y$$

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

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

Equilibrium number of cases:

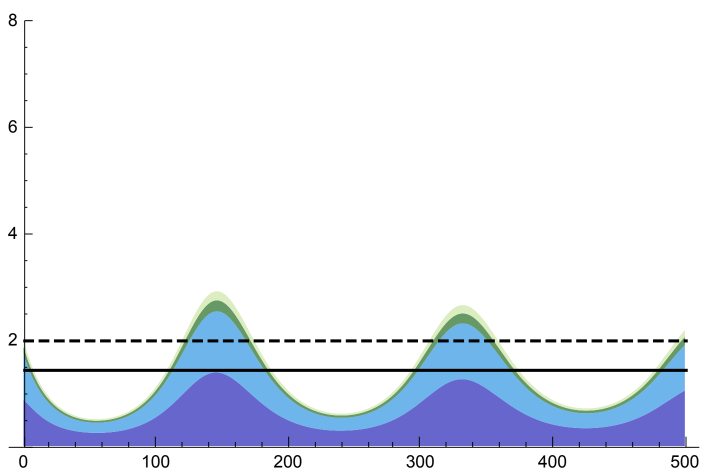
In[∘]:=
```
100 neweq[partemp] // N
```

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, ■}}, {2 → {{1}, ■}},
     {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
  Plot[100 (TRYδ ((1 - p) TRYβ - TRYκ))/((1 - p) TRYβ (TRYδ + TRYκ TRYconvert)) /. p → 0,
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 neweq[partemp] /. p → TRYp /. f → TRYf /. β → TRYβ /. κ → TRYκ /. δ → TRYδ /.
     q → TRYconvert, {t, 0, maxtime}, PlotStyle → {Black}]
 ]
```

Out[∘]=



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, 8/10 TRYδ, 8/10 TRYδ0, TRYκ, 8/10};
```

Equilibrium number of cases:

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

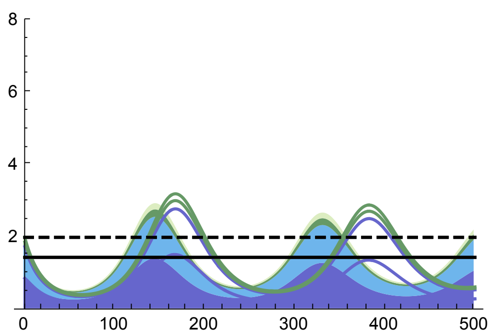
Out[∘]=
```
1.4468
```

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 → {■, ■, ■, ■}],
  Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 neweq[partemp] /. p → TRYp /. f → TRYf /. β → TRYβ /. κ → TRYκ /. δ → 8/10 TRYδ /.
    q → 8/10 TRYconvert, {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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*)
TRYκ = 1 / 5; (*Five day infectious period*)
TRYδ = 1 / 125; (*Waning rate based on Menegale et al. (2023)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

Adding in a rate of switching classes:

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

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

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

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

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

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

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

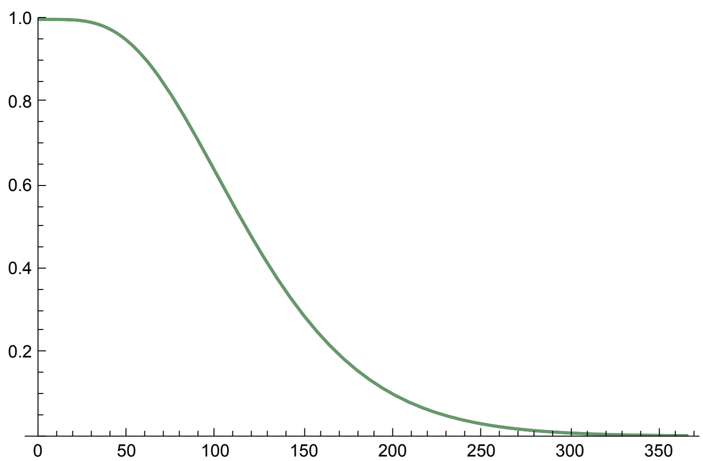
Out[∘]=
$$\left\{\text{s0} \to \frac{12}{25},\ \text{i0} \to \frac{1}{50},\ \text{r0} \to \frac{1}{2}\right\}$$

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 / (TRYδO n)], t]),
  {t, 0, 365}, PlotRange → {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```

Out[∘]=



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_, β_, δY_, δO_, κ_, q_, rate_}, start] :=
 solution[{p, f, older, β, δY, δO, κ, q, rate}, start] =
  Block[{ages = 2, stages = 2, n = 5},
   dsdt[j_, jj_, t_] = (1 - q) * κ[j, jj] * i[j, jj, t] + n * δ[j, jj] * r[n, j, jj, t] - Sum[
        m[jj, kk] × β[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] × β[jj, kk] * i[k, kk, t], {k, 1, ages},
        {kk, 1, stages}] * s[j, jj, t] - κ[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 * κ[j, jj] * i[j, jj, t] - n * δ[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 * δ[j, jj] * r[nn - 1, j, jj, t] - n * δ[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),
     β[j_, k_] → β, δ[1, jj_] → δY, δ[2, jj_] → δO, κ[j_, jj_] → κ};
   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] r0/n, {nn, 1, n}]},
        {j, 1, ages}, {jj, 1, stages}]] /. start, -1];
   NDSolve[Flatten[{nstart /. pars, neqns /. pars}], nvars, {t, 0, maxtime}]
  ]
```

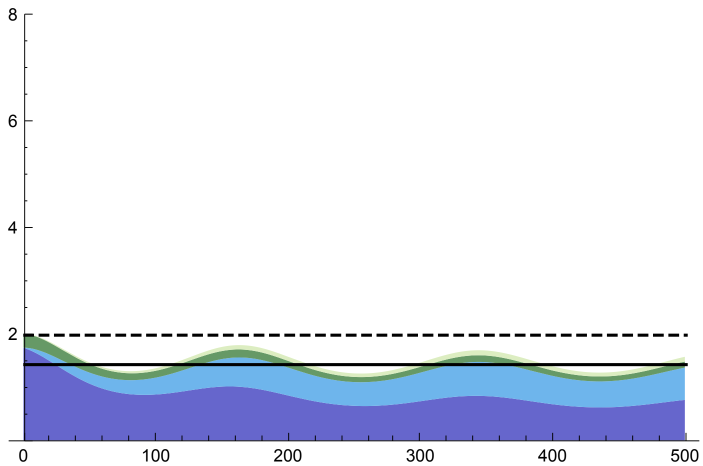
In[∘]:=
```
all = Flatten[Table[{j, jj}, {j, 1, ages}, {jj, 1, stages}], 1]
```
Out[∘]=
```
{{1, 1}, {1, 2}, {2, 1}, {2, 2}}
```
In[∘]:=
```
labels = {"<70,None", "<70,NPI", "70+,None", "70+,NPI"};
```
In[∘]:=
```
colours = {RGBColor[0.4, 0.4, 0.8], ColorData["Pastel", 1],
   RGBColor[0.4, 0.6, 0.4], 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_, δO_, κ_, q_, rate_}] =
```
$$\frac{1}{2\,(-1+p)^2\,\beta\,(\delta+q\,\kappa)}\,\delta\,\Big((1+f\,(-2+p))\,(-1+p)\,p\,\beta-(2+(-2+p)\,p)\,\kappa+2\,\sqrt{4\,(-1+f)\,(-1+p)\,p\,\beta\,\kappa+((-1+p)\,(-1+f\,p)\,\beta-p\,\kappa)^2}-p\,\sqrt{4\,(-1+f)\,(-1+p)\,p\,\beta\,\kappa+((-1+p)\,(-1+f\,p)\,\beta-p\,\kappa)^2}\Big)\;/.\;\delta\to\delta Y$$
```
 (*Doesn't consider age differences here in waning*);
```
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYδ, TRYδO, 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, ■}}, {2 → {{1}, ■}},
     {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
  Plot[100 TRYδ ((1 - p) TRYβ - TRYκ) / ((1 - p) TRYβ (TRYδ + TRYκ TRYconvert)) /. p → 0,
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 neweq[partemp], {t, 0, maxtime}, PlotStyle → {Black}]
 ]
```

Out[∘]=



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, 8/10 TRYδ, 8/10 TRYδ0, TRYκ, 8/10, TRYrate};
```

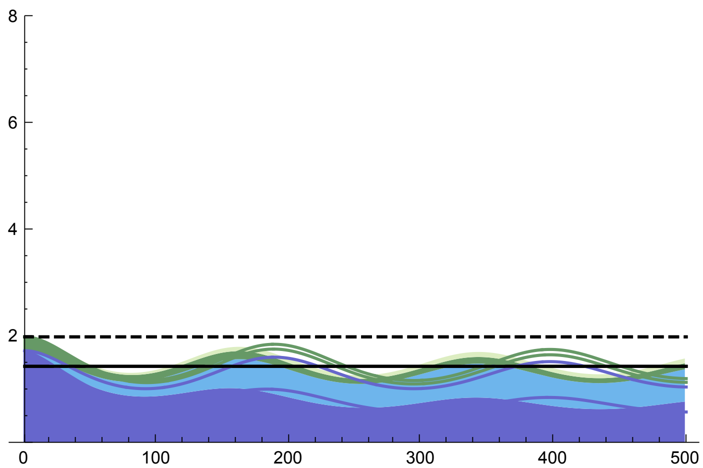
In[∘]:=
```
100 neweq[partemp] // N
```

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 → {■, ■, ■, ■}],
  Plot[100 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 neweq[partemp], {t, 0, maxtime}, PlotStyle → {Black}]
 ]
```

Out[∘]=


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*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)*)
TRYδO = 1 / 125; (*No clear age difference noted in Menegale et al. (2023)*)
TRYconvert = 10 / 10; (*Only this fraction of cases seroconvert or boost immunity*)
```

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

Adding in a rate of switching classes:

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

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

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

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

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

$\frac{\text{TRY}\beta}{\text{TRY}\kappa}$ // 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):

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

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

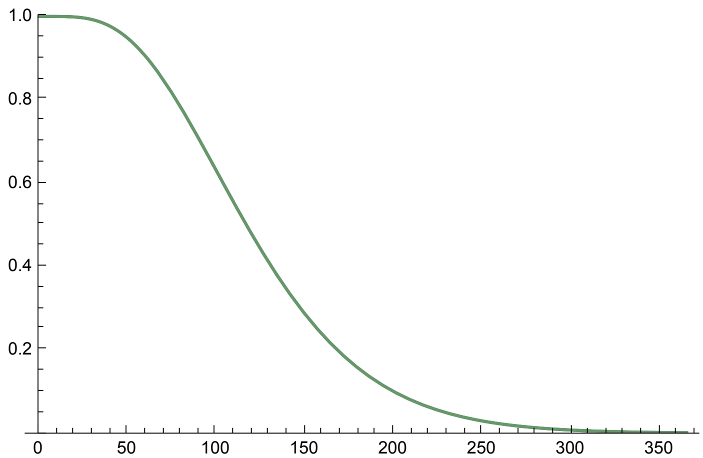
Out[∘]= $\left\{s0 \to \frac{12}{25},\ i0 \to \frac{1}{50},\ r0 \to \frac{1}{2}\right\}$

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 / (TRYδO n)], t]),
  {t, 0, 365}, PlotRange → {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```

Out[∘]=



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_, β_, δY_, δO_, κ_, q_, rate_}, start] :=
 solution[{p, f, older, β, δY, δO, κ, q, rate}, start] =
  Block[{ages = 2, stages = 2, n = 5},
   dsdt[j_, jj_, t_] = (1 - q) * κ[j, jj] * i[j, jj, t] + n * δ[j, jj] * r[n, j, jj, t] - Sum[
       m[jj, kk] × β[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] × β[jj, kk] * i[k, kk, t], {k, 1, ages},
       {kk, 1, stages}] * s[j, jj, t] - κ[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 * κ[j, jj] * i[j, jj, t] - n * δ[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 * δ[j, jj] * r[nn - 1, j, jj, t] - n * δ[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),
     β[j_, k_] → β, δ[1, jj_] → δY, δ[2, jj_] → δO, κ[j_, jj_] → κ};
   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] 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):

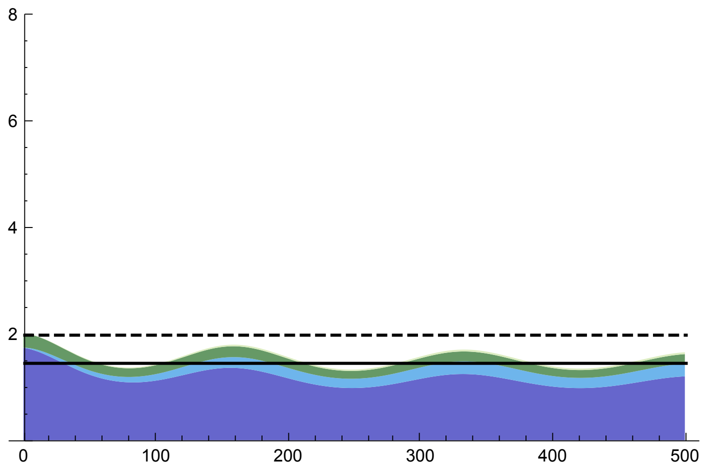
```
In[•]:= neweq[{p_, f_, older_, β_, δY_, δO_, κ_, q_, rate_}] =
```

$$\frac{1}{2\,(-1+p)^2\,\beta\,(\delta+q\,\kappa)}\,\delta\,\Big((1+f\,(-2+p))\,(-1+p)\,p\,\beta-(2+(-2+p)\,p)\,\kappa+2\,\sqrt{4\,(-1+f)\,(-1+p)\,p\,\beta\,\kappa+((-1+p)\,(-1+f\,p)\,\beta-p\,\kappa)^2}-p\,\sqrt{4\,(-1+f)\,(-1+p)\,p\,\beta\,\kappa+((-1+p)\,(-1+f\,p)\,\beta-p\,\kappa)^2}\Big)\ /.\ \delta\to\delta Y$$

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

In[•]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYδ, TRYδO, 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, ■}}, {2 → {{1}, ■}},
      {3 → {{2}, ■}}, {4 → {{3}, ■}}}],
  Plot[100 (TRYδ ((1 - p) TRYβ - TRYϰ)) / ((1 - p) TRYβ (TRYδ + TRYϰ TRYconvert)) /. p → 0,
    {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 neweq[partemp], {t, 0, maxtime}, PlotStyle → {Black}]
 ]
```

Out[∘]=



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, 8/10 TRYδ, 8/10 TRYδ0, TRYϰ, 8/10, TRYrate};
```

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

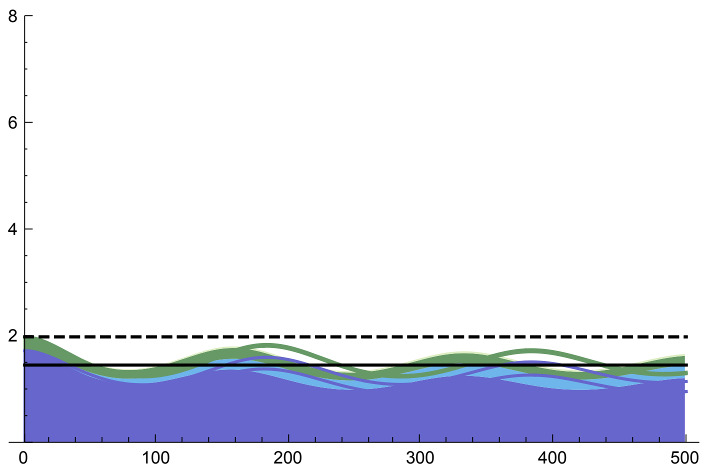
Out[∘]= 1.47119

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 → {■, ■, ■, ■}],
  Plot[100 TRYδ (TRYβ - TRYκ) / (TRYβ (TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 neweq[partemp], {t, 0, maxtime}, PlotStyle → {Black}]
 ]
```

Out[∘]=



In[∘]:=

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

Alternative: SIR model (with leaky variants; Figure S3)

→ Consistent results (accounting for impact on resistant classes)

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

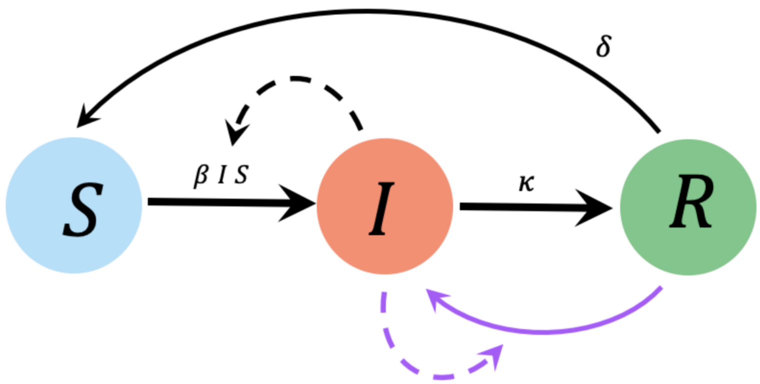


Figure S2A: more transmissible (variant NOT leaky; equivalent to n=1 explored above)

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)*)
TRYδO = 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;
```

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

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

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

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

Out[∘]= $\{\beta V \to 0.590208\}$

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).

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

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

Out[∘]= 0.0254283

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

Out[∘]= 0.0254283

Starting equilibrium would be (r0 includes all of the resistance classes):
$\left\{s \to \frac{\kappa}{\beta},\ i \to \frac{\delta\,(\beta - \kappa)}{\beta\,(\delta + q\,\kappa)}\right\}$

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

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

[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_, 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}] + 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] → 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}], 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	■

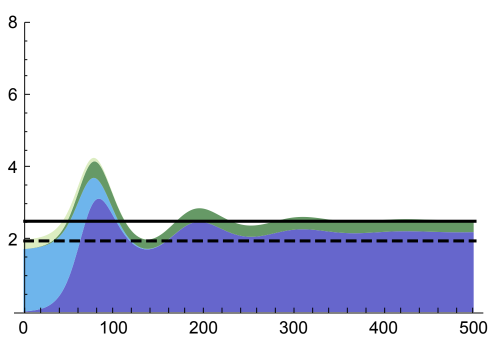
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδ0, TRYϰ, TRYconvert};
```

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 (TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 (TRYδ (TRYβV - TRYϰ))/(TRYβV (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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[∘]= {0.381045}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50))/(p0 / (1 - p0)) /. 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)*)
TRYδO = 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;
```

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

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

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

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

Out[∘]= $\{\beta\text{V} \to 0.534528\}$

In[∘]:= TRYβV = βV /. %;

% increase in β:

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

Out[∘]= 28.2868

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

New equilibrium:

In[∘]:= $\text{neweq} = \frac{\text{leak}\,\beta2-\delta-\kappa+\sqrt{\text{leak}^2\,\beta2^2+2\,\text{leak}\,\beta2\,(\delta-\kappa)-4\,\text{leak}\,\delta\,\kappa+(\delta+\kappa)^2}}{2\,\text{leak}\,\beta2}$ /. β2 → TRYβV /. δ → TRYδ /. κ → TRYκ /. leak → TRYleak

Out[∘]= 0.0320409

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

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

In[∘]:= start = $\left\{s0 \to \frac{TRY\varkappa}{TRY\beta}, i0 \to \frac{TRY\delta\ (TRY\beta - TRY\varkappa)}{TRY\beta\ (TRY\delta + TRY\varkappa\ TRYconvert)}, r0 \to 1 - \frac{TRY\varkappa}{TRY\beta} - \frac{TRY\delta\ (TRY\beta - TRY\varkappa)}{TRY\beta\ (TRY\delta + TRY\varkappa\ TRYconvert)}\right\}$

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

[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_, 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}] + 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] → 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}], 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}}
```

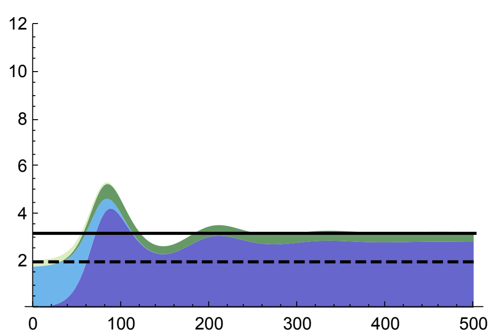
```
In[∘]:= labels = {"<70,Res", "<70,Mutant", "70+,Res", "70+,Mutant"};
```

```
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, TRYδO, 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 (TRYδ (TRYβ - TRYκ)) / (TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
           PlotStyle → {Black, Dashed}],
          Plot[100 neweq, {t, 0, maxtime}, PlotStyle → {Black}],
          ImageSize → 250
        ]
```

Out[∘]=



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

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

Out[∘]= {0.388291}

In[∘]:= Solve$\left[\text{Exp[s 50]} == \left(\frac{\text{p50 / (1 - p50)}}{\text{p0 / (1 - p0)}} \text{ /. p50} \to \text{\% /. p0} \to 1 - \text{TRYf}\right), \text{s}\right]$[[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[∘]:= $\frac{\text{TRY}\beta\text{V} - \text{TRY}\beta}{\text{TRY}\beta}$ TRYκ + TRYleak $\left(\frac{\text{TRY}\kappa\ \text{TRYconvert}\ (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta\ (\text{TRY}\delta + \text{TRY}\kappa\ \text{TRYconvert})}\right)$ TRYβV // N

Out[∘]= 0.0833

% rise in the endemic equilibrium:

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

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)*)
TRYδO = 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 → $\frac{\delta\ (\beta-\kappa)}{\beta\ (\delta+q\ \kappa)}$

In[∘]:=
```
Solve[δ (β - κ)/(β (δ + q κ)) == inf, β]
```

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

In[∘]:=
```
TRYinf = 1 / 50; (*Assumed initial endemic frequency of infected individuals*)
TRYβ = TRYδ TRYκ / (TRYδ - TRYinf TRYδ - TRYconvert TRYinf TRYκ);

TRYβ/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[
  TRYleak (1 - TRYκ/TRYβ - TRYδ (TRYβ - TRYκ)/(TRYβ (TRYδ + TRYκ TRYconvert))) βV + (βV - TRYβ)/TRYβ TRYκ == 0.0833, βV]]
```

Out[∘]= {βV → 0.488448}

In[∘]:=
```
TRYβV = βV /. %;
```

% increase in β:

In[∘]:=
```
100 * (TRYβV - TRYβ)/TRYβ
```

Out[∘]= 17.2276

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

New equilibrium:

In[∘]:=
```
neweq = (leak β2 - δ - κ + Sqrt[leak^2 β2^2 + 2 leak β2 (δ - κ) - 4 leak δ κ + (δ + κ)^2])/(2 leak β2) /. β2 → TRYβV /.
    δ → TRYδ /. κ → TRYκ /. leak → TRYleak
```

Out[∘]= 0.0413158

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

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

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

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

[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_, 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}] + 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] → 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}], 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	■

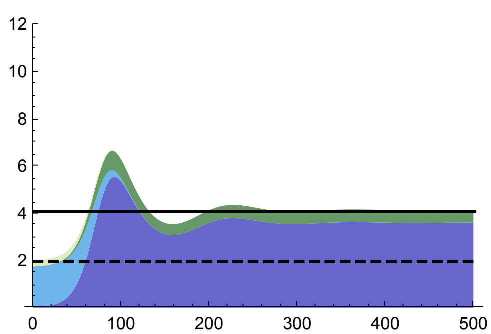
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYκ, TRYconvert};
```

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 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 neweq, {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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[∘]= {0.393131}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. 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 → 0.083219}

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

% rise in the endemic equilibrium:

In[∘]:=
```
100 * (neweq - TRYinf) / 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)*)
TRYδO = 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;
```

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

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

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

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

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

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

Out[∘]= 2.08333

Variant has the same transmissibility:

In[∘]:= TRYβV = TRYβ;

but infects earlier during waning by allowing leaky immunity.

New equilibrium:

In[∘]:= neweq =

$\frac{\text{leak}\ \beta 2 - \delta - \varkappa + \sqrt{\text{leak}^2\ \beta 2^2 + 2\ \text{leak}\ \beta 2\ (\delta-\varkappa) - 4\ \text{leak}\ \delta\ \varkappa + (\delta+\varkappa)^2}}{2\ \text{leak}\ \beta 2}$ /. leak → TRYleak /.

β2 → TRYβV /. δ → TRYδ /. ϰ → TRYϰ // N

Out[∘]= 0.0768382

Starting equilibrium would be (r0 includes all of the resistance classes):
$\left\{s \to \frac{\kappa}{\beta},\ i \to \frac{\delta\ (\beta-\kappa)}{\beta\ (\delta+q\,\kappa)}\right\}$

In[∘]:= $\text{start} = \left\{s0 \to \frac{\text{TRY}\varkappa}{\text{TRY}\beta},\ i0 \to \frac{\text{TRY}\delta\ (\text{TRY}\beta - \text{TRY}\varkappa)}{\text{TRY}\beta\ (\text{TRY}\delta + \text{TRY}\varkappa\ \text{TRYconvert})},\right.$

$\left. r0 \to 1 - \frac{\text{TRY}\varkappa}{\text{TRY}\beta} - \frac{\text{TRY}\delta\ (\text{TRY}\beta - \text{TRY}\varkappa)}{\text{TRY}\beta\ (\text{TRY}\delta + \text{TRY}\varkappa\ \text{TRYconvert})}\right\}$

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

[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_, 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}] + 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] → 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}], 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	■

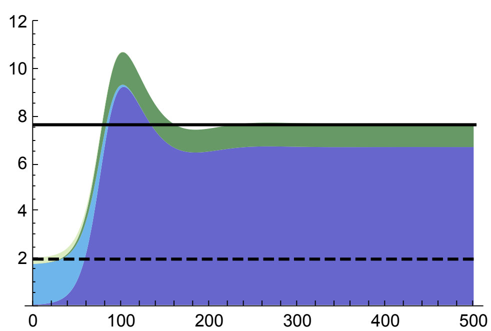
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYϰ, TRYconvert};
```

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 (TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 neweq, {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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[∘]= {0.398831}

In[∘]:=
```
Solve[Exp[s 50] == (p50 / (1 - p50))/(p0 / (1 - p0)) /. 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 → 0.0836956}

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[∘]= 0.0833333

% rise in the endemic equilibrium:

In[∘]:=
```
100 * (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:

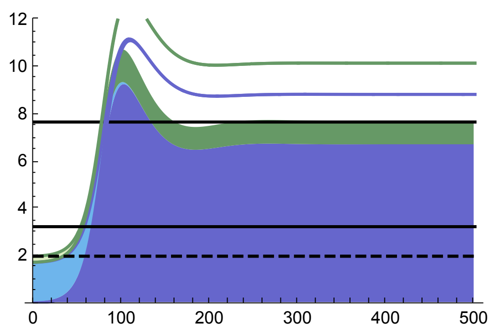
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, 8/10 TRYδ, 8/10 TRYδO, TRYϰ, 8/10};
```

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 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 ((TRYδ/(1-TRYx)) (TRYβV - TRYκ))/(TRYβV ((TRYδ/(1-TRYx)) + TRYκ TRYconvert)), {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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)*)
TRYδO = 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[]=

$$\left\{\{S \to 1, I1 \to 0, R \to 0\}, \left\{S \to \frac{\delta - \kappa + \beta1\,\xi1 + \sqrt{\delta^2 + (\kappa - \beta1\,\xi1)^2 + 2\,\delta\,(\kappa + \beta1\,\xi1 - 2\,\kappa\,\xi1)}}{2\,\beta1\,(-1 + \xi1)},\right.\right.$$

$$I1 \to -\frac{\delta + \kappa - \beta1\,\xi1 + \sqrt{\delta^2 + (\kappa - \beta1\,\xi1)^2 + 2\,\delta\,(\kappa + \beta1\,\xi1 - 2\,\kappa\,\xi1)}}{2\,\beta1\,\xi1},$$

$$\left.R \to -\frac{\delta + \kappa + \beta1\,\xi1 - 2\,\kappa\,\xi1 + \sqrt{\delta^2 + (\kappa - \beta1\,\xi1)^2 + 2\,\delta\,(\kappa + \beta1\,\xi1 - 2\,\kappa\,\xi1)}}{2\,\beta1\,(-1 + \xi1)\,\xi1}\right\},$$

$$\left\{S \to \frac{\delta - \kappa + \beta1\,\xi1 - \sqrt{\delta^2 + (\kappa - \beta1\,\xi1)^2 + 2\,\delta\,(\kappa + \beta1\,\xi1 - 2\,\kappa\,\xi1)}}{2\,\beta1\,(-1 + \xi1)},\right.$$

$$I1 \to \frac{-\delta - \kappa + \beta1\,\xi1 + \sqrt{\delta^2 + (\kappa - \beta1\,\xi1)^2 + 2\,\delta\,(\kappa + \beta1\,\xi1 - 2\,\kappa\,\xi1)}}{2\,\beta1\,\xi1},$$

$$\left.\left.R \to -\frac{\delta + \kappa + \beta1\,\xi1 - 2\,\kappa\,\xi1 - \sqrt{\delta^2 + (\kappa - \beta1\,\xi1)^2 + 2\,\delta\,(\kappa + \beta1\,\xi1 - 2\,\kappa\,\xi1)}}{2\,\beta1\,(-1 + \xi1)\,\xi1}\right\}\right\}$$

```
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 → TRYleak) == 1, β1]
```

Out[]=

$$\left\{\left\{\beta1 \to \frac{2}{49}\left(-24 - \sqrt{1066}\right)\right\}, \left\{\beta1 \to \frac{2}{49}\left(-24 + \sqrt{1066}\right)\right\}\right\}$$

In[∘]:=
```
TRYβ = β1 /. %[[2]]
```

Out[∘]= $\frac{2}{49}\left(-24+\sqrt{1066}\right)$

In[∘]:=
```
(*TRYβ= TRYδ TRYκ / (TRYδ-TRYinf TRYδ-TRYconvert TRYinf TRYκ);*)

TRYβ/TRYκ // N
```

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 + (βV - TRYβ)/TRYβ TRYκ == 0.0833, βV]]
```

Out[∘]= {βV → 0.479481}

In[∘]:=
```
TRYβV = βV /. %;
```

and infects earlier during waning by allowing leaky immunity.

New equilibrium:

In[∘]:=
```
neweq =
  (-δ - κ + β1 ξ1 + Sqrt[δ^2 + (κ - β1 ξ1)^2 + 2 δ (κ + β1 ξ1 - 2 κ ξ1)]) / (2 β1 ξ1) /. ξ1 → TRYleakV /. β1 → TRYβV /.
    δ → TRYδ /. κ → TRYκ // N
```

Out[∘]= 0.0340037

[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_, 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}] + 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_] = TRYleakV 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_] = TRYleak Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] * r[j, 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] - TRYleakV Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t] -
     TRYleak Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] * r[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}], 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	

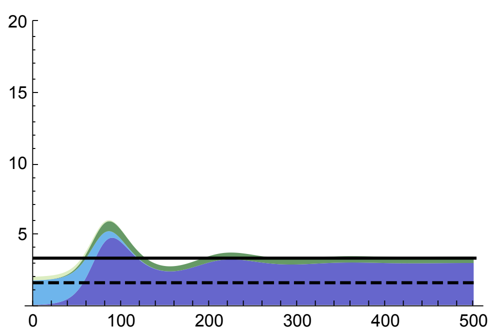
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYκ, TRYconvert};
```

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 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 neweq, {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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))/(p0 / (1 - p0)) /. 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)*)
TRYδO = 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 == 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[∘]=
$$\left\{\{S\to 1,\ I1\to 0,\ R\to 0\},\ \left\{S\to \frac{\delta-\kappa+\beta1\,\xi1+\sqrt{\delta^2+(\kappa-\beta1\,\xi1)^2+2\,\delta\,(\kappa+\beta1\,\xi1-2\,\kappa\,\xi1)}}{2\,\beta1\,(-1+\xi1)},\right.\right.$$
$$I1\to -\frac{\delta+\kappa-\beta1\,\xi1+\sqrt{\delta^2+(\kappa-\beta1\,\xi1)^2+2\,\delta\,(\kappa+\beta1\,\xi1-2\,\kappa\,\xi1)}}{2\,\beta1\,\xi1},$$
$$\left.R\to -\frac{\delta+\kappa+\beta1\,\xi1-2\,\kappa\,\xi1+\sqrt{\delta^2+(\kappa-\beta1\,\xi1)^2+2\,\delta\,(\kappa+\beta1\,\xi1-2\,\kappa\,\xi1)}}{2\,\beta1\,(-1+\xi1)\,\xi1}\right\},$$
$$\left\{S\to \frac{\delta-\kappa+\beta1\,\xi1-\sqrt{\delta^2+(\kappa-\beta1\,\xi1)^2+2\,\delta\,(\kappa+\beta1\,\xi1-2\,\kappa\,\xi1)}}{2\,\beta1\,(-1+\xi1)},\right.$$
$$I1\to \frac{-\delta-\kappa+\beta1\,\xi1+\sqrt{\delta^2+(\kappa-\beta1\,\xi1)^2+2\,\delta\,(\kappa+\beta1\,\xi1-2\,\kappa\,\xi1)}}{2\,\beta1\,\xi1},$$
$$\left.\left.R\to -\frac{\delta+\kappa+\beta1\,\xi1-2\,\kappa\,\xi1-\sqrt{\delta^2+(\kappa-\beta1\,\xi1)^2+2\,\delta\,(\kappa+\beta1\,\xi1-2\,\kappa\,\xi1)}}{2\,\beta1\,(-1+\xi1)\,\xi1}\right\}\right\}$$

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 → TRYleak) == 1, β1]
```

Out[∘]=
$$\left\{\left\{\beta1\to \frac{2}{49}\left(-24-\sqrt{1066}\right)\right\},\ \left\{\beta1\to \frac{2}{49}\left(-24+\sqrt{1066}\right)\right\}\right\}$$

In[∘]:=
```
TRYβ = β1 /. %[[2]]
```

Out[∘]=
$$\frac{2}{49}\left(-24+\sqrt{1066}\right)$$

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

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

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[∘]:=
$$\text{Flatten}\left[\text{Solve}\left[(\text{TRYleakV} - \text{TRYleak})\ (\text{r0 /. start})\ \beta V + \frac{\beta V - \text{TRY}\beta}{\text{TRY}\beta}\ \text{TRY}\kappa == 0.0833,\ \beta V\right]\right]$$

Out[∘]=
```
{βV → 0.428203}
```

In[∘]:=
```
TRYβV = βV /. %;
```

and infects earlier during waning by allowing leaky immunity.

New equilibrium:

In[∘]:=
$$\text{neweq} = \frac{-\delta - \kappa + \beta 1\ \xi 1 + \sqrt{\delta^2 + (\kappa - \beta 1\ \xi 1)^2 + 2\ \delta\ (\kappa + \beta 1\ \xi 1 - 2\ \kappa\ \xi 1)}}{2\ \beta 1\ \xi 1}\ \text{/. } \xi 1 \to \text{TRYleakV /. } \beta 1 \to \text{TRY}\beta\text{V /. } \delta \to \text{TRY}\delta\text{ /. } \kappa \to \text{TRY}\kappa\text{ // N}$$

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_, 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}] + 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_] = TRYleakV 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_] = TRYleak Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] * r[j, 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] - TRYleakV Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t] -
     TRYleak Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] * r[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}], 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	■

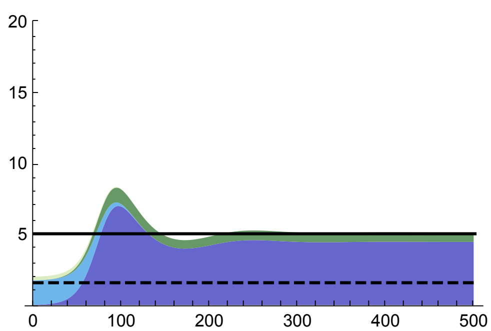
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYϰ, TRYconvert};
```

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 (TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 neweq, {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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[∘]= {0.392738}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50))/(p0 / (1 - p0)) /. 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)*)
TRYδO = 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}]
```

Out[∘]=
$$\left\{\{S\to 1,\ I1\to 0,\ R\to 0\},\ \left\{S\to \frac{\delta-\kappa+\beta 1\ \xi 1+\sqrt{\delta^2+(\kappa-\beta 1\ \xi 1)^2+2\,\delta\,(\kappa+\beta 1\ \xi 1-2\,\kappa\,\xi 1)}}{2\,\beta 1\,(-1+\xi 1)},\right.\right.$$
$$I1\to -\frac{\delta+\kappa-\beta 1\ \xi 1+\sqrt{\delta^2+(\kappa-\beta 1\ \xi 1)^2+2\,\delta\,(\kappa+\beta 1\ \xi 1-2\,\kappa\,\xi 1)}}{2\,\beta 1\,\xi 1},$$
$$\left.R\to -\frac{\delta+\kappa+\beta 1\ \xi 1-2\,\kappa\,\xi 1+\sqrt{\delta^2+(\kappa-\beta 1\ \xi 1)^2+2\,\delta\,(\kappa+\beta 1\ \xi 1-2\,\kappa\,\xi 1)}}{2\,\beta 1\,(-1+\xi 1)\,\xi 1}\right\},$$
$$\left\{S\to \frac{\delta-\kappa+\beta 1\ \xi 1-\sqrt{\delta^2+(\kappa-\beta 1\ \xi 1)^2+2\,\delta\,(\kappa+\beta 1\ \xi 1-2\,\kappa\,\xi 1)}}{2\,\beta 1\,(-1+\xi 1)},\right.$$
$$I1\to \frac{-\delta-\kappa+\beta 1\ \xi 1+\sqrt{\delta^2+(\kappa-\beta 1\ \xi 1)^2+2\,\delta\,(\kappa+\beta 1\ \xi 1-2\,\kappa\,\xi 1)}}{2\,\beta 1\,\xi 1},$$
$$\left.\left.R\to -\frac{\delta+\kappa+\beta 1\ \xi 1-2\,\kappa\,\xi 1-\sqrt{\delta^2+(\kappa-\beta 1\ \xi 1)^2+2\,\delta\,(\kappa+\beta 1\ \xi 1-2\,\kappa\,\xi 1)}}{2\,\beta 1\,(-1+\xi 1)\,\xi 1}\right\}\right\}$$

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 → TRYleak) == 1, β1]
```

Out[∘]=
$$\left\{\left\{\beta 1\to \frac{2}{49}\left(-24-\sqrt{1066}\right)\right\},\ \left\{\beta 1\to \frac{2}{49}\left(-24+\sqrt{1066}\right)\right\}\right\}$$

In[∘]:=
```
TRYβ = β1 /. %[[2]]
```

Out[∘]=
$$\frac{2}{49}\left(-24+\sqrt{1066}\right)$$

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

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

Out[∘]=
```
1.76524
```

Variant has the same transmissibility:

In[∘]:=
```
TRYβV = TRYβ;
```

but infects earlier during waning by allowing leaky immunity.

New equilibrium:

In[∘]:=
```
neweq =
  (-δ - κ + β1 ξ1 + Sqrt[δ^2 + (κ - β1 ξ1)^2 + 2 δ (κ + β1 ξ1 - 2 κ ξ1)])/(2 β1 ξ1) /. ξ1 → TRYleakV /. β1 → TRYβV /.
    δ → TRYδ /. κ → TRYκ // N
```

$$\frac{-\delta-\kappa+\beta 1\,\xi 1+\sqrt{\delta^2+(\kappa-\beta 1\,\xi 1)^2+2\,\delta\,(\kappa+\beta 1\,\xi 1-2\,\kappa\,\xi 1)}}{2\,\beta 1\,\xi 1}$$

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_, 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}] + 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_] = TRYleakV 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_] = TRYleak Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] * r[j, 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] - TRYleakV Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[j, t] -
     TRYleak Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] * r[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}], 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]}
```

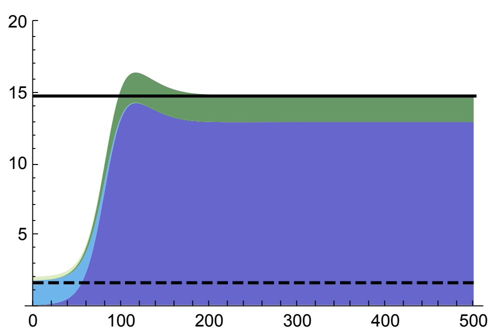
Out[∘]=
```
{■, ■, ■, ■}
```

```
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, TRYδO, 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 (TRYδ (TRYβ - TRYϰ))/(TRYβ (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime},
           PlotStyle → {Black, Dashed}],
          Plot[100 neweq, {t, 0, maxtime}, PlotStyle → {Black}],
          ImageSize → 250
         ]
```

Out[•]=



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[•]= {0.399126}
```

In[∘]:=
```
Solve[Exp[s 50] == (p50 / (1 - p50)) / (p0 / (1 - p0)) /. 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: SIR_n model (with leaky variants)

→ Consistent results (accounting for impact on resistant classes with n=5)

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)*)
TRYδO = 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[∘]=

$$\Big\{\{I1[t]\to 0,\ R[1,t]\to 0,\ R[2,t]\to 0,\ R[3,t]\to 0,\ R[4,t]\to 0,\ R[5,t]\to 0\},$$

$$\Big\{S[t]\to \frac{3125\,\delta^5\,\kappa}{\beta 1\,(5\,\delta + \text{leak}\,\beta 1\,I1[t])^5},\ R[1,t]\to \frac{\kappa\,I1[t]}{5\,\delta + \text{leak}\,\beta 1\,I1[t]},$$

$$R[2,t]\to \frac{5\,\delta\,\kappa\,I1[t]}{(5\,\delta + \text{leak}\,\beta 1\,I1[t])^2},\ R[3,t]\to \frac{25\,\delta^2\,\kappa\,I1[t]}{(5\,\delta + \text{leak}\,\beta 1\,I1[t])^3},$$

$$R[4,t]\to \frac{125\,\delta^3\,\kappa\,I1[t]}{(5\,\delta + \text{leak}\,\beta 1\,I1[t])^4},\ R[5,t]\to \frac{625\,\delta^4\,\kappa\,I1[t]}{(5\,\delta + \text{leak}\,\beta 1\,I1[t])^5}\Big\}\Big\}$$

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 /. δ → TRYδ /.
    ϰ → TRYϰ /. leak → TRYleak) == 1, β1]
```

Out[∘]=
```
{{β1 → -4.47...}, {β1 → 0.361...}, {β1 → -29.4... - 6.27... i},
 {β1 → -29.4... + 6.27... i}, {β1 → -17.5... - 11.8... i}, {β1 → -17.5... + 11.8... i}}
```

In[∘]:=
```
TRYβ = β1 /. %[[2]]
```

Out[∘]=
```
0.361...
```

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

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

Out[∘]= 1.807

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

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

Out[∘]= {βV → 0.511924}

In[∘]:=
```
TRYβV = βV /. %;
```

% increase in β:

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

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;
```

Equilibrium once variant fixes:

In[∘]:=
```
Sort[Solve[
    (S[t] + I1[t] + Sum[R[j, t], {j, 1, TRYn - TRYm}] /. startme /. δ → TRYδ /. κ → TRYκ /.
        leak → TRYleak /. β1 → TRYβV) == 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] → -2.92923}, {I1[t] → -1.48102 - 0.598745 i},
 {I1[t] → -1.48102 + 0.598745 i}, {I1[t] → -0.475548 - 0.774942 i},
 {I1[t] → -0.475548 + 0.774942 i}, {I1[t] → 0.0287181}}
```

Out[∘]=
```
0.0287181
```

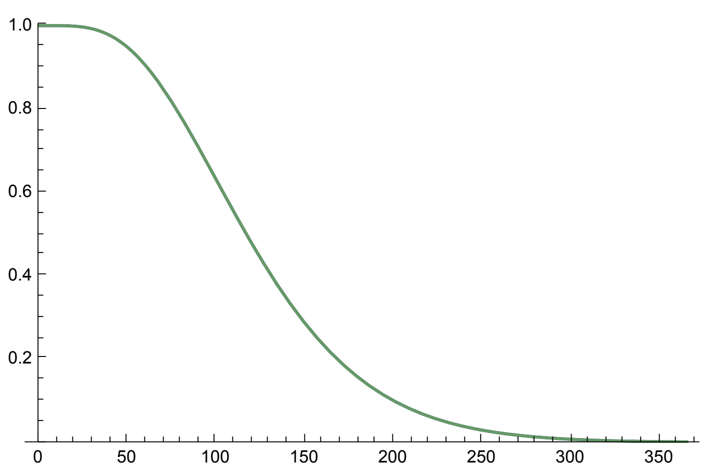
Starting equilibrium would be (r0 includes all of the n resistance classes and is just an approximate start):

In[∘]:=
```
start = {s0 → S[t], i0 → TRYinf, r0 → 1 - S[t] - TRYinf} /. startme /. I1[t] -> TRYinf /.
       δ → TRYδ /. κ → TRYκ /. leak → TRYleak /. β1 → TRYβ;
```

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 / (TRYδO TRYn)], t]),
  {t, 0, 365}, PlotRange → {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```

Out[∘]=



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_, β_, βV_, δY_, δO_, κ_, q_}, start] :=
 solution[{p, f, older, β, βV, δY, δO, κ, q}, start] =
  Block[{ages = 2, stages = 2, n = TRYn},
   dsdt[j_, t_] =
    (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] + n * δ[j] * r[n, 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}] *
      Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] + Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] *
      s[j, t]  + TRYleak * Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] *
      Sum[r[nn, j, t], {nn, 1, TRYn}] - 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] +
     TRYleak * Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] *
      Sum[r[nn, j, t], {nn, 1, TRYn}]  - κ[j, 2] * i[j, 2, t];
   drdt[1, j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] -
     n * δ[j] * r[1, j, t] -
     TRYleak * Sum[β[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 * δ[j] * r[nn - 1, j, t] - n * δ[j] * r[nn, j, t] -
       TRYleak * Sum[β[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 * δ[j] * r[nn - 1, j, t] - Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] -
       TRYleak Sum[β[k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * r[nn, j, t] -
       n * δ[j] * r[nn, 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}],
        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]) 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   ■ )
```

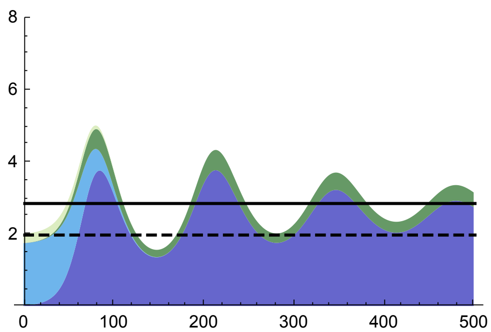
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, TRYϰ, TRYconvert};
```

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 TRYinf, {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 neweq, {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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

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

Out[∘]= {0.385458}

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

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[∘]:=
$$\frac{\texttt{TRY}\beta\texttt{V - TRY}\beta}{\texttt{TRY}\beta} \texttt{TRY}\kappa\texttt{ + Sum[R[j, t], \{j, 1 + TRYn - TRYm, TRYn\}] TRY}\beta\texttt{V /. startme /.}$$
$$\texttt{I1[t]} \to \texttt{TRYinf /. }\delta \to \texttt{TRY}\delta\texttt{ /. }\kappa \to \texttt{TRY}\kappa\texttt{ /. leak} \to \texttt{TRYleak /. }\beta\texttt{1} \to \texttt{TRY}\beta\texttt{V // N}$$

Out[∘]= 0.0833

New equilibrium:

In[∘]:= `neweq // N`

Out[∘]= 0.0287181

% rise in the endemic equilibrium:

In[∘]:=
```
100 * (% - TRYinf) / 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)*)
TRYδO = 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[∘]= $\{\{I1[t]\to 0, R[1,t]\to 0, R[2,t]\to 0, R[3,t]\to 0, R[4,t]\to 0, R[5,t]\to 0\},$

$\{S[t]\to \frac{3125\,\delta^5\,\kappa}{\beta 1\,(5\,\delta + \text{leak}\,\beta 1\,I1[t])^5}, R[1,t]\to \frac{\kappa\,I1[t]}{5\,\delta + \text{leak}\,\beta 1\,I1[t]},$

$R[2,t]\to \frac{5\,\delta\,\kappa\,I1[t]}{(5\,\delta + \text{leak}\,\beta 1\,I1[t])^2}, R[3,t]\to \frac{25\,\delta^2\,\kappa\,I1[t]}{(5\,\delta + \text{leak}\,\beta 1\,I1[t])^3},$

$R[4,t]\to \frac{125\,\delta^3\,\kappa\,I1[t]}{(5\,\delta + \text{leak}\,\beta 1\,I1[t])^4}, R[5,t]\to \frac{625\,\delta^4\,\kappa\,I1[t]}{(5\,\delta + \text{leak}\,\beta 1\,I1[t])^5}\}\}$

```
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 /. δ → TRYδ /.
          κ → TRYκ /. leak → TRYleak) == 1, β1]
```

Out[∘]= {{β1 → -4.47…}, {β1 → 0.361…}, {β1 → -29.4… - 6.27… i},
{β1 → -29.4… + 6.27… i}, {β1 → -17.5… - 11.8… i}, {β1 → -17.5… + 11.8… i}}

```
In[∘]:= TRYβ = β1 /. %[[2]]
```

Out[∘]= 0.361…

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

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

Out[∘]= 1.807

Variant has the same transmissibility:

```
In[∘]:= TRYβV = TRYβ;
```

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 /. δ → TRYδ /. κ → TRYκ /.
        leak → TRYleak /. β1 → TRYβV) == 1, I1[t]] // N]
neweq =
 I1[
   t] /.
  Last[
   %]
```

Out[∘]=
```
{{I1[t] → -4.6949}, {I1[t] → -1.60065 - 1.25807 i}, {I1[t] → -1.60065 + 1.25807 i},
 {I1[t] → -1.45384}, {I1[t] → -0.752823}, {I1[t] → 0.034828}}
```

Out[∘]=
```
0.034828
```

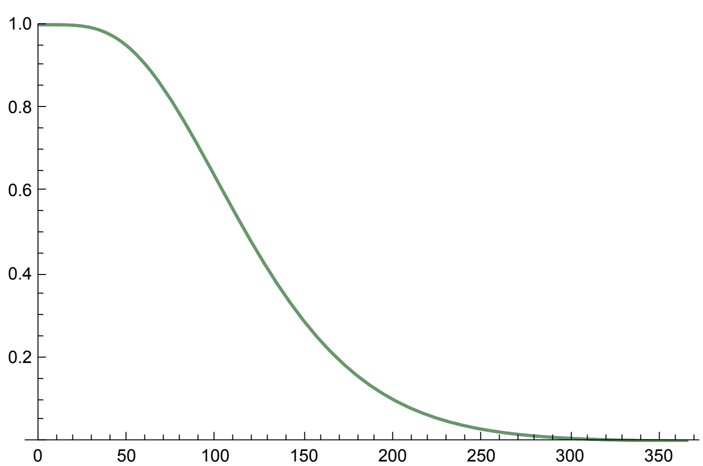
Starting equilibrium would be (r0 includes all of the n resistance classes and is just an approximate start):

In[∘]:=
```
start = {s0 → S[t], i0 → TRYinf, r0 → 1 - S[t] - TRYinf} /. startme /. I1[t] -> TRYinf /.
      δ → TRYδ /. κ → TRYκ /. leak → TRYleak /. β1 → TRYβ;
```

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 / (TRYδO TRYn)], t]),
  {t, 0, 365}, PlotRange → {All, {0, 1}}, PlotStyle -> RGBColor[0.4, 0.6, 0.4]]
]
```

Out[∘]=



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_, β_, βV_, δY_, δO_, κ_, q_}, start] :=
```

```
solution[{p, f, older, β, βV, δY, δO, κ, q}, start] =
 Block[{ages = 2, stages = 2, n = TRYn},
  dsdt[j_, t_] =
   (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] + n * δ[j] * r[n, 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}] *
     Sum[r[nn, j, t], {nn, n + 1 - TRYm, n}] + Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] *
     s[j, t] + TRYleak * Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] *
     Sum[r[nn, j, t], {nn, 1, TRYn}] - 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] +
    TRYleak * Sum[β[k, 2] * i[k, 2, t], {k, 1, ages}] *
     Sum[r[nn, j, t], {nn, 1, TRYn}] - κ[j, 2] * i[j, 2, t];
  drdt[1, j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] -
    n * δ[j] * r[1, j, t] -
    TRYleak * Sum[β[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 * δ[j] * r[nn - 1, j, t] - n * δ[j] * r[nn, j, t] -
      TRYleak * Sum[β[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 * δ[j] * r[nn - 1, j, t] - Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * r[nn, j, t] -
      TRYleak Sum[β[k, kk] * i[k, kk, t], {k, 1, ages}, {kk, 1, stages}] * r[nn, j, t] -
      n * δ[j] * r[nn, 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}],
       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]) 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[∘]= { , , , }
```

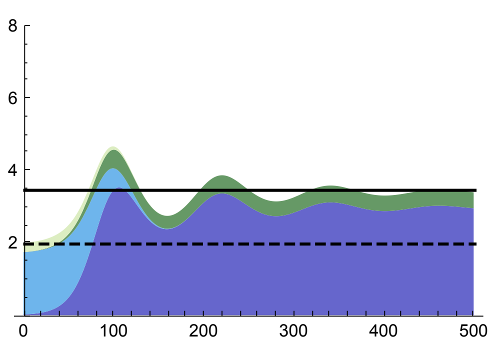
```
In[∘]:= coltab = Join[{{1 → {0, colours[[1]]}}},
           Table[{i -> {{i - 1}, colours[[i]]}}, {i, 2, Length[all]}]];
        Table[{labels[[i]], colours[[i]]}, {i, 1, Length[all]}] // MatrixForm
Out[∘]//MatrixForm=
   <70,Res
   <70,Mutant
   70+,Res
   70+,Mutant
```

```
In[∘]:= partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, TRYδ, TRYδO, 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 TRYinf, {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
          Plot[100 neweq, {t, 0, maxtime}, PlotStyle → {Black}],
          ImageSize → 250
         ]
Out[∘]=
```



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

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

Out[•]= {0.223271}

In[•]:=
```
Solve[Exp[s 50] == ( (p50 / (1 - p50)) / (p0 / (1 - p0)) /. 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 → 0.0669682}

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[•]= 0.0666864

New equilibrium:

In[•]:= `neweq // N`

Out[•]= 0.034828

% rise in the endemic equilibrium:

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

Out[•]= 74.1399

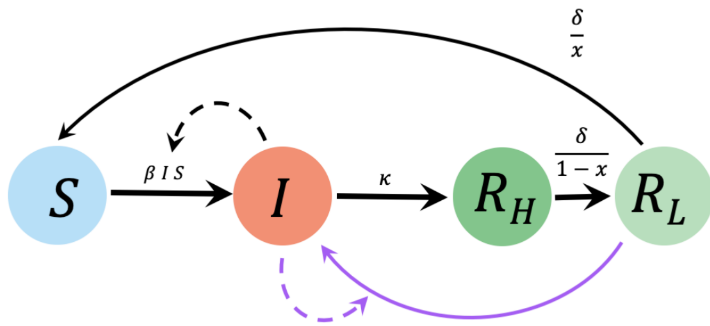
In[•]:=
```
Clear[solution, i, s, r, ages, stages, n, neqns, nstart, nvars, didt, dsdt, drdt];
```

Alternative: SIR$_2$ model (more panels in Figure S2)

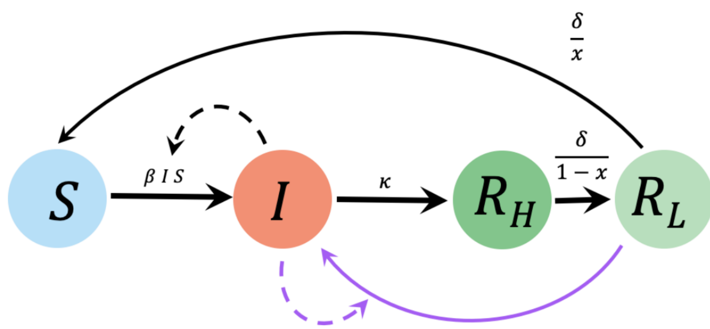
→ Less oscillatory

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.

In[◦]:=



Out[◦]=



We let the waning rate in the two classes be:

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

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

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

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)*)
TRYδO = 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;
```

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

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

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

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

Out[∘]= $\{\beta V \to 0.590208\}$

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

In[◦]:=
```
start = {s0 → TRYκ/TRYβ, i0 → TRYδ (TRYβ - TRYκ)/(TRYβ (TRYδ + TRYκ TRYconvert)),
   r0 → 1 - TRYκ/TRYβ - TRYδ (TRYβ - TRYκ)/(TRYβ (TRYδ + TRYκ TRYconvert))}
```

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

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

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

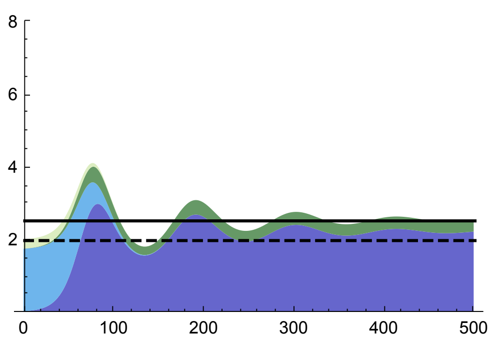
In[◦]:=
```
Clear[solution]
solution[{p_, f_, older_, β_, βV_, δY_, δO_, κ_, q_}, start] :=
 solution[{p, f, older, β, βV, δY, δO, κ, q}, start] =
  Block[{ages = 2, stages = 2},
   dsdt[j_, t_] = (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] + δ[j]/TRYx * rL[j, t] -
     Sum[β[k, kk] * i[k, 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}] * 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}] - δ[j]/(1 - TRYx) * rH[j, t];
   drLdt[j_, t_] = δ[j]/(1 - TRYx) * rH[j, t] - δ[j]/TRYx * 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, TRYδO, 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 (TRYδ (TRYβ - TRYκ)) / (TRYβ (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime},
   PlotStyle → {Black, Dashed}],
  Plot[100 (TRYδ (TRYβV - TRYκ)) / (TRYβV (TRYδ + TRYκ TRYconvert)), {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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[∘]= {0.380632}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. 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[∘]:=
```
(TRYβV - TRYβ) / TRYβ TRYκ + TRYx ((TRYκ TRYconvert (TRYβ - TRYκ)) / (TRYβ (TRYδ + TRYκ TRYconvert))) TRYβV // N
```

Out[∘]= 0.201342

New equilibrium:

In[∘]:=
```
((TRYδ + Δδ) (TRYβV - TRYϰ) / (TRYβV ((TRYδ + Δδ) + TRYϰ TRYconvert))) /. Δδ -> TRYx / (1 - TRYx) TRYδ // N
```

Out[∘]= 0.041321

% rise in the endemic equilibrium:

In[∘]:=
```
100 * (% - TRYinf) / 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:

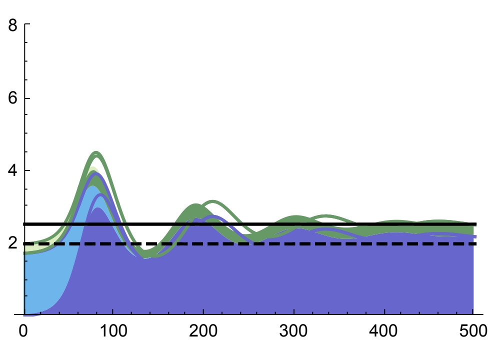
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, 8/10 TRYδ, 8/10 TRYδ0, TRYϰ, 8/10};
```

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 TRYδ (TRYβ - TRYϰ) / (TRYβ (TRYδ + TRYϰ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 TRYδ (TRYβV - TRYϰ) / (TRYβV (TRYδ + TRYϰ TRYconvert)), {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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 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)*)
TRYδO = 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;
```

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

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

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

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

In[*]:= TRYδ / (1 - x) - TRYδ // Factor

Out[*]= $-\frac{x}{125\ (-1+x)}$

In[*]:= $\frac{\text{TRY}\delta + \Delta\delta}{\text{TRY}\delta}$ /. $\Delta\delta$ -> $\frac{\text{TRYx}}{1-\text{TRYx}}$ TRYδ // 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 resistance classes):
$\left\{s \to \frac{\kappa}{\beta}, i \to \frac{\delta(\beta-\kappa)}{\beta(\delta+q\kappa)}\right\}$

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

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

[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_, 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}] + δ[j]/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}] - δ[j]/(1 - TRYx) * rH[j, t];
   drLdt[j_, t_] = δ[j]/(1 - TRYx) * rH[j, t] -
     δ[j]/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, TRYδO, 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}, ■}}}],
```

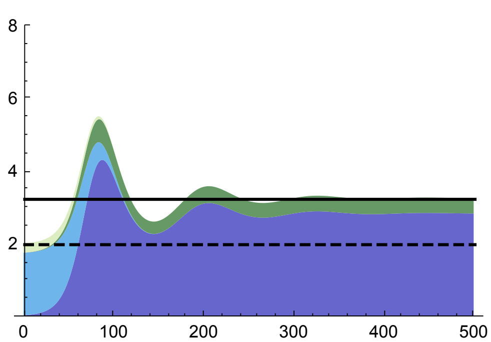
$$\text{Plot}\left[100\,\frac{\text{TRY}\delta\ (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta\ (\text{TRY}\delta + \text{TRY}\kappa\ \text{TRYconvert})},\ \{t, 0, \text{maxtime}\},\right.$$

$$\left.\text{PlotStyle} \to \{\text{Black}, \text{Dashed}\}\right],$$

$$\text{Plot}\left[100\,\frac{\frac{\text{TRY}\delta}{1-\text{TRYx}}\ (\text{TRY}\beta\text{V} - \text{TRY}\kappa)}{\text{TRY}\beta\text{V}\left(\frac{\text{TRY}\delta}{1-\text{TRYx}} + \text{TRY}\kappa\ \text{TRYconvert}\right)},\ \{t, 0, \text{maxtime}\},\ \text{PlotStyle} \to \{\text{Black}\}\right],$$

```
  ImageSize → 250
 ]
```

Out[∘]=



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[∘]= {0.385766}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. 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 → 0.0825995}

This is consistent with the predicted selection coefficient:

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

Out[∘]= 0.0833333

New equilibrium:

In[∘]:=
```
(((TRYδ + Δδ) (TRYβV - TRYϰ)) / (TRYβV ((TRYδ + Δδ) + TRYϰ TRYconvert))) /. Δδ -> TRYx / (1 - TRYx) TRYδ // N
```

Out[∘]= 0.0325

% rise in the endemic equilibrium:

In[∘]:=
```
100 * (% - TRYinf) / 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, TRYβ, TRYβV, 8/10 TRYδ, 8/10 TRYδ0, TRYϰ, 8/10};
```

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

Showing the % of the population infectious:

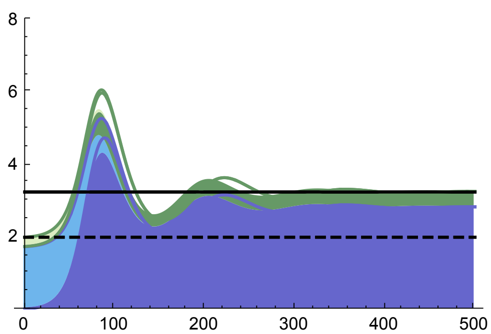
In[∘]:=
```
plot2 = Show[plot1,
  Plot[Evaluate@Table[ Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
       solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
   {t, 0, maxtime}, PlotRange → {Automatic, {0, maxy}},
   PlotStyle → {■, ■, ■, ■}],
```

$$\text{Plot}\left[100\ \frac{\text{TRY}\delta\ (\text{TRY}\beta - \text{TRY}\kappa)}{\text{TRY}\beta\ (\text{TRY}\delta + \text{TRY}\kappa\ \text{TRYconvert})},\ \{t, 0, \text{maxtime}\},\ \text{PlotStyle} \to \{\text{Black}, \text{Dashed}\}\right],$$

$$\text{Plot}\left[100\ \frac{\frac{\text{TRY}\delta}{1-\text{TRYx}}\ (\text{TRY}\beta\text{V} - \text{TRY}\kappa)}{\text{TRY}\beta\text{V}\ \left(\frac{\text{TRY}\delta}{1-\text{TRYx}} + \text{TRY}\kappa\ \text{TRYconvert}\right)},\ \{t, 0, \text{maxtime}\},\ \text{PlotStyle} \to \{\text{Black}\}\right],$$

```
  ImageSize → 250
 ]
```

Out[∘]=



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)*)
TRYδO = 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;
```
$\mathrm{i} \to \frac{\delta\ (\beta-\kappa)}{\beta\ (\delta+\mathrm{q}\ \kappa)}$

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

Out[∘]= $\left\{\left\{\beta \to -\frac{\delta\ \kappa}{-\delta+\mathrm{inf}\ \delta+\mathrm{inf}\ \mathrm{q}\ \kappa}\right\}\right\}$

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

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

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

Out[∘]= 2.08333

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

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

Out[∘]= $\{\beta\mathrm{V} \to 0.488448\}$

In[∘]:= TRYβV = βV /. %;

% increase in β:

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

Out[∘]= 17.2276

and infects earlier during waning.

Specifically, the mean waning rate (once fixed) increases by 25%:

In[∘]:= TRYδ / (1 - x) - TRYδ // Factor

Out[∘]= $-\frac{\mathrm{x}}{125\ (-1+\mathrm{x})}$

In[∘]:= $\frac{\text{TRY}\delta + \Delta\delta}{\text{TRY}\delta}$ /. $\Delta\delta$ -> $\frac{\text{TRYx}}{1 - \text{TRYx}}$ TRYδ // 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):
$\left\{s \to \frac{\kappa}{\beta},\ i \to \frac{\delta\ (\beta-\kappa)}{\beta\ (\delta+q\ \kappa)}\right\}$

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

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

[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_, δO_, κ_, q_}, start] :=
         solution[{p, f, older, β, βV, δY, δO, κ, q}, start] =
          Block[{ages = 2, stages = 2},
                                                                                δ[j]
           dsdt[j_, t_] = (1 - q) * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] + ---- * rL[j, t] -
                                                                                TRYx
             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];
                                                                              δ[j]
           drHdt[j_, t_] = q * Sum[κ[j, jj] * i[j, jj, t], {jj, 1, stages}] - -------- * rH[j, t];
                                                                            1 - TRYx
                            δ[j]
           drLdt[j_, t_] = -------- * rH[j, t] -
                           1 - TRYx
             δ[j]
             ---- * rL[j, t] - Sum[β[k, 1] * i[k, 1, t], {k, 1, ages}] * rL[j, t];
             TRYx
           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, TRYδO, TRYϰ, TRYconvert};
```

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

Showing the % of the population infectious:

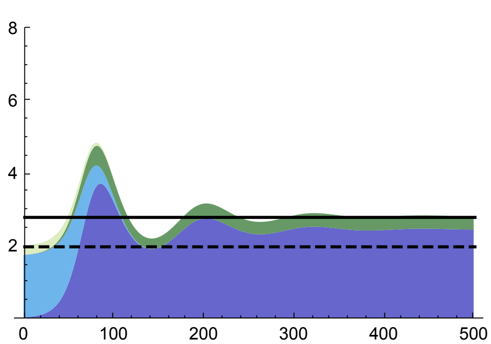
In[∘]:=
```
plot1 = Show[
  Plot[Evaluate@Table[ Sum[100 * i[all[[c, 1]], all[[c, 2]], t] /.
       solution[partemp, start], {c, 1, jcum}], {jcum, 1, Length[all]}],
   {t, 0, maxtime}, PlotRange → {Automatic, {0, maxy}},
   PlotStyle → None, Filling → {{1 → {0, }}, {2 → {{1}, }},
     {3 → {{2}, }},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

$$\text{Plot}\left[100\,\frac{\text{TRY}\delta\ (\text{TRY}\beta - \text{TRY}\varkappa)}{\text{TRY}\beta\ (\text{TRY}\delta + \text{TRY}\varkappa\ \text{TRYconvert})},\ \{t, 0, \text{maxtime}\},\ \text{PlotStyle} \to \{\text{Black}, \text{Dashed}\}\right],$$

$$\text{Plot}\left[100\,\frac{\frac{\text{TRY}\delta}{1-\text{TRYx}}\ (\text{TRY}\beta\text{V} - \text{TRY}\varkappa)}{\text{TRY}\beta\text{V}\left(\frac{\text{TRY}\delta}{1-\text{TRYx}} + \text{TRY}\varkappa\ \text{TRYconvert}\right)},\ \{t, 0, \text{maxtime}\},\ \text{PlotStyle} \to \{\text{Black}\}\right],$$

```
  ImageSize → 250
 ]
```

Out[∘]=



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[∘]= {0.384602}

In[∘]:=
```
Solve[Exp[s 50] == ((p50 / (1 - p50)) / (p0 / (1 - p0)) /. 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 → 0.0825012}

This is consistent with the predicted selection coefficient:

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

Out[∘]= 0.0833

New equilibrium:

In[∘]:=
```
(((TRYδ + Δδ) (TRYβV - TRYϰ)) / (TRYβV ((TRYδ + Δδ) + TRYϰ TRYconvert))) /. Δδ -> TRYx / (1 - TRYx) TRYδ // N
```

Out[∘]= 0.028121

% rise in the endemic equilibrium:

In[∘]:=
```
100 * (% - TRYinf) / 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:

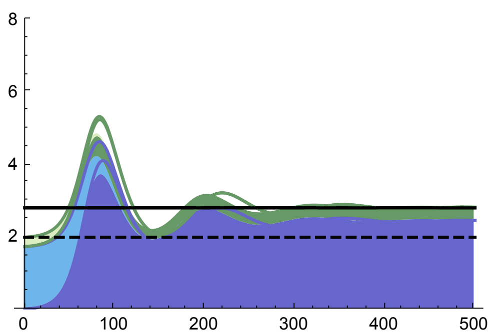
In[∘]:=
```
partemp = {TRYp, TRYf, TRYolder, TRYβ, TRYβV, 8/10 TRYδ, 8/10 TRYδ0, TRYϰ, 8/10};
```

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 (TRYδ (TRYβ - TRYκ))/(TRYβ (TRYδ + TRYκ TRYconvert)),
   {t, 0, maxtime}, PlotStyle → {Black, Dashed}],
  Plot[100 (TRYδ/(1-TRYx) (TRYβV - TRYκ))/(TRYβV (TRYδ/(1-TRYx) + TRYκ TRYconvert)), {t, 0, maxtime}, PlotStyle → {Black}],
  ImageSize → 250
 ]
```

Out[∘]=



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];
```