No intervention

Model equations

Notations:

Capital letter is the resistance profile of the strain, small letter is the drug it is treated with

For example Sf is sensitive, treated with front-line drug

Prevalence of a strain is the sum of equilibrium prevalence of that strain under each treatement

For example: prevalence of the sensitive strain S = Sf + Sl

In[365]:=
```
ClearAll["Global`*"]
```

In[203]:=
```
dSfdt = b (Sf + Sl) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Sf (a + g + d);
```

In[204]:=
```
dSldt = a Sf - Sl (g + d);
```

In[205]:=
```
dFfdt = b (Ff + Fl) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Ff (a + d + c);
```

In[206]:=
```
dFldt = a Ff - Fl (g + d + c) ;
```

In[207]:=
```
dLfdt = b (Lf + Ll) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Lf (a + g + d + c);
```

In[208]:=
```
dLldt = a Lf - Ll (d + c);
```

In[209]:=
```
dMfdt = b (Mf + Ml) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Mf (a + d + 2 c);
```

In[210]:=
```
dMldt = a Mf - Ml (d + 2 c);
```

Determining equilibrium:

In[211]:=
```
FullSimplify[
 Solve[dSfdt == 0 && dSldt == 0 && dFfdt == 0 && dFldt == 0 && dLfdt == 0 &&
   dLldt == 0 && dMfdt == 0 && dMldt == 0 , {Sf, Sl, Ff, Fl, Lf, Ll, Mf, Ml}]]
```

Out[211]=

$$\Big\{\{Sf \to 0, Sl \to 0, Ff \to 0, Fl \to 0, Lf \to 0, Ll \to 0, Mf \to 0, Ml \to 0\},$$

$$\Big\{Sf \to 0, Sl \to 0, Ff \to 0, Fl \to 0, Lf \to 0, Ll \to 0, Mf \to \frac{(b-2c-d)\,(2c+d)}{b\,(a+2c+d)}, Ml \to \frac{a\,(b-2c-d)}{b\,(a+2c+d)}\Big\}, \Big\{Sf \to \frac{(b-d-g)\,(d+g)}{b\,(a+d+g)},$$

$$Sl \to \frac{a\,(b-d-g)}{b\,(a+d+g)}, Ff \to 0, Fl \to 0, Lf \to 0, Ll \to 0, Mf \to 0, Ml \to 0\Big\},$$

$$\Big\{Sf \to 0, Sl \to 0, Ff \to -\frac{(c+d+g)\,(-((b-c-d)\,(c+d+g))+a\,(-b+c+d+g))}{b\,(a+c+d+g)^2},$$

$$Fl \to \frac{a\,(b-c-d)\,(a+c+d)-a\,(a-b+c+d)\,g}{b\,(a+c+d+g)^2}, Lf \to 0, Ll \to 0, Mf \to 0, Ml \to 0\Big\},$$

$$\Big\{Sf \to 0, Sl \to 0, Ff \to 0, Fl \to 0, Lf \to \frac{(c+d)\,(-((a+c+d)\,(-b+c+d))-(c+d)\,g)}{b\,(a+c+d)^2},$$

$$Ll \to \frac{a\,(b-c-d)\,(a+c+d)-a\,(c+d)\,g}{b\,(a+c+d)^2}, Mf \to 0, Ml \to 0\Big\}\Big\}$$

R0s and equilibria

So the equilibrium of each strain under each treatment is (only one strain will be present at equilibrium)

In[738]:= $Sf = \frac{(b - d - g)\ (d + g)}{b\ (a + d + g)};$

In[739]:= $Sl = \frac{a\ (b - d - g)}{b\ (a + d + g)};$

In[740]:= $Ff = -\frac{(c + d + g)\ (-((b - c - d)\ (c + d + g)) + a\ (-b + c + d + g))}{b\ (a + c + d + g)^2};$

In[741]:= $Fl = \frac{a\ (b - c - d)\ (a + c + d) - a\ (a - b + c + d)\ g}{b\ (a + c + d + g)^2};$

In[742]:= $Lf = \frac{(c + d)\ (-((a + c + d)\ (-b + c + d)) - (c + d)\ g)}{b\ (a + c + d)^2};$

In[743]:= $Ll = \frac{a\ (b - c - d)\ (a + c + d) - a\ (c + d)\ g}{b\ (a + c + d)^2};$

In[744]:= $Mf = \frac{(b - 2\ c - d)\ (2\ c + d)}{b\ (a + 2\ c + d)};$

In[745]:= $Ml = \frac{a\ (b - 2\ c - d)}{b\ (a + 2\ c + d)};$

And the overall equilibrium prevalence for each strain are:

In[746]:= `Seq = Sf + Sl;`

In[747]:= `Feq = Ff + Fl;`

In[748]:= `Leq = Lf + Ll;`

In[749]:= `Meq = Mf + Ml;`

Deducing the R0: R0 for a given strain is 1 - 1/Eq:

In[750]:= `r0S = Factor[1 / (1 - Seq)]`

Out[750]= $\frac{b}{d + g}$

In[751]:= `r0F = Factor[1 / (1 - Feq)]`

Out[751]= $\frac{b\ (a + c + d + g)}{(a + c + d)\ (c + d + g)}$

In[752]:= `r0L = Factor[1 / (1 - Leq)]`

Out[752]= $\frac{b\ (a + c + d)}{(c + d)\ (a + c + d + g)}$

In[753]:=
```
r0M = Factor[1 / (1 - Meq)]
```
Out[753]= $\frac{b}{2\,c + d}$

Possible scenarios and boundary conditions

What are the possible situations (i.e. which strain can be the fittest before intervention?), and what are the conditions for each of these situation?

In each case we must evaluate weather there exist conditions where the R0 of a given strain is higher than all others

This must be evaluated with the constraint that the equilibrium prevalence of this strain treated by frontline drug is higher than the equilibrium prevalence of the same strain treated by last line drug, because the definition of a front-line drug is that it is used more.

We also add as a condition that these have to be non-zero equilibrium

```
(* Evaluation below shows that there are conditions of S to be the fittest,
but this is an irreleavant situation to study here,
as we are interested in the problem of AMR *)

Reduce[r0S > r0F && r0S > r0L && r0S > r0M &&
  a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && Sf > Sl > 0]
```

Out[239]= $g > 0 \;\&\&\; \left(\left(\frac{g}{2} < c \le -\frac{g}{2} + \frac{1}{2}\sqrt{5}\sqrt{g^2} \;\&\&\; d > \frac{-c^2 - c\,g + g^2}{2\,c - g} \;\&\&\; \frac{-c^2 - c\,d + d\,g + g^2}{c} < a < d + g \;\&\&\; b > d + g\right) \;||\; \left(-\frac{g}{2} + \frac{1}{2}\sqrt{5}\sqrt{g^2} < c < g \;\&\&\; d > 0 \;\&\&\; \frac{-c^2 - c\,d + d\,g + g^2}{c} < a < d + g \;\&\&\; b > d + g\right) \;||\; (c \ge g \;\&\&\; d > 0 \;\&\&\; 0 < a < d + g \;\&\&\; b > d + g)\right)$

```
(* Evaluations below show that the L strain cannot be the fittest,
within the aforementionned constraints.
  Indeed, r0L > r0F before intervention requires a > c+d,
which is the condition required for Lf<
 Ll meaning that the front-line drug is used less. Hence,
the L strain cannot become fitter than the F strain as long as the front-
 line drug is used more,
which will always be the case owing the the definition of front-
 line drug. Hence, the L strain cannot become the fittest*)
```

In[251]:=
```
Reduce[r0L > r0F && r0L > r0M && r0L > r0S &&
  a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && Lf > Ll > 0]
```
Out[251]= False

In[250]:=
```
Reduce[r0L > r0F && a > 0 && b > 0 && c > 0 && d > 0 && g > 0]
```

Out[250]= $d > 0 \&\& c > 0 \&\& a > c + d \&\& 0 < g < \frac{a^2 - c^2 - 2\,c\,d - d^2}{c + d} \&\& b > 0$

In[249]:=
```
Reduce[Lf < Ll > 0 && a > 0 && b > 0 && c > 0 && d > 0 && g > 0]
```

Out[249]= $d > 0 \&\& c > 0 \&\& a > c + d \&\& g > 0 \&\& b > \frac{a\,c + c^2 + a\,d + 2\,c\,d + d^2 + c\,g + d\,g}{a + c + d}$

```
(* Evaluations below show that the
  M strain will become the fittest as long as a <
 2c+d (the other conditions are simply variation of value of d depending
    on c for equilibrium to exist, but the constrain is in a
     The meaning of this condition is understood when looking
     the Mf and Ml. a < 2c+d means that the front line
      drug is used more when the M strain is the fittest*)
```

In[252]:=
```
Reduce[r0M > r0F && r0M > r0L && r0M > r0S &&
  a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && Mf > Ml > 0]
```

Out[252]= $g > 0 \&\& \left(\left(0 < c \leq \frac{g}{3} \&\& d > 0 \&\& \frac{-c^2 - c\,d - c\,g}{c - g} < a < 2\,c + d \&\& b > 2\,c + d\right) \,||\, \left(\frac{g}{3} < c < \frac{g}{2} \&\& d > \frac{-3\,c^2 + c\,g}{2\,c - g} \&\& \frac{-c^2 - c\,d - c\,g}{c - g} < a < 2\,c + d \&\& b > 2\,c + d\right)\right)$

In[253]:=
```
Reduce[Mf > Ml > 0 && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 ]
```

Out[253]= $d > 0 \&\& c > 0 \&\& b > 2\,c + d \&\& 0 < a < 2\,c + d \&\& g > 0$

(* We also see that a has the be greater than a treshold $\frac{-c^2-c\,d-c\,g}{c-g}$. Below this treshold, F becomes fitter than M *)

In[256]:=
```
Reduce[r0M > r0F && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 ]
```

Out[256]= $g > 0 \&\& 0 < c < g \&\& d > 0 \&\& a > \frac{-c^2 - c\,d - c\,g}{c - g} \&\& b > 0$

```
(* Finally, and that will be important for later,
we also see that the only possible order of strains when M is the fittest is M>
 F>L>S, any other order leads to "False" evaluation *)
```

In[258]:=
```
Reduce[r0M > r0L > r0S > r0S && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && Mf > Ml > 0]
```

Out[258]= False

```
(* indeed we showed before that L cannot be
  fitter than F as long as the front-line drug is used more,
so we know that it will necessarily be F>L. We can then show that if M>
 L (M fittest), S is necessarily below L. Indeed,
```
S>L requires a< $\frac{-c^2-c\ d}{c-g}$. But we already showed that M>F requires a> $\frac{-c^2-c\ d-c\ g}{c-g}$,
which is higher than $\frac{-c^2-c\ d}{c-g}$. Hence, in conditons for M to be fittest,
the condition for S>L cannot be met. Hence we will necessarily have L>
 S. Hence overall, the only possible order is M>F>L>S *)

In[273]:= Reduce[r0S > r0L && a > 0 && b > 0 && c > 0 && d > 0 && g > 0]

Out[273]= $g > 0\ \&\&\ \left(\left(0 < c < g\ \&\&\ d > 0\ \&\&\ 0 < a < \frac{-c^2 - c\ d}{c - g}\ \&\&\ b > 0\right)\ ||\ (c \geq g\ \&\&\ d > 0\ \&\&\ a > 0\ \&\&\ b > 0)\right)$

(* Finally for the F strain can become the fittest.
 It requires a< $\frac{-c^2-c\ d-c\ g}{c-g}$, to be fitter than M, as shown above.
 We already showed that L cannot be fitter than F unless last-
 line drug is used more.
 There are conditions for S fitter than F even when F>M,
but again that is not a releavant scenario.
 So we just know that it is possible to have F fittest,
where in this case it will necessitate a< $\frac{-c^2-c\ d-c\ g}{c-g}$, for F to be fitter than M*)

Reduce[r0F > r0M && a > 0 && b > 0 && c > 0 && d > 0 && g > 0]

Out[307]= $$g > 0\ \&\&\ \left(\left(0 < c \leq \frac{g}{2}\ \&\&\ d > 0\ \&\&\ 0 < a < \frac{-c^2 - c\ d - c\ g}{c - g}\ \&\&\ b > \frac{a\ c + c^2 + a\ d + 2\ c\ d + d^2 + a\ g + c\ g + d\ g}{a + c + d + g}\right)\ ||\ \left(c > \frac{g}{2}\ \&\&\ d > 0\ \&\&\ 0 < a < c + d + g\ \&\&\ b > \frac{a\ c + c^2 + a\ d + 2\ c\ d + d^2 + a\ g + c\ g + d\ g}{a + c + d + g}\right)\right)$$

SO IN SUMMARY:

- Although S can be the fittest, we disregard this scenario which would not necessitate an intervention to tackle AMR

- L cannot be the fittest unless the front-line drug is used more

- Then, M can be fittest as long as a<2c+d, which is the condition for front-line drug to be used more when M is fittest

- If M fittest, we showed that there is only one order of strains possible.

- If the escalation rate continues to decrease through, the F>M. Hence F can become the fittest, which will necessitate $a < \frac{-c^2-c\ d-c\ g}{c-g}$**, to overcome M.**

- There are various order of strains possible when F fittest.

Adjuvant

Notations:
Notations are as before, but we add the prefix: adj for “adjuvant”, and then Fline or Lline for front-line intervention of last-line intervention

Front-line adjuvant

Model equations

```
In[310]:= ClearAll["Global`*"]

In[311]:= adjFlinedSfdt = b (Sf + Sl) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Sf (a + g + d);

In[312]:= adjFlinedSldt = a Sf - Sl (g + d);

In[313]:= adjFlinedFfdt = b (Ff + Fl) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Ff (a + d + c + e);

In[314]:= adjFlinedFldt = a Ff - Fl (g + d + c);

In[315]:= adjFlinedLfdt = b (Lf + Ll) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Lf (a + g + d + c);

In[316]:= adjFlinedLldt = a Lf - Ll (d + c);

In[317]:= adjFlinedMfdt = b (Mf + Ml) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Mf (a + d + 2 c + e);

In[318]:= adjFlinedMldt = a Mf - Ml (d + 2 c);
```

Determining equilibrium

In[319]:= Solve[adjFlinedSfdt == 0 && adjFlinedSldt == 0 && adjFlinedFfdt == 0 && adjFlinedFldt == 0 && adjFlinedLfdt == 0 && adjFlinedLldt == 0 && adjFlinedMfdt == 0 && adjFlinedMldt == 0 , {Sf, Sl, Ff, Fl, Lf, Ll, Mf, Ml}]

Out[319]=
$$\left\{\{Sf\to 0,\ Sl\to 0,\ Ff\to 0,\ Fl\to 0,\ Lf\to 0,\ Ll\to 0,\ Mf\to 0,\ Ml\to 0\},\right.$$
$$\left\{Sf\to \frac{(b-d-g)\ (d+g)}{b\ (a+d+g)},\ Sl\to \frac{a\ (b-d-g)}{b\ (a+d+g)},\ Ff\to 0,\ Fl\to 0,\ Lf\to 0,\ Ll\to 0,\ Mf\to 0,\ Ml\to 0\right\},\ \{Sf\to 0,\ Sl\to 0,\ Ff\to 0,\ Fl\to 0,\ Lf\to 0,\ Ll\to 0,$$
$$Mf\to -\frac{(2c+d)\ \left(-a b+2 a c-2 b c+4 c^2+a d-b d+4 c d+d^2+2 c e+d e\right)}{b\ (a+2c+d)^2},$$
$$Ml\to \frac{a\ \left(a b-2 a c+2 b c-4 c^2-a d+b d-4 c d-d^2-2 c e-d e\right)}{b\ (a+2c+d)^2}\},\ \{Sf\to 0,\ Sl\to 0,$$
$$Ff\to 0,\ Fl\to 0,\ Lf\to -\frac{(c+d)\ \left(-a b+a c-b c+c^2+a d-b d+2 c d+d^2+c g+d g\right)}{b\ (a+c+d)^2},$$
$$Ll\to \frac{a\ \left(a b-a c+b c-c^2-a d+b d-2 c d-d^2-c g-d g\right)}{b\ (a+c+d)^2},$$
$$Mf\to 0,\ Ml\to 0\},\ \{Sf\to 0,\ Sl\to 0,\ Ff\to$$
$$-\frac{(c+d+g)\ \left(-a b+a c-b c+c^2+a d-b d+2 c d+d^2+c e+d e+a g-b g+c g+d g+e g\right)}{b\ (a+c+d+g)^2},$$
$$Fl\to \frac{a\ \left(a b-a c+b c-c^2-a d+b d-2 c d-d^2-c e-d e-a g+b g-c g-d g-e g\right)}{b\ (a+c+d+g)^2},$$
$$\left. Lf\to 0,\ Ll\to 0,\ Mf\to 0,\ Ml\to 0\}\right\}$$

So the equilibrium of each strain under each treatment is (only one strain will be present at equilibrium)

In[382]:= $$\text{adjFlineSf} = \frac{(b-d-g)\ (d+g)}{b\ (a+d+g)};$$

In[383]:= $$\text{adjFlineSl} = \frac{a\ (b-d-g)}{b\ (a+d+g)};$$

In[384]:= $$\text{adjFlineFf} = -\frac{(c+d+g)\ \left(-a b+a c-b c+c^2+a d-b d+2 c d+d^2+c e+d e+a g-b g+c g+d g+e g\right)}{b\ (a+c+d+g)^2};$$

In[385]:= $$\text{adjFlineFl} = \frac{a\ \left(a b-a c+b c-c^2-a d+b d-2 c d-d^2-c e-d e-a g+b g-c g-d g-e g\right)}{b\ (a+c+d+g)^2};$$

In[386]:= $$\text{adjFlineLf} = -\frac{(c+d)\ \left(-a b+a c-b c+c^2+a d-b d+2 c d+d^2+c g+d g\right)}{b\ (a+c+d)^2};$$

In[387]:= $$\text{adjFlineLl} = \frac{a\ \left(a b-a c+b c-c^2-a d+b d-2 c d-d^2-c g-d g\right)}{b\ (a+c+d)^2};$$

In[388]:=
$$adjFlineMf = -\frac{(2c+d)\left(-ab+2ac-2bc+4c^2+ad-bd+4cd+d^2+2ce+de\right)}{b\,(a+2c+d)^2};$$

In[389]:=
$$adjFlineMl = \frac{a\left(ab-2ac+2bc-4c^2-ad+bd-4cd-d^2-2ce-de\right)}{b\,(a+2c+d)^2};$$

In[390]:= And the overall equilibrium prevalence for each strain are :

```
In[390]:= adjFlineSeq = (adjFlineSf + adjFlineSl);

In[391]:= adjFlineFeq = (adjFlineFf + adjFlineFl);

In[392]:= adjFlineLeq = (adjFlineLf + adjFlineLl);

In[393]:= adjFlineMeq = (adjFlineMf + adjFlineMl);
```

▪ R0 under front-line intervention

```
In[394]:= r0Sf = Factor[1 / (1 - adjFlineSeq )]
```

Out[394]=
$$\frac{b}{d+g}$$

```
In[395]:= r0Ff = Factor[1 / (1 - adjFlineFeq )]
```

Out[395]=
$$\frac{b\,(a+c+d+g)}{(a+c+d+e)\,(c+d+g)}$$

```
In[396]:= r0Lf = Factor[1 / (1 - adjFlineLeq )]
```

Out[396]=
$$\frac{b\,(a+c+d)}{(c+d)\,(a+c+d+g)}$$

```
In[397]:= r0Mf = Factor[1 / (1 - adjFlineMeq )]
```

Out[397]=
$$\frac{b\,(a+2c+d)}{(2c+d)\,(a+2c+d+e)}$$

Last-line adjuvant

▪ Model equations

```
In[339]:= adjLlinedSfdt =
    b (Sf + Sl) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Sf (a + g + d);

In[340]:= adjLlinedSldt = a Sf - Sl (g + d);

In[341]:= adjLlinedFfdt =
    b (Ff + Fl) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Ff (a + d + c);

In[342]:= adjLlinedFldt = a Ff - Fl (g + d + c);

In[343]:= adjLlinedLfdt =
    b (Lf + Ll) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Lf (a + g + d + c);

In[344]:= adjLlinedLldt = a Lf - Ll (d + c + e);

In[345]:= adjLlinedMfdt =
    b (Mf + Ml) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Mf (a + d + 2 c);
```

In[346]:=
```
adjLlinedMldt = a Mf - Ml (d + 2 c + e);
```

Determining equilibrium

In[347]:=
```
Solve[adjLlinedSfdt == 0 && adjLlinedSldt == 0 && adjLlinedFfdt == 0 &&
  adjLlinedFldt == 0 && adjLlinedLfdt == 0 && adjLlinedLldt == 0 &&
  adjLlinedMfdt == 0 && adjLlinedMldt == 0 , {Sf, Sl, Ff, Fl, Lf, Ll, Mf, Ml}]
```

Out[347]=

$$\left\{\{Sf\to 0, Sl\to 0, Ff\to 0, Fl\to 0, Lf\to 0, Ll\to 0, Mf\to 0, Ml\to 0\}, \left\{Sf\to \frac{(b-d-g)\ (d+g)}{b\ (a+d+g)}, Sl\to \frac{a\ (b-d-g)}{b\ (a+d+g)}, Ff\to 0, Fl\to 0, Lf\to 0, Ll\to 0, Mf\to 0, Ml\to 0\right\}, \right.$$

$$\left\{Sf\to 0, Sl\to 0, Ff\to -\frac{(c+d+g)\ \left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+a\,g-b\,g+c\,g+d\,g\right)}{b\ (a+c+d+g)^2}, Fl\to \frac{a\ \left(a\,b-a\,c+b\,c-c^2-a\,d+b\,d-2\,c\,d-d^2-a\,g+b\,g-c\,g-d\,g\right)}{b\ (a+c+d+g)^2}, Lf\to 0, Ll\to 0, Mf\to 0, Ml\to 0\right\},$$

$$\left\{Sf\to 0, Sl\to 0, Ff\to 0, Fl\to 0, Lf\to 0, Ll\to 0, Mf\to -\frac{(2\,c+d+e)\ \left(-a\,b+2\,a\,c-2\,b\,c+4\,c^2+a\,d-b\,d+4\,c\,d+d^2+a\,e-b\,e+2\,c\,e+d\,e\right)}{b\ (a+2\,c+d+e)^2}, Ml\to \frac{a\ \left(a\,b-2\,a\,c+2\,b\,c-4\,c^2-a\,d+b\,d-4\,c\,d-d^2-a\,e+b\,e-2\,c\,e-d\,e\right)}{b\ (a+2\,c+d+e)^2}\right\},$$

$$\left.\left\{Sf\to 0, Sl\to 0, Ff\to 0, Fl\to 0, Lf\to -\frac{(c+d+e)\ \left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+a\,e-b\,e+c\,e+d\,e+c\,g+d\,g+e\,g\right)}{b\ (a+c+d+e)^2}, Ll\to \frac{a\ \left(a\,b-a\,c+b\,c-c^2-a\,d+b\,d-2\,c\,d-d^2-a\,e+b\,e-c\,e-d\,e-c\,g-d\,g-e\,g\right)}{b\ (a+c+d+e)^2}, Mf\to 0, Ml\to 0\right\}\right\}$$

(*So the equilibrium of each strain under each treatment is (only one strain will be present at equilibrium) *)

In[398]:=
$$adjLlineSf = \frac{(b-d-g)\ (d+g)}{b\ (a+d+g)};$$

In[399]:=
$$adjLlineSl = \frac{a\ (b-d-g)}{b\ (a+d+g)};$$

In[400]:=
$$adjLlineFf = -\frac{(c+d+g)\ \left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+a\,g-b\,g+c\,g+d\,g\right)}{b\ (a+c+d+g)^2};$$

In[401]:=
$$adjLlineFl = \frac{a\ \left(a\,b-a\,c+b\,c-c^2-a\,d+b\,d-2\,c\,d-d^2-a\,g+b\,g-c\,g-d\,g\right)}{b\ (a+c+d+g)^2};$$

In[402]:=
$$adjLlineLf = -\frac{(c+d+e)\ \left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+a\,e-b\,e+c\,e+d\,e+c\,g+d\,g+e\,g\right)}{b\ (a+c+d+e)^2};$$

In[403]:=
$$\text{adjLlineLl} = \frac{a\,(a\,b - a\,c + b\,c - c^2 - a\,d + b\,d - 2\,c\,d - d^2 - a\,e + b\,e - c\,e - d\,e - c\,g - d\,g - e\,g)}{b\,(a + c + d + e)^2};$$

In[404]:=
$$\text{adjLlineMf} = -\frac{(2\,c + d + e)\,(-a\,b + 2\,a\,c - 2\,b\,c + 4\,c^2 + a\,d - b\,d + 4\,c\,d + d^2 + a\,e - b\,e + 2\,c\,e + d\,e)}{b\,(a + 2\,c + d + e)^2};$$

In[405]:=
$$\text{adjLlineMl} = \frac{a\,(a\,b - 2\,a\,c + 2\,b\,c - 4\,c^2 - a\,d + b\,d - 4\,c\,d - d^2 - a\,e + b\,e - 2\,c\,e - d\,e)}{b\,(a + 2\,c + d + e)^2};$$

(*And the overall equilibrium prevalence for each strain are*)

```
In[406]:= adjLlineSeq = (adjLlineSf + adjLlineSl);
In[407]:= adjLlineFeq = (adjLlineFf + adjLlineFl);
In[408]:= adjLlineLeq = (adjLlineLf + adjLlineLl);
In[409]:= adjLlineMeq = (adjLlineMf + adjLlineMl);
```

▪ R0 under last-line intervention

```
In[410]:= r0Sl = Factor[1 / (1 - adjLlineSeq )]
```

Out[410]= $\frac{b}{d + g}$

```
In[411]:= r0Fl = Factor[1 / (1 - adjLlineFeq )]
```

Out[411]= $\frac{b\,(a + c + d + g)}{(a + c + d)\,(c + d + g)}$

```
In[412]:= r0Ll = Factor[1 / (1 - adjLlineLeq )]
```

Out[412]= $\frac{b\,(a + c + d + e)}{(c + d + e)\,(a + c + d + g)}$

```
In[413]:= r0Ml = Factor[1 / (1 - adjLlineMeq )]
```

Out[413]= $\frac{b\,(a + 2\,c + d + e)}{(a + 2\,c + d)\,(2\,c + d + e)}$

Public health analysis for Adjuvant

▪ If F was the fittest strain before intervention

There is no need to go too much into the equations for this case.
The last-line intervention does not affect the fitness of the F strain (r0Fl = r0F), so under last-line intervention, that strain will remain the fittest.
The front-line intervention reduces the fitness of all strains or leave it equal (r0Xf <= r0X)
[Indeed, denominator of r0Ff is bigger, for same numerator, so r0Ff<r0F. And r0Sf = r0S, and r0Lf = r0L]
Depending on exact parameter, different strain may become the fittest (another strain than F can become fittest under front-line intervention, leading to strain replacement at equilibrium). But regardless, since the fitness of all strains get reduced under the front -line intervention, and F was the fittest before intervention, it necessarily follows that any strain selected under front-line will be

of lower fitness than the strain selected under de last-line intervention, which is the front-line resistant one.

- **If M was the fittest strain before intervention**

We can see that the difference in R0 between the M strain under front-line and last-line intervention, is lower than zero, as long as a<2c+d
This condition is simply the condition for front-line drug to be used more, when M is the fittest before intervention, which we have assumed.
Hence, if the intervention does not lead to strain replacement, the R0 under front-line intervention is lower, implying a better public health benefit.

In[437]:= `Factor[FullSimplify[r0Mf - r0Ml]]`

Out[437]= $$-\frac{b\,e\,\left(-a^2+4\,c^2+4\,c\,d+d^2+2\,c\,e+d\,e\right)}{(2\,c+d)\,(a+2\,c+d)\,(2\,c+d+e)\,(a+2\,c+d+e)}$$

In[438]:= $$\text{Reduce}\left[-\frac{b\,e\,\left(-a^2+4\,c^2+4\,c\,d+d^2+2\,c\,e+d\,e\right)}{(2\,c+d)\,(a+2\,c+d)\,(2\,c+d+e)\,(a+2\,c+d+e)}<0\;\&\&\; a>0\;\&\&\;b>0\;\&\&\;c>0\;\&\&\;d>0\;\&\&\;g>0\;\&\&\;e>0\right]$$

Out[438]= $$g>0\;\&\&\;d>0\;\&\&\;c>0\;\&\&\;\left((0<a\leq 2\,c+d\;\&\&\;e>0\;\&\&\;b>0)\;||\;\left(a>2\,c+d\;\&\&\;e>\frac{a^2-4\,c^2-4\,c\,d-d^2}{2\,c+d}\;\&\&\;b>0\right)\right)$$

We must also consider how they may lead to strains other than the multi-drug resistant strain becoming fittest.
Contrary to the previous scenario starting with F strain fittest, the fitness of the M strain is affected under both the front-line and the last-line intervention.
Hence both intervention can lead to a strain replacement. We need to evaluate which strain would become the fittest under each intervention, and compare the fitness of those two strains.

UNDER FRONT-LINE INTERVENTION: The L strain can become the fittest

We can see from the evaluation below that above a certain threshold for **e**, the L strain becomes fitter than the M strain.
Note that in the output below, this threshold for e exists when $g>\frac{a\,c+c^2+c\,d}{c+d}$*, which is equivalent to* $a>\frac{-c^2-c\,d-c\,g}{c-g}$*, which is a condition that is met as we have assumed that M is the fittest strain here, and r0M > r0F requires* $a>\frac{-c^2-c\,d-c\,g}{c-g}$

In[456]:= `Reduce[r0Lf > r0Mf && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && e > 0]`

Out[456]= $$d>0\;\&\&\;c>0\;\&\&\;a>0\;\&\&\;\left(\left(0<g\leq\frac{a\,c+c^2+c\,d}{c+d}\;\&\&\;e>0\;\&\&\;b>0\right)\;||\;\left(g>\frac{a\,c+c^2+c\,d}{c+d}\;\&\&\; e>\frac{-a^2\,c-3\,a\,c^2-2\,c^3-2\,a\,c\,d-3\,c^2\,d-c\,d^2+a\,c\,g+2\,c^2\,g+a\,d\,g+3\,c\,d\,g+d^2\,g}{2\,a\,c+2\,c^2+a\,d+3\,c\,d+d^2}\;\&\&\; b>0\right)\right)$$

In[457]:= `Reduce[r0M > r0F && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 ]`

Out[457]= $g > 0 \&\& 0 < c < g \&\& d > 0 \&\& a > \frac{-c^2 - c\,d - c\,g}{c - g} \&\& b > 0$

Rewriting the expression for that threshold it reads:

In[447]:= `FullSimplify[` $\frac{-a^2 c - 3 a c^2 - 2 c^3 - 2 a c d - 3 c^2 d - c d^2 + a c g + 2 c^2 g + a d g + 3 c d g + d^2 g}{2 a c + 2 c^2 + a d + 3 c d + d^2}$ `]`

Out[447]= $-\frac{(a + 2 c + d)\,(a c + (c + d)\,(c - g))}{(a + c + d)\,(2 c + d)}$

This L strain is fitter than the S strain under front-line intervention, as long as a> $\frac{c^2+c\,d}{g-c}$, which is necessarily true here as we have assumed for this scenario that r0M>r0F (M was fittest originally), which requires a > $\frac{c^2+c\,d+c\,g}{g-c}$, which implies that a> $\frac{c^2+c\,d}{g-c}$ condition is met.

In[458]:= `Reduce[r0Lf > r0Sf && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && e > 0]`

Out[458]= $g > 0 \&\& 0 < c < g \&\& d > 0 \&\& a > \frac{-c^2 - c\,d}{c - g} \&\& b > 0 \&\& e > 0$

Similarly, this L strain is necessarily fitter than the F strain under front-line intervention, whenever a > $\frac{c^2+c\,d+c\,g}{g-c}$ and the treshold are met

In[467]:= `Reduce[r0Lf > r0Ff && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && e > 0 && r0M > r0F && r0M > r0L && r0M > r0S && Mf > Ml > 0]`

Out[467]= $d > 0 \&\& c > 0 \&\& c < a < 2 c + d \&\& g > \frac{a\,c + c^2 + c\,d}{a - c} \&\&$
$e > \frac{-a^2 g + c^2 g + 2 c\,d\,g + d^2 g + c\,g^2 + d\,g^2}{a\,c + c^2 + a\,d + 2 c\,d + d^2 + a\,g + c\,g + d\,g} \&\& b > 2 c + d$

Similarly, this L strain is necessarily fitter than the F strain under front-line intervention, whenever g > $\frac{a^2-c^2-2\,c\,d-d^2}{c+d}$ and e > $\frac{-a^2 g+c^2 g+2\,c\,d\,g+d^2 g+c\,g^2+d\,g^2}{a\,c+c^2+a\,d+2\,c\,d+d^2+a\,g+c\,g+d\,g}$. These two conditions are met, as this threshold for ***e*** is lower than the threshold leading L > M (i.e L becomes fitter than F before becoming fitter than M), so it's already met, and similarly, this threshold for ***g*** *is also lower than the threshold* g > $\frac{a\,c+c^2+c\,d}{a-c}$ *which we have already assumed for r0M > r0F , whenever a<2c+d, which is met too*

In[470]:= `Reduce[r0Lf > r0Ff && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && e > 0 ]`

Out[470]= $d > 0 \&\& c > 0 \&\&$
$\left(\left(0 < a \le c + d \&\& g > 0 \&\& e > \frac{-a^2 g + c^2 g + 2 c\,d\,g + d^2 g + c\,g^2 + d\,g^2}{a\,c + c^2 + a\,d + 2 c\,d + d^2 + a\,g + c\,g + d\,g} \&\& b > 0\right) \,||\right.$
$\left(a > c + d \&\& \left(\left(0 < g \le \frac{a^2 - c^2 - 2 c\,d - d^2}{c + d} \&\& e > 0 \&\& b > 0\right) \,||\right.\right.$
$\left.\left.\left.\left(g > \frac{a^2 - c^2 - 2 c\,d - d^2}{c + d} \&\& e > \frac{-a^2 g + c^2 g + 2 c\,d\,g + d^2 g + c\,g^2 + d\,g^2}{a\,c + c^2 + a\,d + 2 c\,d + d^2 + a\,g + c\,g + d\,g} \&\& b > 0\right)\right)\right)\right)$

In[472]:= $\text{Reduce}\left[\frac{a\,c + c^2 + c\,d}{c + d} > \frac{a^2 - c^2 - 2\,c\,d - d^2}{c + d}\ \&\&\ a > 0\ \&\&\ c > 0\ \&\&\ d > 0\right]$

Out[472]= $d > 0\ \&\&\ c > 0\ \&\&\ 0 < a < 2\,c + d$

UNDER LAST-LINE INTERVENTION: The F strain can become the fittest

We can see from the evaluation below that above a certain threshold for **e**, the F strain becomes fitter than the M strain.

Note that in the output below, this threshold for e exists when $g > \frac{a\,c+c^2+c\,d}{c+d}$*, which is equivalent to* $a > \frac{-c^2-c\,d-c\,g}{c-g}$*, which is a condition that is met as we have assumed that M is the fittest strain here, and r0M > r0F requires* $a > \frac{-c^2-c\,d-c\,g}{c-g}$

In[473]:= `Reduce[r0Fl > r0Ml && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && e > 0]`

Out[473]= $c > 0\ \&\&\ \Big((0 < a \le c\ \&\&\ d > 0\ \&\&\ g > 0\ \&\&\ e > 0\ \&\&\ b > 0)\ ||$
$\Big(a > c\ \&\&\ d > 0\ \&\&\ \Big(\Big(0 < g \le \frac{a\,c + c^2 + c\,d}{a - c}\ \&\&\ e > 0\ \&\&\ b > 0\Big)\ ||\ \Big(g > \frac{a\,c + c^2 + c\,d}{a - c}\ \&\&$
$e > \frac{-a^2\,c - 3\,a\,c^2 - 2\,c^3 - 2\,a\,c\,d - 3\,c^2\,d - c\,d^2 + a^2\,g + a\,c\,g - 2\,c^2\,g + a\,d\,g - c\,d\,g}{a^2 + 2\,a\,c + c^2 + a\,d + c\,d + c\,g}\ \&\&$
$b > 0\Big)\Big)\Big)\Big)$

Rewriting the expression for that threshold it reads:

In[474]:= $\text{FullSimplify}\left[\frac{-a^2\,c - 3\,a\,c^2 - 2\,c^3 - 2\,a\,c\,d - 3\,c^2\,d - c\,d^2 + a^2\,g + a\,c\,g - 2\,c^2\,g + a\,d\,g - c\,d\,g}{a^2 + 2\,a\,c + c^2 + a\,d + c\,d + c\,g}\right]$

Out[474]= $-\frac{(a + 2\,c + d)\ (a\ (c - g) + c\ (c + d + g))}{(a + c)\ (a + c + d) + c\,g}$

This F strain is fitter than the S strain under last-line intervention, as long as a<2c+d (condition for front-line drug to be used more) and $c < \frac{g}{2}$, which is the condition for M > S before intervention

In[482]:= $\text{Reduce}\left[\text{r0Fl} < \text{r0Sl}\ \&\&\ a > 0\ \&\&\ b > 0\ \&\&\ c > 0\ \&\&\ d > 0\ \&\&\ g > 0\ \&\&\ e > 0\ \&\&\ a < 2\,c + d\ \&\&\ c < \frac{g}{2}\right]$

Out[482]= `False`

In[483]:= `Reduce[r0M > r0S && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && e > 0]`

Out[483]= $a > 0\ \&\&\ g > 0\ \&\&\ 0 < c < \frac{g}{2}\ \&\&\ d > 0\ \&\&\ b > 0\ \&\&\ e > 0$

And this F strain is also fitter than the L strain under last-line intervention, as long as a<2c+d (condition for front-line drug to be used more) and $a < \frac{-c^2-c\,d+c\,g+d\,g}{c}$, which is the condition for M > L before intervention, which is met here since M was the fittest

In[491]:= Reduce$\left[\right.$r0Fl < r0Ll && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && e > 0 && a < 2 c + d && a < $\frac{-c^2 - c\,d + c\,g + d\,g}{c}\left.\right]$

Out[491]= False

In[492]:= Reduce[r0M > r0L && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && e > 0]

Out[492]= $g > 0 \;\&\&\; 0 < c < g \;\&\&\; d > 0 \;\&\&\; 0 < a < \frac{-c^2 - c\,d + c\,g + d\,g}{c} \;\&\&\; b > 0 \;\&\&\; e > 0$

SO, WHEN BOTH INTERVENTIONS LEAD TO STRAIN REPLACEMENT, where:
front-line intervention replaces M --> L
last-line intervention replaces M --> F

Which intervention is best? --> We see that r0Lf < r0Fl, as long as a<2c+d, which again is the condition for front line drug to be used more initially in this scenario, to this condition is met

Notes, on the below output: $g > \frac{a^2-c^2-2\,c\,d-d^2}{c+d}$ is met:
We know that for r0M>r0L, requires $a < \frac{-c^2-c\,d+c\,g+d\,g}{c}$, which is equivalent to $g > \frac{a\,c+c^2+c\,d}{c+d}$ (which itself is equivlanet for $a > \frac{-c^2-c\,d-c\,g}{c-g}$), which was the condition for M > F before intervention (M was fittest originally).
And if condition $g > \frac{a\,c+c^2+c\,d}{c+d}$ is met, then condition $g > \frac{a^2-c^2-2\,c\,d-d^2}{c+d}$ is also met as long as a<2 c+d, because $\frac{a^2-c^2-2\,c\,d-d^2}{c+d} < \frac{a\,c+c^2+c\,d}{c+d}$ as long as a<2 c+d, which we have assumed for front-line drug to be used more.
Hence we can simply summarise: " r0Lf < r0Fl as long as a<2 c+d, which we have assumed owing to definition of front-line drug being used more"

In[527]:= Reduce[r0Lf < r0Fl && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && e > 0 && a < 2 c + d]

Out[527]= $e > 0 \;\&\&\; d > 0 \;\&\&\; c > 0 \;\&\&\; \left((0 < a \leq c + d \;\&\&\; g > 0 \;\&\&\; b > 0) \;||\; \left(c + d < a < 2\,c + d \;\&\&\; g > \frac{a^2 - c^2 - 2\,c\,d - d^2}{c + d} \;\&\&\; b > 0\right)\right)$

In[528]:= Reduce$\left[\frac{a\,c + c^2 + c\,d}{c + d} > \frac{a^2 - c^2 - 2\,c\,d - d^2}{c + d}\right.$ && a > 0 && b > 0 && c > 0 && d > 0 && g > 0$\left.\right]$

Out[528]= $b > 0 \;\&\&\; d > 0 \;\&\&\; c > 0 \;\&\&\; 0 < a < 2\,c + d \;\&\&\; g > 0$

We see that the threshold e for last-line intervention to lead to replacement M --> F is lower than the threshold for front-line intervention to lead to the replacement M --> L.
Said otherwise, the last-line intervention achieves to replace the M strain by a treatable one (F) before the front-line intervention does.
But in this case, we can also show that the fitness of the selected strain under last line intervention is higher than the R0 of the selected strain under front line intervention (r0Fl > r0Mf) within

this range of efficacy

In[533]:=
```
Reduce[r0Fl < r0Mf && a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && e > 0 &&
  e > (-a^2 c - 3 a c^2 - 2 c^3 - 2 a c d - 3 c^2 d - c d^2 + a^2 g + a c g - 2 c^2 g + a d g - c d g)/(a^2 + 2 a c + c^2 + a d + c d + c g) &&
  e < -((a + 2 c + d) (a c + (c + d) (c - g)))/((a + c + d) (2 c + d))]
```

Out[533]= False

Diagnostic (with “efficacy” parameter)

Notations:

Notations are as before, but we add the prefix: diag for “diagnostic”, and then Fline or Lline for front-line intervention of last-line intervention

Note about the t parameter:

The parameter t is simply a rate of diagnosis, in order to have a measure of efficacy as we can have for the adjuvant (parameter e)

If t = 1, then people are always treated according to the diagnostic result, and the model reduces to the original model we had for the paper

If 0<t<1, then the diagnostic is not perfect, or not perfectly used/implemented. This is just to allow having a plot that mirrors what we get for the adjuvant model, where we see how the R0 change with the efficacy of the intervention. It’s an easier plot to visualise the difference between the original R0 (at x-axis = 0) and the new R0 (intervention efficacy/implementation rate is non-zero), and also to illustrate how the intervention can lead to strain replacement when they are efficient enough.

- **Model equations**

In[558]:=
```
ClearAll["Global`*"]
```

In[559]:=
```
diagFlinedSfdt =
  (b (Sf + Sl)) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Sf (a + g + d);
```

In[560]:=
```
diagFlinedSldt = a Sf - Sl (g + d);
```

In[561]:=
```
diagFlinedFfdt =
  (1 - t) b (Ff + Fl) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Ff (a + d + c);
```

In[562]:=
```
diagFlinedFldt =
  t b (Ff + Fl) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) + a Ff - Fl (g + d + c);
```

In[563]:=
```
diagFlinedLfdt =
  (b (Lf + Ll)) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Lf (a + g + d + c);
```

In[564]:=
```
diagFlinedLldt = a Lf - Ll (d + c);
```

In[565]:=
```
diagFlinedMfdt =
  (1 - t) b (Mf + Ml) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Mf (a + d + 2 c);
```

In[566]:=
```
diagFlinedMldt =
  t b (Mf + Ml) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) + a Mf - Ml (d + 2 c);
```

Determining equilibrium

```
(* Solving for equilibrium *)
```

In[567]:=
```
Solve[diagFlinedSfdt == 0 && diagFlinedSldt == 0 && diagFlinedFfdt == 0 &&
  diagFlinedFldt == 0 && diagFlinedLfdt == 0 && diagFlinedLldt == 0 &&
  diagFlinedMfdt == 0 && diagFlinedMldt == 0 , {Sf, Sl, Ff, Fl, Lf, Ll, Mf, Ml}]
```

Out[567]=

$$\Big\{\{Sf \to 0, Sl \to 0, Ff \to 0, Fl \to 0, Lf \to 0, Ll \to 0, Mf \to 0, Ml \to 0\},$$

$$\Big\{Sf \to \frac{(b-d-g)\ (d+g)}{b\ (a+d+g)},\ Sl \to \frac{a\ (b-d-g)}{b\ (a+d+g)},\ Ff \to 0,\ Fl \to 0,$$

$$Lf \to 0, Ll \to 0, Mf \to 0, Ml \to 0\Big\}, \Big\{Sf \to 0, Sl \to 0, Ff \to 0, Fl \to 0,$$

$$Lf \to -\frac{(c+d)\ \left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+c\,g+d\,g\right)}{b\ (a+c+d)^2},$$

$$Ll \to \frac{a\ \left(a\,b-a\,c+b\,c-c^2-a\,d+b\,d-2\,c\,d-d^2-c\,g-d\,g\right)}{b\ (a+c+d)^2},\ Mf \to 0,\ Ml \to 0\Big\},$$

$$\Big\{Sf \to 0, Sl \to 0, Ff \to 0, Fl \to 0, Lf \to 0, Ll \to 0, Mf \to -\frac{(b-2\,c-d)\ (2\,c+d) \times (-1+t)}{b\ (a+2\,c+d)},$$

$$Ml \to \frac{(b-2\,c-d)\ (a+2\,c\,t+d\,t)}{b\ (a+2\,c+d)}\Big\}, \Big\{Sf \to 0, Sl \to 0, Ff \to$$

$$\frac{(c+d+g)\ (-1+t)\ \left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+a\,g-b\,g+c\,g+d\,g+b\,g\,t\right)}{b\ (a+c+d+g-g\,t)^2},$$

$$Fl \to -\frac{(a+c\,t+d\,t)\ \left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+a\,g-b\,g+c\,g+d\,g+b\,g\,t\right)}{b\ (a+c+d+g-g\,t)^2},$$

$$Lf \to 0, Ll \to 0, Mf \to 0, Ml \to 0\Big\}\Big\}$$

(* So the equilibrium of each strain under each
  treatment is (only one strain will be present at equilibrium) *)

In[568]:=
$$diagFlineSf = \frac{(b-d-g)\ (d+g)}{b\ (a+d+g)};$$

In[569]:=
$$diagFlineSl = \frac{a\ (b-d-g)}{b\ (a+d+g)};$$

In[570]:=
$$diagFlineFf = \frac{(c+d+g)\ (-1+t)\ \left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+a\,g-b\,g+c\,g+d\,g+b\,g\,t\right)}{b\ (a+c+d+g-g\,t)^2};$$

In[571]:=
$$diagFlineFl = -\frac{(a+c\,t+d\,t)\ \left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+a\,g-b\,g+c\,g+d\,g+b\,g\,t\right)}{b\ (a+c+d+g-g\,t)^2};$$

In[572]:= $$\text{diagFlineLf} = -\frac{(c+d)\left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+c\,g+d\,g\right)}{b\,(a+c+d)^2};$$

In[573]:= $$\text{diagFlineLl} = \frac{a\left(a\,b-a\,c+b\,c-c^2-a\,d+b\,d-2\,c\,d-d^2-c\,g-d\,g\right)}{b\,(a+c+d)^2};$$

In[574]:= $$\text{diagFlineMf} = -\frac{(b-2\,c-d)\,(2\,c+d)\times(-1+t)}{b\,(a+2\,c+d)};$$

In[575]:= $$\text{diagFlineMl} = \frac{(b-2\,c-d)\,(a+2\,c\,t+d\,t)}{b\,(a+2\,c+d)};$$

In[544]:= (* And the overall equilibrium prevalence for each strain are *)

```
In[580]:= diagFlineSeq = (diagFlineSf + diagFlineSl);
In[581]:= diagFlineFeq = (diagFlineFf + diagFlineFl);
In[582]:= diagFlineLeq = (diagFlineLf + diagFlineLl);
In[584]:= diagFlineMeq = (diagFlineMf + diagFlineMl);
```

- **R0 under front-line diagnostic**

```
In[617]:= r0Sf = Factor[1 / (1 - diagFlineSeq )]
```

Out[617]= $$\frac{b}{d+g}$$

```
In[618]:= r0Ff = Factor[1 / (1 - diagFlineFeq )]
```

Out[618]= $$\frac{b\,(a+c+d+g-g\,t)}{(a+c+d)\,(c+d+g)}$$

```
In[619]:= r0Lf = Factor[1 / (1 - diagFlineLeq )]
```

Out[619]= $$\frac{b\,(a+c+d)}{(c+d)\,(a+c+d+g)}$$

```
In[620]:= r0Mf = Factor[1 / (1 - diagFlineMeq )]
```

Out[620]= $$\frac{b}{2\,c+d}$$

Last line diagnostic (V2)

- **Model equations**

```
(*ClearAll["Global`*"]*)

In[590]:= diagLlinedSfdt =
  (b (Sf + Sl)) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Sf (a + g + d);

In[591]:= diagLlinedSldt = a Sf - Sl (g + d);

In[592]:= diagLlinedFfdt = b (Ff + Fl) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Ff (a + d + c);

In[593]:= diagLlinedFldt = a Ff - Fl (g + d + c);
```

In[594]:=
```
diagLlinedLfdt =
  (b (Lf + Ll)) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Lf ((1 - t) a + g + d + c);
```

In[595]:=
```
diagLlinedLldt = (1 - t) a Lf - Ll (d + c);
```

In[596]:=
```
diagLlinedMfdt =
  b (Mf + Ml) (1 - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Mf ((1 - t) a + d + 2 c);
```

In[597]:=
```
diagLlinedMldt = (1 - t) a Mf - Ml (d + 2 c);
```

Determining equilibrium

```
(* Solving for equilibrium *)
```

In[598]:=
```
Solve[diagLlinedSfdt == 0 && diagLlinedSldt == 0 && diagLlinedFfdt == 0 &&
  diagLlinedFldt == 0 && diagLlinedLfdt == 0 && diagLlinedLldt == 0 &&
  diagLlinedMfdt == 0 && diagLlinedMldt == 0 , {Sf, Sl, Ff, Fl, Lf, Ll, Mf, Ml}]
```

Out[598]=

$$\left\{\{Sf \to 0, Sl \to 0, Ff \to 0, Fl \to 0, Lf \to 0, Ll \to 0, Mf \to 0, Ml \to 0\}, \left\{Sf \to \frac{(b-d-g)\ (d+g)}{b\ (a+d+g)},\right.\right.$$
$$\left. Sl \to \frac{a\ (b-d-g)}{b\ (a+d+g)}, Ff \to 0, Fl \to 0, Lf \to 0, Ll \to 0, Mf \to 0, Ml \to 0\right\}, \left\{Sf \to 0, Sl \to 0,\right.$$
$$Ff \to -\frac{(c+d+g)\ \left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+a\,g-b\,g+c\,g+d\,g\right)}{b\ (a+c+d+g)^2},$$
$$Fl \to \frac{a\ \left(a\,b-a\,c+b\,c-c^2-a\,d+b\,d-2\,c\,d-d^2-a\,g+b\,g-c\,g-d\,g\right)}{b\ (a+c+d+g)^2},$$
$$\left. Lf \to 0, Ll \to 0, Mf \to 0, Ml \to 0\right\},$$
$$\left\{Sf \to 0, Sl \to 0, Ff \to 0, Fl \to 0, Lf \to 0, Ll \to 0, Mf \to \frac{(b-2\,c-d)\ (2\,c+d)}{b\ (a+2\,c+d-a\,t)},\right.$$
$$\left. Ml \to \frac{a\ (b-2\,c-d)\ (-1+t)}{b\ (-a-2\,c-d+a\,t)}\right\}, \left\{Sf \to 0, Sl \to 0, Ff \to 0, Fl \to 0,\right.$$
$$Lf \to -\frac{(c+d)\ \left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+c\,g+d\,g+a\,b\,t-a\,c\,t-a\,d\,t\right)}{b\ (a+c+d-a\,t)^2},$$
$$Ll \to \frac{a\ (-1+t)\ \left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+c\,g+d\,g+a\,b\,t-a\,c\,t-a\,d\,t\right)}{b\ (-a-c-d+a\,t)^2},$$
$$\left.\left. Mf \to 0, Ml \to 0\right\}\right\}$$

(*So the equilibrium of each strain under each treatment is (only one strain will be present at equilibrium)*)

In[600]:=
$$diagLlineSf = \frac{(b-d-g)\ (d+g)}{b\ (a+d+g)};$$

In[601]:=
$$diagLlineSl = \frac{a\ (b-d-g)}{b\ (a+d+g)};$$

In[602]:=
$$diagLlineFf = -\frac{(c+d+g)\ \left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+a\,g-b\,g+c\,g+d\,g\right)}{b\ (a+c+d+g)^2};$$

In[603]:= diagLlineFl = $\frac{a\left(a\,b-a\,c+b\,c-c^2-a\,d+b\,d-2\,c\,d-d^2-a\,g+b\,g-c\,g-d\,g\right)}{b\,(a+c+d+g)^2}$;

In[604]:= diagLlineLf =
$-\frac{(c+d)\left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+c\,g+d\,g+a\,b\,t-a\,c\,t-a\,d\,t\right)}{b\,(a+c+d-a\,t)^2}$;

In[605]:= diagLlineLl =
$\frac{a\,(-1+t)\left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+c\,g+d\,g+a\,b\,t-a\,c\,t-a\,d\,t\right)}{b\,(-a-c-d+a\,t)^2}$;

In[606]:= diagLlineMf = $\frac{(b-2\,c-d)\,(2\,c+d)}{b\,(a+2\,c+d-a\,t)}$;

In[607]:= diagLlineMl = $\frac{a\,(b-2\,c-d)\,(-1+t)}{b\,(-a-2\,c-d+a\,t)}$;

```
(*And the overall equilibrium prevalence for each strain are*)
```

In[608]:= diagLlineSeq = (diagLlineSf + diagLlineSl);

In[609]:= diagLlineFeq = (diagLlineFf + diagLlineFl);

In[610]:= diagLlineLeq = (diagLlineLf + diagLlineLl);

In[611]:= diagLlineMeq = (diagLlineMf + diagLlineMl);

■ R0 under last-line diagnostic

In[621]:= r0Sl = Factor[1 / (1 - diagLlineSeq)]

Out[621]= $\frac{b}{d+g}$

In[622]:= r0Fl = Factor[1 / (1 - diagLlineFeq)]

Out[622]= $\frac{b\,(a+c+d+g)}{(a+c+d)\,(c+d+g)}$

In[623]:= r0Ll = Factor[1 / (1 - diagLlineLeq)]

Out[623]= $\frac{b\,(a+c+d-a\,t)}{(c+d)\,(a+c+d+g-a\,t)}$

In[624]:= r0Ml = Factor[1 / (1 - diagLlineMeq)]

Out[624]= $\frac{b}{2\,c+d}$

Public health analysis for Diagnostic

■ If F was the fittest strain before intervention

It follows the exact same logic as before:

The last-line intervention does not affect the fitness of the F strain (r0Fl = r0F), so under last-line intervention, that strain will remain the fittest.

The front-line intervention reduces the fitness of all strains or leave it equal (r0Xf <= r0X)
[Indeed, r0Ff has same denominator as r0F, but -gt is remove from its numerator, so it is r0Ff < r0F. For the other strains, the diagnostic has no effect]
Depending on exact parameter, different strain may become the fittest (another strain than F can become fittest under front-line intervention, leading to strain replacement at equilibrium). But regardless, since the fitness of all strains get reduced under the front -line intervention, and F was the fittest before intervention, it necessarily follows that any strain selected under front-line will be of lower fitness than the strain selected under de last-line intervention, which is the front-line resistant one.

- **If M was the fittest strain before intervention**

Here the diagnostic simply bring no benefit on its on. Indeed, the diagnostic has no effect on the fitness of the M strain, r0M = r0Ml = r0Mf = $\frac{b}{2\,c+d}$
Hence, this M strain will remain the fittest (cannot be replaced by another strain) and front-line or last-line diagnostics makes no difference.

New drug (with “efficacy” parameter)

Notations:
Notations are as before, but we add the prefix: new for “new drug”, and then Fline or Lline for front-line intervention of last-line intervention

Note about the t parameter:
The parameter t is simply a rate of usage of that new drug, in order to have a measure of efficacy as we can have for the adjuvant (parameter e)
If t = 1, then people are always stick to using this new drug in the pipeline, and that simplifies to the model we used for the submitted paper
If 0<t<1, then some GP use that new drug but some other don’t (e.g. that new drug is not available to everyone, or not known by all GPs)

This is just to allow having a plot that mirrors what we get for the adjuvant model, where we see how the R0 change with the efficacy of the intervention. It’s an easier plot to visualise the difference between the original R0 (at x-axis = 0) and the new R0 (intervention efficacy/implementation rate is non-zero), and also to illustrate how the intervention can lead to strain replacement when they are efficient enough.

Front-line new drug

- **Model equations**

```
In[663]:= ClearAll["Global`*"]

In[664]:= newFlinedSndt = t * (b (Sn + Sf + Sl))
              (1 - Sn - Fn - Ln - Mn - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Sn (a + g + d);
```

```
In[665]:= newFlinedSfdt =
    (1 - t) * (b (Sn + Sf + Sl)) (1 - Sn - Fn - Ln - Mn - Sf - Ff - Lf - Mf - Sl -
       Fl - Ll - Ml) + a Sn - Sf (a + g + d);

In[666]:= newFlinedSldt = a Sf - Sl (g + d);

In[667]:= newFlinedFndt = t * (b (Fn + Ff + Fl))
      (1 - Sn - Fn - Ln - Mn - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Fn (a + g + d + c);

In[668]:= newFlinedFfdt =
    (1 - t) * (b (Fn + Ff + Fl)) (1 - Sn - Fn - Ln - Mn - Sf - Ff - Lf - Mf - Sl -
       Fl - Ll - Ml) + a Fn - Ff (a + d + c);

In[669]:= newFlinedFldt =  a Ff - Fl (g + d + c);

In[670]:= newFlinedLndt = t * (b (Ln + Lf + Ll))
      (1 - Sn - Fn - Ln - Mn - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Ln (a + g + d + c);

In[671]:= newFlinedLfdt =
    (1 - t) * (b (Ln + Lf + Ll)) (1 - Sn - Fn - Ln - Mn - Sf - Ff - Lf - Mf - Sl -
       Fl - Ll - Ml) + a Ln - Lf (a + g + d + c);

In[672]:= newFlinedLldt = a Lf - Ll (d + c);

In[673]:= newFlinedMndt =
    t * (b (Mn + Mf + Ml)) (1 - Sn - Fn - Ln - Mn - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) -
     Mn (a + g + d + 2 c);

In[674]:= newFlinedMfdt =
    (1 - t) * (b (Mn + Mf + Ml)) (1 - Sn - Fn - Ln - Mn - Sf - Ff - Lf - Mf - Sl -
       Fl - Ll - Ml) + a Mn - Mf (a + d + 2 c);

In[675]:= newFlinedMldt = a Mf - Ml (d + 2 c);
```

■ Determining equilibrium

```
(* Solving for equilibrium *)

In[676]:= Solve[newFlinedSndt == 0 && newFlinedSfdt == 0 && newFlinedSldt == 0 &&
    newFlinedFndt == 0 && newFlinedFfdt == 0 && newFlinedFldt == 0 &&
    newFlinedLndt == 0 && newFlinedLfdt == 0 && newFlinedLldt == 0 &&
    newFlinedMndt == 0 && newFlinedMfdt == 0 && newFlinedMldt == 0,
   {Sn, Sf, Sl, Fn, Ff, Fl, Ln, Lf, Ll, Mn, Mf, Ml}]
```

Out[676]=

$$\Big\{\{Sn\to 0,\ Sf\to 0,\ Sl\to 0,\ Fn\to 0,\ Ff\to 0,\ Fl\to 0,\ Ln\to 0,\ Lf\to 0,\ Ll\to 0,\ Mn\to 0,\ Mf\to 0,\ Ml\to 0\},\ \Big\{Sn\to \frac{(b-d-g)\ (d+g)\ t}{b\ (a+d+g)},\ Sf\to \frac{1}{-a-d-g}$$

$$\left(-\frac{a\,d}{a+d+g}-\frac{d^2}{a+d+g}+\frac{a\,d^2}{b\ (a+d+g)}+\frac{d^3}{b\ (a+d+g)}-\frac{a\,g}{a+d+g}-\frac{2\,d\,g}{a+d+g}+\frac{2\,a\,d\,g}{b\ (a+d+g)}+\frac{3\,d^2\,g}{b\ (a+d+g)}-\frac{g^2}{a+d+g}+\frac{a\,g^2}{b\ (a+d+g)}+\frac{3\,d\,g^2}{b\ (a+d+g)}+\frac{g^3}{b\ (a+d+g)}+\frac{d^2\,t}{a+d+g}-\frac{d^3\,t}{b\ (a+d+g)}+\frac{2\,d\,g\,t}{a+d+g}-\frac{3\,d^2\,g\,t}{b\ (a+d+g)}+\frac{g^2\,t}{a+d+g}-\frac{3\,d\,g^2\,t}{b\ (a+d+g)}-\frac{g^3\,t}{b\ (a+d+g)}\right),$$

$$\mathrm{Sl}\to \frac{1}{-a\,d-d^2-a\,g-2\,d\,g-g^2}\left(-\frac{a^2\,d}{a+d+g}-\frac{a\,d^2}{a+d+g}+\frac{a^2\,d^2}{b\,(a+d+g)}+\frac{a\,d^3}{b\,(a+d+g)}-\frac{a^2\,g}{a+d+g}-\frac{2\,a\,d\,g}{a+d+g}+\frac{2\,a^2\,d\,g}{b\,(a+d+g)}+\frac{3\,a\,d^2\,g}{b\,(a+d+g)}-\frac{a\,g^2}{a+d+g}+\frac{a^2\,g^2}{b\,(a+d+g)}+\frac{3\,a\,d\,g^2}{b\,(a+d+g)}+\frac{a\,g^3}{b\,(a+d+g)}+\frac{a\,d^2\,t}{a+d+g}-\frac{a\,d^3\,t}{b\,(a+d+g)}+\frac{2\,a\,d\,g\,t}{a+d+g}-\frac{3\,a\,d^2\,g\,t}{b\,(a+d+g)}+\frac{a\,g^2\,t}{a+d+g}-\frac{3\,a\,d\,g^2\,t}{b\,(a+d+g)}-\frac{a\,g^3\,t}{b\,(a+d+g)}\right),$$

$$\mathrm{Fn}\to 0,\ \mathrm{Ff}\to 0,\ \mathrm{Fl}\to 0,\ \mathrm{Ln}\to 0,\ \mathrm{Lf}\to 0,\ \mathrm{Ll}\to 0,\ \mathrm{Mn}\to 0,\ \mathrm{Mf}\to 0,\ \mathrm{Ml}\to 0\Big\},$$

$$\Big\{\mathrm{Sn}\to 0,\ \mathrm{Sf}\to 0,\ \mathrm{Sl}\to 0,\ \mathrm{Fn}\to 0,\ \mathrm{Ff}\to 0,\ \mathrm{Fl}\to 0,\ \mathrm{Ln}\to 0,\ \mathrm{Lf}\to 0,\ \mathrm{Ll}\to 0,$$

$$\mathrm{Mn}\to -\frac{(2\,c+d)\,t\,\left(-a\,b+2\,a\,c-2\,b\,c+4\,c^2+a\,d-b\,d+4\,c\,d+d^2-b\,g+2\,c\,g+d\,g+b\,g\,t\right)}{b\,(a+2\,c+d+g-g\,t)^2},$$

$$\mathrm{Mf}\to \Big((2\,c+d)\,(a+2\,c+d+g-2\,c\,t-d\,t-g\,t)\,\left(a\,b-2\,a\,c+2\,b\,c-4\,c^2-a\,d+b\,d-4\,c\,d-d^2+b\,g-2\,c\,g-d\,g-b\,g\,t\right)\Big)\Big/\Big(a^3\,b+6\,a^2\,b\,c+12\,a\,b\,c^2+8\,b\,c^3+3\,a^2\,b\,d+12\,a\,b\,c\,d+12\,b\,c^2\,d+3\,a\,b\,d^2+6\,b\,c\,d^2+b\,d^3+2\,a^2\,b\,g+8\,a\,b\,c\,g+8\,b\,c^2\,g+4\,a\,b\,d\,g+8\,b\,c\,d\,g+2\,b\,d^2\,g+a\,b\,g^2+2\,b\,c\,g^2+b\,d\,g^2-2\,a^2\,b\,g\,t-8\,a\,b\,c\,g\,t-8\,b\,c^2\,g\,t-4\,a\,b\,d\,g\,t-8\,b\,c\,d\,g\,t-2\,b\,d^2\,g\,t-2\,a\,b\,g^2\,t-4\,b\,c\,g^2\,t-2\,b\,d\,g^2\,t+a\,b\,g^2\,t^2+2\,b\,c\,g^2\,t^2+b\,d\,g^2\,t^2\Big),$$

$$\mathrm{Ml}\to -\Big(\Big(a\,(a+2\,c+d+g-2\,c\,t-d\,t-g\,t)\,\left(-a\,b+2\,a\,c-2\,b\,c+4\,c^2+a\,d-b\,d+4\,c\,d+d^2-b\,g+2\,c\,g+d\,g+b\,g\,t\right)\Big)\Big/\Big(b\,(a+2\,c+d)\,(a+2\,c+d+g-g\,t)^2\Big)\Big)\Big\},$$

$$\Big\{\mathrm{Sn}\to 0,\ \mathrm{Sf}\to 0,\ \mathrm{Sl}\to 0,\ \mathrm{Fn}\to 0,\ \mathrm{Ff}\to 0,\ \mathrm{Fl}\to 0,\ \mathrm{Ln}\to$$

$$\Big((c+d)\,(a+c+d+g)\,t\,\left(a^2\,b-a^2\,c+2\,a\,b\,c-2\,a\,c^2+b\,c^2-c^3-a^2\,d+2\,a\,b\,d-4\,a\,c\,d+2\,b\,c\,d-3\,c^2\,d-2\,a\,d^2+b\,d^2-3\,c\,d^2-d^3+a\,b\,g-2\,a\,c\,g+b\,c\,g-2\,c^2\,g-2\,a\,d\,g+b\,d\,g-4\,c\,d\,g-2\,d^2\,g-c\,g^2-d\,g^2-a\,b\,g\,t\right)\Big)\Big/\Big(a^4\,b+4\,a^3\,b\,c+6\,a^2\,b\,c^2+4\,a\,b\,c^3+b\,c^4+4\,a^3\,b\,d+12\,a^2\,b\,c\,d+12\,a\,b\,c^2\,d+4\,b\,c^3\,d+6\,a^2\,b\,d^2+12\,a\,b\,c\,d^2+6\,b\,c^2\,d^2+4\,a\,b\,d^3+4\,b\,c\,d^3+b\,d^4+2\,a^3\,b\,g+6\,a^2\,b\,c\,g+6\,a\,b\,c^2\,g+2\,b\,c^3\,g+6\,a^2\,b\,d\,g+12\,a\,b\,c\,d\,g+6\,b\,c^2\,d\,g+6\,a\,b\,d^2\,g+6\,b\,c\,d^2\,g+2\,b\,d^3\,g+a^2\,b\,g^2+2\,a\,b\,c\,g^2+b\,c^2\,g^2+2\,a\,b\,d\,g^2+2\,b\,c\,d\,g^2+b\,d^2\,g^2-2\,a^3\,b\,g\,t-4\,a^2\,b\,c\,g\,t-2\,a\,b\,c^2\,g\,t-4\,a^2\,b\,d\,g\,t-4\,a\,b\,c\,d\,g\,t-2\,a\,b\,d^2\,g\,t-2\,a^2\,b\,g^2\,t-2\,a\,b\,c\,g^2\,t-2\,a\,b\,d\,g^2\,t+a^2\,b\,g^2\,t^2\Big),$$

$$\mathrm{Lf}\to \Big((c+d)\,(a+c+d+g-c\,t-d\,t-g\,t)\,\left(a^2\,b-a^2\,c+2\,a\,b\,c-2\,a\,c^2+b\,c^2-c^3-a^2\,d+2\,a\,b\,d-4\,a\,c\,d+2\,b\,c\,d-3\,c^2\,d-2\,a\,d^2+b\,d^2-3\,c\,d^2-d^3+a\,b\,g-2\,a\,c\,g+b\,c\,g-2\,c^2\,g-2\,a\,d\,g+b\,d\,g-4\,c\,d\,g-2\,d^2\,g-c\,g^2-d\,g^2-a\,b\,g\,t\right)\Big)\Big/\Big(a^4\,b+4\,a^3\,b\,c+6\,a^2\,b\,c^2+4\,a\,b\,c^3+b\,c^4+4\,a^3\,b\,d+12\,a^2\,b\,c\,d+12\,a\,b\,c^2\,d+4\,b\,c^3\,d+6\,a^2\,b\,d^2+12\,a\,b\,c\,d^2+6\,b\,c^2\,d^2+4\,a\,b\,d^3+4\,b\,c\,d^3+b\,d^4+2\,a^3\,b\,g+6\,a^2\,b\,c\,g+6\,a\,b\,c^2\,g+2\,b\,c^3\,g+6\,a^2\,b\,d\,g+12\,a\,b\,c\,d\,g+6\,b\,c^2\,d\,g+6\,a\,b\,d^2\,g+6\,b\,c\,d^2\,g+2\,b\,d^3\,g+a^2\,b\,g^2+2\,a\,b\,c\,g^2+b\,c^2\,g^2+2\,a\,b\,d\,g^2+2\,b\,c\,d\,g^2+b\,d^2\,g^2-2\,a^3\,b\,g\,t-4\,a^2\,b\,c\,g\,t-2\,a\,b\,c^2\,g\,t-4\,a^2\,b\,d\,g\,t-4\,a\,b\,c\,d\,g\,t-2\,a\,b\,d^2\,g\,t-2\,a^2\,b\,g^2\,t-2\,a\,b\,c\,g^2\,t-2\,a\,b\,d\,g^2\,t+a^2\,b\,g^2\,t^2\Big),$$

$$\mathrm{Ll}\to \Big(a\,(a+c+d+g-c\,t-d\,t-g\,t)\,\left(a^2\,b-a^2\,c+2\,a\,b\,c-2\,a\,c^2+b\,c^2-c^3-a^2\,d+2\,a\,b\,d-4\,a\,c\,d+2\,b\,c\,d-3\,c^2\,d-2\,a\,d^2+b\,d^2-3\,c\,d^2-d^3+a\,b\,g-2\,a\,c\,g+b\,c\,g-2\,c^2\,g-2\,a\,d\,g+b\,d\,g-4\,c\,d\,g-2\,d^2\,g-c\,g^2-d\,g^2-a\,b\,g\,t\right)\Big)\Big/$$

$$\left(a^4 b+4 a^3 b c+6 a^2 b c^2+4 a b c^3+b c^4+4 a^3 b d+12 a^2 b c d+12 a b c^2 d+\right.$$
$$4 b c^3 d+6 a^2 b d^2+12 a b c d^2+6 b c^2 d^2+4 a b d^3+4 b c d^3+b d^4+$$
$$2 a^3 b g+6 a^2 b c g+6 a b c^2 g+2 b c^3 g+6 a^2 b d g+12 a b c d g+6 b c^2 d g+$$
$$6 a b d^2 g+6 b c d^2 g+2 b d^3 g+a^2 b g^2+2 a b c g^2+b c^2 g^2+2 a b d g^2+$$
$$2 b c d g^2+b d^2 g^2-2 a^3 b g t-4 a^2 b c g t-2 a b c^2 g t-4 a^2 b d g t-$$
$$\left.4 a b c d g t-2 a b d^2 g t-2 a^2 b g^2 t-2 a b c g^2 t-2 a b d g^2 t+a^2 b g^2 t^2\right),$$
$$\mathrm{Mn}\to 0,\ \mathrm{Mf}\to 0,\ \mathrm{Ml}\to 0\},\ \{\mathrm{Sn}\to 0,\ \mathrm{Sf}\to 0,\ \mathrm{Sl}\to 0,$$
$$\mathrm{Fn}\to\left((a+c+d)\,(c+d+g)\,t\,\left(a^2 b-a^2 c+2 a b c-2 a c^2+b c^2-c^3-a^2 d+2 a b d-4 a c d+\right.\right.$$
$$2 b c d-3 c^2 d-2 a d^2+b d^2-3 c d^2-d^3-a^2 g+2 a b g-3 a c g+2 b c g-2 c^2 g-$$
$$\left.\left.3 a d g+2 b d g-4 c d g-2 d^2 g-a g^2+b g^2-c g^2-d g^2-b c g t-b d g t-b g^2 t\right)\right)\Big/$$
$$\left(a^4 b+4 a^3 b c+6 a^2 b c^2+4 a b c^3+b c^4+4 a^3 b d+12 a^2 b c d+12 a b c^2 d+\right.$$
$$4 b c^3 d+6 a^2 b d^2+12 a b c d^2+6 b c^2 d^2+4 a b d^3+4 b c d^3+b d^4+4 a^3 b g+$$
$$12 a^2 b c g+12 a b c^2 g+4 b c^3 g+12 a^2 b d g+24 a b c d g+12 b c^2 d g+$$
$$12 a b d^2 g+12 b c d^2 g+4 b d^3 g+6 a^2 b g^2+12 a b c g^2+6 b c^2 g^2+12 a b d g^2+$$
$$12 b c d g^2+6 b d^2 g^2+4 a b g^3+4 b c g^3+4 b d g^3+b g^4-2 a^2 b c g t-$$
$$4 a b c^2 g t-2 b c^3 g t-2 a^2 b d g t-8 a b c d g t-6 b c^2 d g t-4 a b d^2 g t-$$
$$6 b c d^2 g t-2 b d^3 g t-2 a^2 b g^2 t-8 a b c g^2 t-6 b c^2 g^2 t-8 a b d g^2 t-$$
$$12 b c d g^2 t-6 b d^2 g^2 t-4 a b g^3 t-6 b c g^3 t-6 b d g^3 t-2 b g^4 t+$$
$$\left.b c^2 g^2 t^2+2 b c d g^2 t^2+b d^2 g^2 t^2+2 b c g^3 t^2+2 b d g^3 t^2+b g^4 t^2\right),$$
$$\mathrm{Ff}\to\left((c+d+g)\,(a+c+d+g-c t-d t-g t)\right.$$
$$\left(a^2 b-a^2 c+2 a b c-2 a c^2+b c^2-c^3-a^2 d+2 a b d-4 a c d+2 b c d-3 c^2 d-\right.$$
$$2 a d^2+b d^2-3 c d^2-d^3-a^2 g+2 a b g-3 a c g+2 b c g-2 c^2 g-3 a d g+$$
$$\left.\left.2 b d g-4 c d g-2 d^2 g-a g^2+b g^2-c g^2-d g^2-b c g t-b d g t-b g^2 t\right)\right)\Big/$$
$$\left(a^4 b+4 a^3 b c+6 a^2 b c^2+4 a b c^3+b c^4+4 a^3 b d+12 a^2 b c d+12 a b c^2 d+\right.$$
$$4 b c^3 d+6 a^2 b d^2+12 a b c d^2+6 b c^2 d^2+4 a b d^3+4 b c d^3+b d^4+4 a^3 b g+$$
$$12 a^2 b c g+12 a b c^2 g+4 b c^3 g+12 a^2 b d g+24 a b c d g+12 b c^2 d g+$$
$$12 a b d^2 g+12 b c d^2 g+4 b d^3 g+6 a^2 b g^2+12 a b c g^2+6 b c^2 g^2+12 a b d g^2+$$
$$12 b c d g^2+6 b d^2 g^2+4 a b g^3+4 b c g^3+4 b d g^3+b g^4-2 a^2 b c g t-$$
$$4 a b c^2 g t-2 b c^3 g t-2 a^2 b d g t-8 a b c d g t-6 b c^2 d g t-4 a b d^2 g t-$$
$$6 b c d^2 g t-2 b d^3 g t-2 a^2 b g^2 t-8 a b c g^2 t-6 b c^2 g^2 t-8 a b d g^2 t-$$
$$12 b c d g^2 t-6 b d^2 g^2 t-4 a b g^3 t-6 b c g^3 t-6 b d g^3 t-2 b g^4 t+$$
$$\left.b c^2 g^2 t^2+2 b c d g^2 t^2+b d^2 g^2 t^2+2 b c g^3 t^2+2 b d g^3 t^2+b g^4 t^2\right),\ \mathrm{Fl}\to$$
$$\left(a\,(a+c+d+g-c t-d t-g t)\,\left(a^2 b-a^2 c+2 a b c-2 a c^2+b c^2-c^3-a^2 d+2 a b d-4 a c\right.\right.$$
$$d+2 b c d-3 c^2 d-2 a d^2+b d^2-3 c d^2-d^3-a^2 g+2 a b g-3 a c g+2 b c g-2 c^2 g-$$
$$\left.\left.3 a d g+2 b d g-4 c d g-2 d^2 g-a g^2+b g^2-c g^2-d g^2-b c g t-b d g t-b g^2 t\right)\right)\Big/$$
$$\left(a^4 b+4 a^3 b c+6 a^2 b c^2+4 a b c^3+b c^4+4 a^3 b d+12 a^2 b c d+12 a b c^2 d+\right.$$
$$4 b c^3 d+6 a^2 b d^2+12 a b c d^2+6 b c^2 d^2+4 a b d^3+4 b c d^3+b d^4+4 a^3 b g+$$
$$12 a^2 b c g+12 a b c^2 g+4 b c^3 g+12 a^2 b d g+24 a b c d g+12 b c^2 d g+$$
$$12 a b d^2 g+12 b c d^2 g+4 b d^3 g+6 a^2 b g^2+12 a b c g^2+6 b c^2 g^2+12 a b d g^2+$$
$$12 b c d g^2+6 b d^2 g^2+4 a b g^3+4 b c g^3+4 b d g^3+b g^4-2 a^2 b c g t-$$
$$4 a b c^2 g t-2 b c^3 g t-2 a^2 b d g t-8 a b c d g t-6 b c^2 d g t-4 a b d^2 g t-$$
$$6 b c d^2 g t-2 b d^3 g t-2 a^2 b g^2 t-8 a b c g^2 t-6 b c^2 g^2 t-8 a b d g^2 t-$$
$$12 b c d g^2 t-6 b d^2 g^2 t-4 a b g^3 t-6 b c g^3 t-6 b d g^3 t-2 b g^4 t+$$
$$\left.b c^2 g^2 t^2+2 b c d g^2 t^2+b d^2 g^2 t^2+2 b c g^3 t^2+2 b d g^3 t^2+b g^4 t^2\right),$$
$$\mathrm{Ln}\to 0,\ \mathrm{Lf}\to 0,\ \mathrm{Ll}\to 0,\ \mathrm{Mn}\to 0,\ \mathrm{Mf}\to 0,$$

```
Ml → 0}}
```

(* So the equilibrium of each strain under each treatment is (only one strain will be present at equilibrium) *)

In[677]:= $$\text{newFlineSn} = \frac{(b-d-g)\,(d+g)\,t}{b\,(a+d+g)};$$

In[678]:= $$\text{newFlineSf} = \frac{1}{-a-d-g}\left(-\frac{a\,d}{a+d+g}-\frac{d^2}{a+d+g}+\frac{a\,d^2}{b\,(a+d+g)}+\frac{d^3}{b\,(a+d+g)}-\frac{a\,g}{a+d+g}-\frac{2\,d\,g}{a+d+g}+\frac{2\,a\,d\,g}{b\,(a+d+g)}+\frac{3\,d^2\,g}{b\,(a+d+g)}-\frac{g^2}{a+d+g}+\frac{a\,g^2}{b\,(a+d+g)}+\frac{3\,d\,g^2}{b\,(a+d+g)}+\frac{g^3}{b\,(a+d+g)}+\frac{d^2\,t}{a+d+g}-\frac{d^3\,t}{b\,(a+d+g)}+\frac{2\,d\,g\,t}{a+d+g}-\frac{3\,d^2\,g\,t}{b\,(a+d+g)}+\frac{g^2\,t}{a+d+g}-\frac{3\,d\,g^2\,t}{b\,(a+d+g)}-\frac{g^3\,t}{b\,(a+d+g)}\right);$$

In[679]:= $$\text{newFlineSl} = \frac{1}{-a\,d-d^2-a\,g-2\,d\,g-g^2}\left(-\frac{a^2\,d}{a+d+g}-\frac{a\,d^2}{a+d+g}+\frac{a^2\,d^2}{b\,(a+d+g)}+\frac{a\,d^3}{b\,(a+d+g)}-\frac{a^2\,g}{a+d+g}-\frac{2\,a\,d\,g}{a+d+g}+\frac{2\,a^2\,d\,g}{b\,(a+d+g)}+\frac{3\,a\,d^2\,g}{b\,(a+d+g)}-\frac{a\,g^2}{a+d+g}+\frac{a^2\,g^2}{b\,(a+d+g)}+\frac{3\,a\,d\,g^2}{b\,(a+d+g)}+\frac{a\,g^3}{b\,(a+d+g)}+\frac{a\,d^2\,t}{a+d+g}-\frac{a\,d^3\,t}{b\,(a+d+g)}+\frac{2\,a\,d\,g\,t}{a+d+g}-\frac{3\,a\,d^2\,g\,t}{b\,(a+d+g)}+\frac{a\,g^2\,t}{a+d+g}-\frac{3\,a\,d\,g^2\,t}{b\,(a+d+g)}-\frac{a\,g^3\,t}{b\,(a+d+g)}\right);$$

In[680]:= $$\text{newFlineFn} = \Big((a+c+d)\,(c+d+g)\,t\,\big(a^2\,b-a^2\,c+2\,a\,b\,c-2\,a\,c^2+b\,c^2-c^3-a^2\,d+2\,a\,b\,d-4\,a\,c\,d+2\,b\,c\,d-3\,c^2\,d-2\,a\,d^2+b\,d^2-3\,c\,d^2-d^3-a^2\,g+2\,a\,b\,g-3\,a\,c\,g+2\,b\,c\,g-2\,c^2\,g-3\,a\,d\,g+2\,b\,d\,g-4\,c\,d\,g-2\,d^2\,g-a\,g^2+b\,g^2-c\,g^2-d\,g^2-b\,c\,g\,t-b\,d\,g\,t-b\,g^2\,t\big)\Big)\,/\,\big(a^4\,b+4\,a^3\,b\,c+6\,a^2\,b\,c^2+4\,a\,b\,c^3+b\,c^4+4\,a^3\,b\,d+12\,a^2\,b\,c\,d+12\,a\,b\,c^2\,d+4\,b\,c^3\,d+6\,a^2\,b\,d^2+12\,a\,b\,c\,d^2+6\,b\,c^2\,d^2+4\,a\,b\,d^3+4\,b\,c\,d^3+b\,d^4+4\,a^3\,b\,g+12\,a^2\,b\,c\,g+12\,a\,b\,c^2\,g+4\,b\,c^3\,g+12\,a^2\,b\,d\,g+24\,a\,b\,c\,d\,g+12\,b\,c^2\,d\,g+12\,a\,b\,d^2\,g+12\,b\,c\,d^2\,g+4\,b\,d^3\,g+6\,a^2\,b\,g^2+12\,a\,b\,c\,g^2+6\,b\,c^2\,g^2+12\,a\,b\,d\,g^2+12\,b\,c\,d\,g^2+6\,b\,d^2\,g^2+4\,a\,b\,g^3+4\,b\,c\,g^3+4\,b\,d\,g^3+b\,g^4-2\,a^2\,b\,c\,g\,t-4\,a\,b\,c^2\,g\,t-2\,b\,c^3\,g\,t-2\,a^2\,b\,d\,g\,t-8\,a\,b\,c\,d\,g\,t-6\,b\,c^2\,d\,g\,t-4\,a\,b\,d^2\,g\,t-6\,b\,c\,d^2\,g\,t-2\,b\,d^3\,g\,t-2\,a^2\,b\,g^2\,t-8\,a\,b\,c\,g^2\,t-6\,b\,c^2\,g^2\,t-8\,a\,b\,d\,g^2\,t-12\,b\,c\,d\,g^2\,t-6\,b\,d^2\,g^2\,t-4\,a\,b\,g^3\,t-6\,b\,c\,g^3\,t-6\,b\,d\,g^3\,t-2\,b\,g^4\,t+b\,c^2\,g^2\,t^2+2\,b\,c\,d\,g^2\,t^2+b\,d^2\,g^2\,t^2+2\,b\,c\,g^3\,t^2+2\,b\,d\,g^3\,t^2+b\,g^4\,t^2\big);$$

In[681]:=
```
newFlineFf = ((c + d + g) (a + c + d + g - c t - d t - g t)
      (a^2 b - a^2 c + 2 a b c - 2 a c^2 + b c^2 - c^3 - a^2 d + 2 a b d - 4 a c d + 2 b c d - 3 c^2 d -
        2 a d^2 + b d^2 - 3 c d^2 - d^3 - a^2 g + 2 a b g - 3 a c g + 2 b c g - 2 c^2 g - 3 a d g +
        2 b d g - 4 c d g - 2 d^2 g - a g^2 + b g^2 - c g^2 - d g^2 - b c g t - b d g t - b g^2 t)) /
    (a^4 b + 4 a^3 b c + 6 a^2 b c^2 + 4 a b c^3 + b c^4 + 4 a^3 b d + 12 a^2 b c d + 12 a b c^2 d +
      4 b c^3 d + 6 a^2 b d^2 + 12 a b c d^2 + 6 b c^2 d^2 + 4 a b d^3 + 4 b c d^3 + b d^4 + 4 a^3 b g + 12 a^2 b c g +
      12 a b c^2 g + 4 b c^3 g + 12 a^2 b d g + 24 a b c d g + 12 b c^2 d g + 12 a b d^2 g + 12 b c d^2 g +
      4 b d^3 g + 6 a^2 b g^2 + 12 a b c g^2 + 6 b c^2 g^2 + 12 a b d g^2 + 12 b c d g^2 + 6 b d^2 g^2 +
      4 a b g^3 + 4 b c g^3 + 4 b d g^3 + b g^4 - 2 a^2 b c g t - 4 a b c^2 g t - 2 b c^3 g t - 2 a^2 b d g t -
      8 a b c d g t - 6 b c^2 d g t - 4 a b d^2 g t - 6 b c d^2 g t - 2 b d^3 g t - 2 a^2 b g^2 t - 8 a b c g^2 t -
      6 b c^2 g^2 t - 8 a b d g^2 t - 12 b c d g^2 t - 6 b d^2 g^2 t - 4 a b g^3 t - 6 b c g^3 t - 6 b d g^3 t -
      2 b g^4 t + b c^2 g^2 t^2 + 2 b c d g^2 t^2 + b d^2 g^2 t^2 + 2 b c g^3 t^2 + 2 b d g^3 t^2 + b g^4 t^2);
```

In[682]:=
```
newFlineFl =
   (a (a + c + d + g - c t - d t - g t) (a^2 b - a^2 c + 2 a b c - 2 a c^2 + b c^2 - c^3 - a^2 d + 2 a b d - 4 a c
          d + 2 b c d - 3 c^2 d - 2 a d^2 + b d^2 - 3 c d^2 - d^3 - a^2 g + 2 a b g - 3 a c g + 2 b c g - 2 c^2 g -
        3 a d g + 2 b d g - 4 c d g - 2 d^2 g - a g^2 + b g^2 - c g^2 - d g^2 - b c g t - b d g t - b g^2 t)) /
    (a^4 b + 4 a^3 b c + 6 a^2 b c^2 + 4 a b c^3 + b c^4 + 4 a^3 b d + 12 a^2 b c d + 12 a b c^2 d +
      4 b c^3 d + 6 a^2 b d^2 + 12 a b c d^2 + 6 b c^2 d^2 + 4 a b d^3 + 4 b c d^3 + b d^4 + 4 a^3 b g + 12 a^2 b c g +
      12 a b c^2 g + 4 b c^3 g + 12 a^2 b d g + 24 a b c d g + 12 b c^2 d g + 12 a b d^2 g + 12 b c d^2 g +
      4 b d^3 g + 6 a^2 b g^2 + 12 a b c g^2 + 6 b c^2 g^2 + 12 a b d g^2 + 12 b c d g^2 + 6 b d^2 g^2 +
      4 a b g^3 + 4 b c g^3 + 4 b d g^3 + b g^4 - 2 a^2 b c g t - 4 a b c^2 g t - 2 b c^3 g t - 2 a^2 b d g t -
      8 a b c d g t - 6 b c^2 d g t - 4 a b d^2 g t - 6 b c d^2 g t - 2 b d^3 g t - 2 a^2 b g^2 t - 8 a b c g^2 t -
      6 b c^2 g^2 t - 8 a b d g^2 t - 12 b c d g^2 t - 6 b d^2 g^2 t - 4 a b g^3 t - 6 b c g^3 t - 6 b d g^3 t -
      2 b g^4 t + b c^2 g^2 t^2 + 2 b c d g^2 t^2 + b d^2 g^2 t^2 + 2 b c g^3 t^2 + 2 b d g^3 t^2 + b g^4 t^2);
```

In[685]:=
```
newFlineLn =
   ((c + d) (a + c + d + g) t (a^2 b - a^2 c + 2 a b c - 2 a c^2 + b c^2 - c^3 - a^2 d + 2 a b d - 4 a c d +
        2 b c d - 3 c^2 d - 2 a d^2 + b d^2 - 3 c d^2 - d^3 + a b g - 2 a c g + b c g -
        2 c^2 g - 2 a d g + b d g - 4 c d g - 2 d^2 g - c g^2 - d g^2 - a b g t)) /
    (a^4 b + 4 a^3 b c + 6 a^2 b c^2 + 4 a b c^3 + b c^4 + 4 a^3 b d + 12 a^2 b c d + 12 a b c^2 d + 4 b c^3 d +
      6 a^2 b d^2 + 12 a b c d^2 + 6 b c^2 d^2 + 4 a b d^3 + 4 b c d^3 + b d^4 + 2 a^3 b g + 6 a^2 b c g + 6 a b c^2 g +
      2 b c^3 g + 6 a^2 b d g + 12 a b c d g + 6 b c^2 d g + 6 a b d^2 g + 6 b c d^2 g + 2 b d^3 g + a^2 b g^2 +
      2 a b c g^2 + b c^2 g^2 + 2 a b d g^2 + 2 b c d g^2 + b d^2 g^2 - 2 a^3 b g t - 4 a^2 b c g t - 2 a b c^2 g t -
      4 a^2 b d g t - 4 a b c d g t - 2 a b d^2 g t - 2 a^2 b g^2 t - 2 a b c g^2 t - 2 a b d g^2 t + a^2 b g^2 t^2);
```

In[687]:=
```
newFlineLf =
   ((c + d) (a + c + d + g - c t - d t - g t) (a^2 b - a^2 c + 2 a b c - 2 a c^2 + b c^2 - c^3 - a^2 d +
        2 a b d - 4 a c d + 2 b c d - 3 c^2 d - 2 a d^2 + b d^2 - 3 c d^2 - d^3 + a b g - 2 a c g +
        b c g - 2 c^2 g - 2 a d g + b d g - 4 c d g - 2 d^2 g - c g^2 - d g^2 - a b g t)) /
    (a^4 b + 4 a^3 b c + 6 a^2 b c^2 + 4 a b c^3 + b c^4 + 4 a^3 b d + 12 a^2 b c d + 12 a b c^2 d + 4 b c^3 d +
      6 a^2 b d^2 + 12 a b c d^2 + 6 b c^2 d^2 + 4 a b d^3 + 4 b c d^3 + b d^4 + 2 a^3 b g + 6 a^2 b c g + 6 a b c^2 g +
      2 b c^3 g + 6 a^2 b d g + 12 a b c d g + 6 b c^2 d g + 6 a b d^2 g + 6 b c d^2 g + 2 b d^3 g + a^2 b g^2 +
      2 a b c g^2 + b c^2 g^2 + 2 a b d g^2 + 2 b c d g^2 + b d^2 g^2 - 2 a^3 b g t - 4 a^2 b c g t - 2 a b c^2 g t -
      4 a^2 b d g t - 4 a b c d g t - 2 a b d^2 g t - 2 a^2 b g^2 t - 2 a b c g^2 t - 2 a b d g^2 t + a^2 b g^2 t^2);
```

In[686]:=
```
newFlineLl =
  (a (a + c + d + g - c t - d t - g t) (a^2 b - a^2 c + 2 a b c - 2 a c^2 + b c^2 - c^3 - a^2 d + 2 a b d -
       4 a c d + 2 b c d - 3 c^2 d - 2 a d^2 + b d^2 - 3 c d^2 - d^3 + a b g - 2 a c g +
       b c g - 2 c^2 g - 2 a d g + b d g - 4 c d g - 2 d^2 g - c g^2 - d g^2 - a b g t)) /
   (a^4 b + 4 a^3 b c + 6 a^2 b c^2 + 4 a b c^3 + b c^4 + 4 a^3 b d + 12 a^2 b c d + 12 a b c^2 d + 4 b c^3 d +
     6 a^2 b d^2 + 12 a b c d^2 + 6 b c^2 d^2 + 4 a b d^3 + 4 b c d^3 + b d^4 + 2 a^3 b g + 6 a^2 b c g + 6 a b c^2 g +
     2 b c^3 g + 6 a^2 b d g + 12 a b c d g + 6 b c^2 d g + 6 a b d^2 g + 6 b c d^2 g + 2 b d^3 g + a^2 b g^2 +
     2 a b c g^2 + b c^2 g^2 + 2 a b d g^2 + 2 b c d g^2 + b d^2 g^2 - 2 a^3 b g t - 4 a^2 b c g t - 2 a b c^2 g t -
     4 a^2 b d g t - 4 a b c d g t - 2 a b d^2 g t - 2 a^2 b g^2 t - 2 a b c g^2 t - 2 a b d g^2 t + a^2 b g^2 t^2);
```

In[688]:=
```
newFlineMn =
  -((2 c + d) t (-a b + 2 a c - 2 b c + 4 c^2 + a d - b d + 4 c d + d^2 - b g + 2 c g + d g + b g t)) /
    (b (a + 2 c + d + g - g t)^2);
```

In[689]:=
```
newFlineMf = ((2 c + d) (a + 2 c + d + g - 2 c t - d t - g t)
      (a b - 2 a c + 2 b c - 4 c^2 - a d + b d - 4 c d - d^2 + b g - 2 c g - d g - b g t)) /
   (a^3 b + 6 a^2 b c + 12 a b c^2 + 8 b c^3 + 3 a^2 b d + 12 a b c d + 12 b c^2 d + 3 a b d^2 +
     6 b c d^2 + b d^3 + 2 a^2 b g + 8 a b c g + 8 b c^2 g + 4 a b d g + 8 b c d g + 2 b d^2 g + a b g^2 +
     2 b c g^2 + b d g^2 - 2 a^2 b g t - 8 a b c g t - 8 b c^2 g t - 4 a b d g t - 8 b c d g t -
     2 b d^2 g t - 2 a b g^2 t - 4 b c g^2 t - 2 b d g^2 t + a b g^2 t^2 + 2 b c g^2 t^2 + b d g^2 t^2);
```

In[690]:=
```
newFlineMl =
  -((a (a + 2 c + d + g - 2 c t - d t - g t) (-a b + 2 a c - 2 b c + 4 c^2 + a d - b d + 4 c d +
         d^2 - b g + 2 c g + d g + b g t)) / (b (a + 2 c + d) (a + 2 c + d + g - g t)^2));
```

In[ ]:=
```
(* And the overall equilibrium prevalence for each strain are *)
```

In[691]:=
```
newFlineSeq = (newFlineSf + newFlineSl + newFlineSn);
```

In[692]:=
```
newFlineFeq = (newFlineFf + newFlineFl + newFlineFn);
```

In[693]:=
```
newFlineLeq = (newFlineLf + newFlineLl + newFlineLn);
```

In[694]:=
```
newFlineMeq = (newFlineMf + newFlineMl + newFlineMn);
```

▪ R0 under front-line new drug

In[695]:=
```
r0Sf = Factor[1 / (1 - newFlineSeq )]
```

Out[695]=
$$\frac{b}{d+g}$$

In[698]:=
```
r0Ff = FullSimplify[Factor[1 / (1 - newFlineFeq )]]
```

Out[698]=
$$\frac{b\left((a+c+d+g)^2-g\,(c+d+g)\,t\right)}{(a+c+d)\,(c+d+g)\,(a+c+d+g)}$$

In[699]:=
```
r0Lf = FullSimplify[Factor[1 / (1 - newFlineLeq )]]
```

Out[699]=
$$\frac{b\,(a+c+d)\,(a+c+d+g)-a\,b\,g\,t}{(c+d)\,(a+c+d+g)^2}$$

In[701]:=
```
r0Mf = FullSimplify[Factor[1 / (1 - newFlineMeq )]]
```

Out[701]=
$$\frac{b\ (a+2\,c+d+g-g\,t)}{(2\,c+d)\ (a+2\,c+d+g)}$$

Last-line new drug

Model equations

In[702]:=
```
newLlinedSfdt = (b (Sn + Sf + Sl))
    (1 - Sn - Fn - Ln - Mn - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Sf (a + g + d);
```

In[703]:=
```
newLlinedSldt =  a Sf - Sl (t * a + g + d);
```

In[704]:=
```
newLlinedSndt = t * a Sl - Sn (g + d);
```

In[705]:=
```
newLlinedFfdt = (b (Fn + Ff + Fl))
    (1 - Sn - Fn - Ln - Mn - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Ff (a + d + c);
```

In[706]:=
```
newLlinedFldt =  a Ff - Fl (t * a + g + d + c);
```

In[707]:=
```
newLlinedFndt =  t * a Fl - Fn (g + d + c);
```

In[708]:=
```
newLlinedLfdt = (b (Ln + Lf + Ll))
    (1 - Sn - Fn - Ln - Mn - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Lf (a + g + d + c);
```

In[709]:=
```
newLlinedLldt =  a Lf - Ll (t * a + d + c);
```

In[710]:=
```
newLlinedLndt = t * a Ll - Ln (g + d + c);
```

In[711]:=
```
newLlinedMfdt = (b (Mn + Mf + Ml))
    (1 - Sn - Fn - Ln - Mn - Sf - Ff - Lf - Mf - Sl - Fl - Ll - Ml) - Mf (a + d + 2 c);
```

In[712]:=
```
newLlinedMldt = a Mf - Ml (t * a + d + 2 c);
```

In[713]:=
```
newLlinedMndt = t * a Ml - Mn (g + d + 2 c);
```

Determining equilibrium

```
(* Solving for equilibrium *)
```

In[714]:=
```
Solve[newLlinedSndt == 0 && newLlinedSfdt == 0 && newLlinedSldt == 0 &&
  newLlinedFndt == 0 && newLlinedFfdt == 0 && newLlinedFldt == 0 &&
  newLlinedLndt == 0 && newLlinedLfdt == 0 && newLlinedLldt == 0 &&
  newLlinedMndt == 0 && newLlinedMfdt == 0 && newLlinedMldt == 0,
 {Sn, Sf, Sl, Fn, Ff, Fl, Ln, Lf, Ll, Mn, Mf, Ml}]
```

Out[714]=
$$\Big\{\{Sn\to 0,\ Sf\to 0,\ Sl\to 0,\ Fn\to 0,\ Ff\to 0,\ Fl\to 0,\ Ln\to 0,\ Lf\to 0,\ Ll\to 0,\ Mn\to 0,\ Mf\to 0,\ Ml\to 0\},\ \Big\{Sn\to \frac{a^2\ (b-d-g)\ t}{b\ (a+d+g)\ (d+g+a\,t)},$$
$$Sf\to \frac{d^2}{(a+d+g)\ (d+g+a\,t)}-\frac{d^3}{b\ (a+d+g)\ (d+g+a\,t)}+\frac{2\,d\,g}{(a+d+g)\ (d+g+a\,t)}-$$
$$\frac{3\,d^2\,g}{b\ (a+d+g)\ (d+g+a\,t)}+\frac{g^2}{(a+d+g)\ (d+g+a\,t)}-\frac{3\,d\,g^2}{b\ (a+d+g)\ (d+g+a\,t)}-$$

$$\frac{g^3}{b\,(a+d+g)\,(d+g+a\,t)}+\frac{a\,d\,t}{(a+d+g)\,(d+g+a\,t)}-\frac{a\,d^2\,t}{b\,(a+d+g)\,(d+g+a\,t)}+$$
$$\frac{a\,g\,t}{(a+d+g)\,(d+g+a\,t)}-\frac{2\,a\,d\,g\,t}{b\,(a+d+g)\,(d+g+a\,t)}-\frac{a\,g^2\,t}{b\,(a+d+g)\,(d+g+a\,t)},$$
$$Sl\to\frac{a\,(b-d-g)\,(d+g)}{b\,(a+d+g)\,(d+g+a\,t)},\ Fn\to 0,\ Ff\to 0,\ Fl\to 0,\ Ln\to 0,$$
$$Lf\to 0,\ Ll\to 0,\ Mn\to 0,\ Mf\to 0,\ Ml\to 0\Big\},$$

$$\Big\{Sn\to 0,\ Sf\to 0,\ Sl\to 0,\ Fn\to 0,\ Ff\to 0,\ Fl\to 0,\ Ln\to 0,\ Lf\to 0,\ Ll\to 0,$$
$$Mn\to\Big(a^2\,t\,\big(2\,a\,b\,c-4\,a\,c^2+4\,b\,c^2-8\,c^3+a\,b\,d-4\,a\,c\,d+4\,b\,c\,d-$$
$$12\,c^2\,d-a\,d^2+b\,d^2-6\,c\,d^2-d^3+a\,b\,g-2\,a\,c\,g+2\,b\,c\,g-4\,c^2\,g-a\,d\,g+$$
$$b\,d\,g-4\,c\,d\,g-d^2\,g+a^2\,b\,t-2\,a^2\,c\,t+2\,a\,b\,c\,t-4\,a\,c^2\,t-a^2\,d\,t+$$
$$a\,b\,d\,t-4\,a\,c\,d\,t-a\,d^2\,t-a^2\,g\,t+a\,b\,g\,t-2\,a\,c\,g\,t-a\,d\,g\,t\big)\Big)\Big/$$
$$\Big(b\,\big(2\,a\,c+4\,c^2+a\,d+4\,c\,d+d^2+a\,g+2\,c\,g+d\,g+a^2\,t+2\,a\,c\,t+a\,d\,t+a\,g\,t\big)^2\Big),$$
$$Mf\to\Big((2\,c+d+g)\times(2\,c+d+a\,t)\times\big(2\,a\,b\,c-4\,a\,c^2+4\,b\,c^2-8\,c^3+a\,b\,d-$$
$$4\,a\,c\,d+4\,b\,c\,d-12\,c^2\,d-a\,d^2+b\,d^2-6\,c\,d^2-d^3+a\,b\,g-2\,a\,c\,g+2\,b\,c\,g-$$
$$4\,c^2\,g-a\,d\,g+b\,d\,g-4\,c\,d\,g-d^2\,g+a^2\,b\,t-2\,a^2\,c\,t+2\,a\,b\,c\,t-4\,a\,c^2\,t-$$
$$a^2\,d\,t+a\,b\,d\,t-4\,a\,c\,d\,t-a\,d^2\,t-a^2\,g\,t+a\,b\,g\,t-2\,a\,c\,g\,t-a\,d\,g\,t\big)\Big)\Big/$$
$$\big(4\,a^2\,b\,c^2+16\,a\,b\,c^3+16\,b\,c^4+4\,a^2\,b\,c\,d+24\,a\,b\,c^2\,d+32\,b\,c^3\,d+a^2\,b\,d^2+12\,a\,b\,c\,d^2+$$
$$24\,b\,c^2\,d^2+2\,a\,b\,d^3+8\,b\,c\,d^3+b\,d^4+4\,a^2\,b\,c\,g+16\,a\,b\,c^2\,g+16\,b\,c^3\,g+2\,a^2\,b\,d\,g+$$
$$16\,a\,b\,c\,d\,g+24\,b\,c^2\,d\,g+4\,a\,b\,d^2\,g+12\,b\,c\,d^2\,g+2\,b\,d^3\,g+a^2\,b\,g^2+4\,a\,b\,c\,g^2+$$
$$4\,b\,c^2\,g^2+2\,a\,b\,d\,g^2+4\,b\,c\,d\,g^2+b\,d^2\,g^2+4\,a^3\,b\,c\,t+16\,a^2\,b\,c^2\,t+16\,a\,b\,c^3\,t+$$
$$2\,a^3\,b\,d\,t+16\,a^2\,b\,c\,d\,t+24\,a\,b\,c^2\,d\,t+4\,a^2\,b\,d^2\,t+12\,a\,b\,c\,d^2\,t+2\,a\,b\,d^3\,t+$$
$$2\,a^3\,b\,g\,t+12\,a^2\,b\,c\,g\,t+16\,a\,b\,c^2\,g\,t+6\,a^2\,b\,d\,g\,t+16\,a\,b\,c\,d\,g\,t+4\,a\,b\,d^2\,g\,t+$$
$$2\,a^2\,b\,g^2\,t+4\,a\,b\,c\,g^2\,t+2\,a\,b\,d\,g^2\,t+a^4\,b\,t^2+4\,a^3\,b\,c\,t^2+4\,a^2\,b\,c^2\,t^2+2\,a^3\,b\,d\,t^2+$$
$$4\,a^2\,b\,c\,d\,t^2+a^2\,b\,d^2\,t^2+2\,a^3\,b\,g\,t^2+4\,a^2\,b\,c\,g\,t^2+2\,a^2\,b\,d\,g\,t^2+a^2\,b\,g^2\,t^2\big),$$
$$Ml\to\Big(a\,(2\,c+d+g)\times\big(2\,a\,b\,c-4\,a\,c^2+4\,b\,c^2-8\,c^3+a\,b\,d-4\,a\,c\,d+4\,b\,c\,d-$$
$$12\,c^2\,d-a\,d^2+b\,d^2-6\,c\,d^2-d^3+a\,b\,g-2\,a\,c\,g+2\,b\,c\,g-4\,c^2\,g-a\,d\,g+$$
$$b\,d\,g-4\,c\,d\,g-d^2\,g+a^2\,b\,t-2\,a^2\,c\,t+2\,a\,b\,c\,t-4\,a\,c^2\,t-a^2\,d\,t+$$
$$a\,b\,d\,t-4\,a\,c\,d\,t-a\,d^2\,t-a^2\,g\,t+a\,b\,g\,t-2\,a\,c\,g\,t-a\,d\,g\,t\big)\Big)\Big/$$
$$\big(4\,a^2\,b\,c^2+16\,a\,b\,c^3+16\,b\,c^4+4\,a^2\,b\,c\,d+24\,a\,b\,c^2\,d+32\,b\,c^3\,d+a^2\,b\,d^2+12\,a\,b\,c\,d^2+$$
$$24\,b\,c^2\,d^2+2\,a\,b\,d^3+8\,b\,c\,d^3+b\,d^4+4\,a^2\,b\,c\,g+16\,a\,b\,c^2\,g+16\,b\,c^3\,g+2\,a^2\,b\,d\,g+$$
$$16\,a\,b\,c\,d\,g+24\,b\,c^2\,d\,g+4\,a\,b\,d^2\,g+12\,b\,c\,d^2\,g+2\,b\,d^3\,g+a^2\,b\,g^2+4\,a\,b\,c\,g^2+$$
$$4\,b\,c^2\,g^2+2\,a\,b\,d\,g^2+4\,b\,c\,d\,g^2+b\,d^2\,g^2+4\,a^3\,b\,c\,t+16\,a^2\,b\,c^2\,t+16\,a\,b\,c^3\,t+$$
$$2\,a^3\,b\,d\,t+16\,a^2\,b\,c\,d\,t+24\,a\,b\,c^2\,d\,t+4\,a^2\,b\,d^2\,t+12\,a\,b\,c\,d^2\,t+2\,a\,b\,d^3\,t+$$
$$2\,a^3\,b\,g\,t+12\,a^2\,b\,c\,g\,t+16\,a\,b\,c^2\,g\,t+6\,a^2\,b\,d\,g\,t+16\,a\,b\,c\,d\,g\,t+4\,a\,b\,d^2\,g\,t+$$
$$2\,a^2\,b\,g^2\,t+4\,a\,b\,c\,g^2\,t+2\,a\,b\,d\,g^2\,t+a^4\,b\,t^2+4\,a^3\,b\,c\,t^2+4\,a^2\,b\,c^2\,t^2+2\,a^3\,b\,d\,t^2+$$
$$4\,a^2\,b\,c\,d\,t^2+a^2\,b\,d^2\,t^2+2\,a^3\,b\,g\,t^2+4\,a^2\,b\,c\,g\,t^2+2\,a^2\,b\,d\,g\,t^2+a^2\,b\,g^2\,t^2\big)\Big\},$$

$$\Big\{Sn\to 0,\ Sf\to 0,\ Sl\to 0,\ Fn\to 0,\ Ff\to 0,\ Fl\to 0,$$
$$Ln\to\Big(a^2\,t\,\big(a\,b\,c-a\,c^2+b\,c^2-c^3+a\,b\,d-2\,a\,c\,d+2\,b\,c\,d-3\,c^2\,d-a\,d^2+$$
$$b\,d^2-3\,c\,d^2-d^3+a\,b\,g-a\,c\,g+b\,c\,g-2\,c^2\,g-a\,d\,g+b\,d\,g-4\,c\,d\,g-$$
$$2\,d^2\,g-c\,g^2-d\,g^2+a^2\,b\,t-a^2\,c\,t+a\,b\,c\,t-a\,c^2\,t-a^2\,d\,t+a\,b\,d\,t-$$
$$2\,a\,c\,d\,t-a\,d^2\,t-a^2\,g\,t+a\,b\,g\,t-2\,a\,c\,g\,t-2\,a\,d\,g\,t-a\,g^2\,t\big)\Big)\Big/$$

$$\left(b\left(a c+c^2+a d+2 c d+d^2+a g+c g+d g+a^2 t+a c t+a d t+a g t\right)^2\right),$$

$$Lf \to \Big((c+d+g)\,(c+d+a t)\,\big(a b c-a c^2+b c^2-c^3+a b d-2 a c d+2 b c d-3 c^2 d-a d^2+b d^2-3 c d^2-d^3+a b g-a c g+b c g-2 c^2 g-a d g+b d g-4 c d g-2 d^2 g-c g^2-d g^2+a^2 b t-a^2 c t+a b c t-a c^2 t-a^2 d t+a b d t-2 a c d t-a d^2 t-a^2 g t+a b g t-2 a c g t-2 a d g t-a g^2 t\big)\Big) \Big/ \left(a^2 b c^2+2 a b c^3+b c^4+2 a^2 b c d+6 a b c^2 d+4 b c^3 d+a^2 b d^2+6 a b c d^2+6 b c^2 d^2+2 a b d^3+4 b c d^3+b d^4+2 a^2 b c g+4 a b c^2 g+2 b c^3 g+2 a^2 b d g+8 a b c d g+6 b c^2 d g+4 a b d^2 g+6 b c d^2 g+2 b d^3 g+a^2 b g^2+2 a b c g^2+b c^2 g^2+2 a b d g^2+2 b c d g^2+b d^2 g^2+2 a^3 b c t+4 a^2 b c^2 t+2 a b c^3 t+2 a^3 b d t+8 a^2 b c d t+6 a b c^2 d t+4 a^2 b d^2 t+6 a b c d^2 t+2 a b d^3 t+2 a^3 b g t+6 a^2 b c g t+4 a b c^2 g t+6 a^2 b d g t+8 a b c d g t+4 a b d^2 g t+2 a^2 b g^2 t+2 a b c g^2 t+2 a b d g^2 t+a^4 b t^2+2 a^3 b c t^2+a^2 b c^2 t^2+2 a^3 b d t^2+2 a^2 b c d t^2+a^2 b d^2 t^2+2 a^3 b g t^2+2 a^2 b c g t^2+2 a^2 b d g t^2+a^2 b g^2 t^2\right),$$

$$Ll \to \Big(a\,(c+d+g)\,\big(a b c-a c^2+b c^2-c^3+a b d-2 a c d+2 b c d-3 c^2 d-a d^2+b d^2-3 c d^2-d^3+a b g-a c g+b c g-2 c^2 g-a d g+b d g-4 c d g-2 d^2 g-c g^2-d g^2+a^2 b t-a^2 c t+a b c t-a c^2 t-a^2 d t+a b d t-2 a c d t-a d^2 t-a^2 g t+a b g t-2 a c g t-2 a d g t-a g^2 t\big)\Big) \Big/ \left(a^2 b c^2+2 a b c^3+b c^4+2 a^2 b c d+6 a b c^2 d+4 b c^3 d+a^2 b d^2+6 a b c d^2+6 b c^2 d^2+2 a b d^3+4 b c d^3+b d^4+2 a^2 b c g+4 a b c^2 g+2 b c^3 g+2 a^2 b d g+8 a b c d g+6 b c^2 d g+4 a b d^2 g+6 b c d^2 g+2 b d^3 g+a^2 b g^2+2 a b c g^2+b c^2 g^2+2 a b d g^2+2 b c d g^2+b d^2 g^2+2 a^3 b c t+4 a^2 b c^2 t+2 a b c^3 t+2 a^3 b d t+8 a^2 b c d t+6 a b c^2 d t+4 a^2 b d^2 t+6 a b c d^2 t+2 a b d^3 t+2 a^3 b g t+6 a^2 b c g t+4 a b c^2 g t+6 a^2 b d g t+8 a b c d g t+4 a b d^2 g t+2 a^2 b g^2 t+2 a b c g^2 t+2 a b d g^2 t+a^4 b t^2+2 a^3 b c t^2+a^2 b c^2 t^2+2 a^3 b d t^2+2 a^2 b c d t^2+a^2 b d^2 t^2+2 a^3 b g t^2+2 a^2 b c g t^2+2 a^2 b d g t^2+a^2 b g^2 t^2\right),$$

$Mn \to 0,\ Mf \to 0,\ Ml \to 0\},\ \{Sn \to 0,\ Sf \to 0,$

$Sl \to 0,$

$$Fn \to \frac{a^2\left(a b-a c+b c-c^2-a d+b d-2 c d-d^2-a g+b g-c g-d g\right) t}{b\,(a+c+d+g)^2\,(c+d+g+a t)},$$

$$Ff \to -\frac{(c+d+g)\left(-a b+a c-b c+c^2+a d-b d+2 c d+d^2+a g-b g+c g+d g\right)}{b\,(a+c+d+g)^2},$$

$$Fl \to -\frac{a\,(c+d+g)\left(-a b+a c-b c+c^2+a d-b d+2 c d+d^2+a g-b g+c g+d g\right)}{b\,(a+c+d+g)^2\,(c+d+g+a t)},$$

$Ln \to 0,\ Lf \to 0,\ Ll \to 0,$

$Mn \to 0,$

$Mf \to 0,$

$Ml \to 0\}\}$

(* So the equilibrium of each strain under each treatment is (only one strain will be present at equilibrium) *)

In[717]:= $$\text{newLlineSn} = \frac{a^2\,(b-d-g)\,t}{b\,(a+d+g)\,(d+g+a\,t)};$$

In[718]:= $$\begin{aligned}\text{newLlineSf} = {} & \frac{d^2}{(a+d+g)\,(d+g+a\,t)} - \frac{d^3}{b\,(a+d+g)\,(d+g+a\,t)} + \frac{2\,d\,g}{(a+d+g)\,(d+g+a\,t)} - \\ & \frac{3\,d^2\,g}{b\,(a+d+g)\,(d+g+a\,t)} + \frac{g^2}{(a+d+g)\,(d+g+a\,t)} - \frac{3\,d\,g^2}{b\,(a+d+g)\,(d+g+a\,t)} - \\ & \frac{g^3}{b\,(a+d+g)\,(d+g+a\,t)} + \frac{a\,d\,t}{(a+d+g)\,(d+g+a\,t)} - \frac{a\,d^2\,t}{b\,(a+d+g)\,(d+g+a\,t)} + \\ & \frac{a\,g\,t}{(a+d+g)\,(d+g+a\,t)} - \frac{2\,a\,d\,g\,t}{b\,(a+d+g)\,(d+g+a\,t)} - \frac{a\,g^2\,t}{b\,(a+d+g)\,(d+g+a\,t)};\end{aligned}$$

In[719]:= $$\text{newLlineSl} = \frac{a\,(b-d-g)\,(d+g)}{b\,(a+d+g)\,(d+g+a\,t)};$$

In[720]:= $$\begin{aligned}&\text{newLlineMn} = \\ &\Big(a^2\,t\,\big(2\,a\,b\,c - 4\,a\,c^2 + 4\,b\,c^2 - 8\,c^3 + a\,b\,d - 4\,a\,c\,d + 4\,b\,c\,d - 12\,c^2\,d - a\,d^2 + b\,d^2 - 6\,c\,d^2 - d^3 + \\ &\quad a\,b\,g - 2\,a\,c\,g + 2\,b\,c\,g - 4\,c^2\,g - a\,d\,g + b\,d\,g - 4\,c\,d\,g - d^2\,g + a^2\,b\,t - 2\,a^2\,c\,t + 2\,a\,b\,c\,t - \\ &\quad 4\,a\,c^2\,t - a^2\,d\,t + a\,b\,d\,t - 4\,a\,c\,d\,t - a\,d^2\,t - a^2\,g\,t + a\,b\,g\,t - 2\,a\,c\,g\,t - a\,d\,g\,t\big)\Big) \Big/ \\ &\Big(b\,\big(2\,a\,c + 4\,c^2 + a\,d + 4\,c\,d + d^2 + a\,g + 2\,c\,g + d\,g + a^2\,t + 2\,a\,c\,t + a\,d\,t + a\,g\,t\big)^2\Big);\end{aligned}$$

In[721]:= $$\begin{aligned}&\text{newLlineMf} = \\ &\Big((2\,c+d+g) \times (2\,c+d+a\,t) \times \big(2\,a\,b\,c - 4\,a\,c^2 + 4\,b\,c^2 - 8\,c^3 + a\,b\,d - 4\,a\,c\,d + 4\,b\,c\,d - \\ &\quad 12\,c^2\,d - a\,d^2 + b\,d^2 - 6\,c\,d^2 - d^3 + a\,b\,g - 2\,a\,c\,g + 2\,b\,c\,g - 4\,c^2\,g - a\,d\,g + \\ &\quad b\,d\,g - 4\,c\,d\,g - d^2\,g + a^2\,b\,t - 2\,a^2\,c\,t + 2\,a\,b\,c\,t - 4\,a\,c^2\,t - a^2\,d\,t + \\ &\quad a\,b\,d\,t - 4\,a\,c\,d\,t - a\,d^2\,t - a^2\,g\,t + a\,b\,g\,t - 2\,a\,c\,g\,t - a\,d\,g\,t\big)\Big) \Big/ \\ &\Big(4\,a^2\,b\,c^2 + 16\,a\,b\,c^3 + 16\,b\,c^4 + 4\,a^2\,b\,c\,d + 24\,a\,b\,c^2\,d + 32\,b\,c^3\,d + a^2\,b\,d^2 + 12\,a\,b\,c\,d^2 + \\ &\quad 24\,b\,c^2\,d^2 + 2\,a\,b\,d^3 + 8\,b\,c\,d^3 + b\,d^4 + 4\,a^2\,b\,c\,g + 16\,a\,b\,c^2\,g + 16\,b\,c^3\,g + 2\,a^2\,b\,d\,g + \\ &\quad 16\,a\,b\,c\,d\,g + 24\,b\,c^2\,d\,g + 4\,a\,b\,d^2\,g + 12\,b\,c\,d^2\,g + 2\,b\,d^3\,g + a^2\,b\,g^2 + 4\,a\,b\,c\,g^2 + \\ &\quad 4\,b\,c^2\,g^2 + 2\,a\,b\,d\,g^2 + 4\,b\,c\,d\,g^2 + b\,d^2\,g^2 + 4\,a^3\,b\,c\,t + 16\,a^2\,b\,c^2\,t + 16\,a\,b\,c^3\,t + \\ &\quad 2\,a^3\,b\,d\,t + 16\,a^2\,b\,c\,d\,t + 24\,a\,b\,c^2\,d\,t + 4\,a^2\,b\,d^2\,t + 12\,a\,b\,c\,d^2\,t + 2\,a\,b\,d^3\,t + \\ &\quad 2\,a^3\,b\,g\,t + 12\,a^2\,b\,c\,g\,t + 16\,a\,b\,c^2\,g\,t + 6\,a^2\,b\,d\,g\,t + 16\,a\,b\,c\,d\,g\,t + 4\,a\,b\,d^2\,g\,t + \\ &\quad 2\,a^2\,b\,g^2\,t + 4\,a\,b\,c\,g^2\,t + 2\,a\,b\,d\,g^2\,t + a^4\,b\,t^2 + 4\,a^3\,b\,c\,t^2 + 4\,a^2\,b\,c^2\,t^2 + 2\,a^3\,b\,d\,t^2 + \\ &\quad 4\,a^2\,b\,c\,d\,t^2 + a^2\,b\,d^2\,t^2 + 2\,a^3\,b\,g\,t^2 + 4\,a^2\,b\,c\,g\,t^2 + 2\,a^2\,b\,d\,g\,t^2 + a^2\,b\,g^2\,t^2\Big);\end{aligned}$$

In[722]:= `newLlineMl =`

$$
\begin{aligned}
&\big(a\,(2c+d+g)\times\big(2abc-4ac^2+4bc^2-8c^3+abd-4acd+4bcd-12c^2d-ad^2+\\
&\quad bd^2-6cd^2-d^3+abg-2acg+2bcg-4c^2g-adg+bdg-\\
&\quad 4cdg-d^2g+a^2bt-2a^2ct+2abct-4ac^2t-a^2dt+\\
&\quad abdt-4acdt-ad^2t-a^2gt+abgt-2acgt-adgt\big)\big)\Big/\\
&\big(4a^2bc^2+16abc^3+16bc^4+4a^2bcd+24abc^2d+32bc^3d+a^2bd^2+12abcd^2+\\
&\quad 24bc^2d^2+2abd^3+8bcd^3+bd^4+4a^2bcg+16abc^2g+16bc^3g+2a^2bdg+\\
&\quad 16abcdg+24bc^2dg+4abd^2g+12bcd^2g+2bd^3g+a^2bg^2+4abcg^2+\\
&\quad 4bc^2g^2+2abdg^2+4bcdg^2+bd^2g^2+4a^3bct+16a^2bc^2t+16abc^3t+\\
&\quad 2a^3bdt+16a^2bcdt+24abc^2dt+4a^2bd^2t+12abcd^2t+2abd^3t+\\
&\quad 2a^3bgt+12a^2bcgt+16abc^2gt+6a^2bdgt+16abcdgt+4abd^2gt+\\
&\quad 2a^2bg^2t+4abcg^2t+2abdg^2t+a^4bt^2+4a^3bct^2+4a^2bc^2t^2+2a^3bdt^2+\\
&\quad 4a^2bcdt^2+a^2bd^2t^2+2a^3bgt^2+4a^2bcgt^2+2a^2bdgt^2+a^2bg^2t^2\big);
\end{aligned}
$$

In[723]:= `newLlineLn =`

$$
\begin{aligned}
&\big(a^2t\,\big(abc-ac^2+bc^2-c^3+abd-2acd+2bcd-3c^2d-ad^2+bd^2-3cd^2-d^3+\\
&\quad abg-acg+bcg-2c^2g-adg+bdg-4cdg-2d^2g-\\
&\quad cg^2-dg^2+a^2bt-a^2ct+abct-ac^2t-a^2dt+abdt-\\
&\quad 2acdt-ad^2t-a^2gt+abgt-2acgt-2adgt-ag^2t\big)\big)\Big/\\
&\big(b\,\big(ac+c^2+ad+2cd+d^2+ag+cg+dg+a^2t+act+adt+agt\big)^2\big);
\end{aligned}
$$

In[724]:= `newLlineLf =`

$$
\begin{aligned}
&\big((c+d+g)\,(c+d+at)\,\big(abc-ac^2+bc^2-c^3+abd-2acd+2bcd-3c^2d-ad^2+\\
&\quad bd^2-3cd^2-d^3+abg-acg+bcg-2c^2g-adg+bdg-4cdg-\\
&\quad 2d^2g-cg^2-dg^2+a^2bt-a^2ct+abct-ac^2t-a^2dt+abdt-\\
&\quad 2acdt-ad^2t-a^2gt+abgt-2acgt-2adgt-ag^2t\big)\big)\Big/\\
&\big(a^2bc^2+2abc^3+bc^4+2a^2bcd+6abc^2d+4bc^3d+a^2bd^2+6abcd^2+\\
&\quad 6bc^2d^2+2abd^3+4bcd^3+bd^4+2a^2bcg+4abc^2g+2bc^3g+2a^2bdg+\\
&\quad 8abcdg+6bc^2dg+4abd^2g+6bcd^2g+2bd^3g+a^2bg^2+2abcg^2+\\
&\quad bc^2g^2+2abdg^2+2bcdg^2+bd^2g^2+2a^3bct+4a^2bc^2t+2abc^3t+\\
&\quad 2a^3bdt+8a^2bcdt+6abc^2dt+4a^2bd^2t+6abcd^2t+2abd^3t+\\
&\quad 2a^3bgt+6a^2bcgt+4abc^2gt+6a^2bdgt+8abcdgt+4abd^2gt+\\
&\quad 2a^2bg^2t+2abcg^2t+2abdg^2t+a^4bt^2+2a^3bct^2+a^2bc^2t^2+2a^3bdt^2+\\
&\quad 2a^2bcdt^2+a^2bd^2t^2+2a^3bgt^2+2a^2bcgt^2+2a^2bdgt^2+a^2bg^2t^2\big);
\end{aligned}
$$

In[725]:= newLlineLl =

$$\left(a\,(c+d+g)\,\left(a\,b\,c-a\,c^2+b\,c^2-c^3+a\,b\,d-2\,a\,c\,d+2\,b\,c\,d-3\,c^2\,d-a\,d^2+b\,d^2-3\,c\,d^2-d^3+a\,b\,g-a\,c\,g+b\,c\,g-2\,c^2\,g-a\,d\,g+b\,d\,g-4\,c\,d\,g-2\,d^2\,g-c\,g^2-d\,g^2+a^2\,b\,t-a^2\,c\,t+a\,b\,c\,t-a\,c^2\,t-a^2\,d\,t+a\,b\,d\,t-2\,a\,c\,d\,t-a\,d^2\,t-a^2\,g\,t+a\,b\,g\,t-2\,a\,c\,g\,t-2\,a\,d\,g\,t-a\,g^2\,t\right)\right)/\left(a^2\,b\,c^2+2\,a\,b\,c^3+b\,c^4+2\,a^2\,b\,c\,d+6\,a\,b\,c^2\,d+4\,b\,c^3\,d+a^2\,b\,d^2+6\,a\,b\,c\,d^2+6\,b\,c^2\,d^2+2\,a\,b\,d^3+4\,b\,c\,d^3+b\,d^4+2\,a^2\,b\,c\,g+4\,a\,b\,c^2\,g+2\,b\,c^3\,g+2\,a^2\,b\,d\,g+8\,a\,b\,c\,d\,g+6\,b\,c^2\,d\,g+4\,a\,b\,d^2\,g+6\,b\,c\,d^2\,g+2\,b\,d^3\,g+a^2\,b\,g^2+2\,a\,b\,c\,g^2+b\,c^2\,g^2+2\,a\,b\,d\,g^2+2\,b\,c\,d\,g^2+b\,d^2\,g^2+2\,a^3\,b\,c\,t+4\,a^2\,b\,c^2\,t+2\,a\,b\,c^3\,t+2\,a^3\,b\,d\,t+8\,a^2\,b\,c\,d\,t+6\,a\,b\,c^2\,d\,t+4\,a^2\,b\,d^2\,t+6\,a\,b\,c\,d^2\,t+2\,a\,b\,d^3\,t+2\,a^3\,b\,g\,t+6\,a^2\,b\,c\,g\,t+4\,a\,b\,c^2\,g\,t+6\,a^2\,b\,d\,g\,t+8\,a\,b\,c\,d\,g\,t+4\,a\,b\,d^2\,g\,t+2\,a^2\,b\,g^2\,t+2\,a\,b\,c\,g^2\,t+2\,a\,b\,d\,g^2\,t+a^4\,b\,t^2+2\,a^3\,b\,c\,t^2+a^2\,b\,c^2\,t^2+2\,a^3\,b\,d\,t^2+2\,a^2\,b\,c\,d\,t^2+a^2\,b\,d^2\,t^2+2\,a^3\,b\,g\,t^2+2\,a^2\,b\,c\,g\,t^2+2\,a^2\,b\,d\,g\,t^2+a^2\,b\,g^2\,t^2\right);$$

In[726]:= $\text{newLlineFn} = \dfrac{a^2\,\left(a\,b-a\,c+b\,c-c^2-a\,d+b\,d-2\,c\,d-d^2-a\,g+b\,g-c\,g-d\,g\right)\,t}{b\,(a+c+d+g)^2\,(c+d+g+a\,t)};$

In[727]:= $\text{newLlineFf} = -\dfrac{(c+d+g)\,\left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+a\,g-b\,g+c\,g+d\,g\right)}{b\,(a+c+d+g)^2};$

In[728]:= $\text{newLlineFl} = -\dfrac{a\,(c+d+g)\,\left(-a\,b+a\,c-b\,c+c^2+a\,d-b\,d+2\,c\,d+d^2+a\,g-b\,g+c\,g+d\,g\right)}{b\,(a+c+d+g)^2\,(c+d+g+a\,t)};$

In[ ]:= (* And the overall equilibrium prevalence for each strain are *)

```
In[729]:= newLlineSeq = (newLlineSf + newLlineSl + newLlineSn);

In[730]:= newLlineFeq = (newLlineFf + newLlineFl + newLlineFn);

In[731]:= newLlineLeq = (newLlineLf + newLlineLl + newLlineLn);

In[732]:= newLlineMeq = (newLlineMf + newLlineMl + newLlineMn);
```

■ R0 under last-line new drug

```
In[733]:= r0Sl = Factor[1 / (1 - newLlineSeq )]
```

Out[733]= $\dfrac{b}{d+g}$

```
In[734]:= r0Fl = Factor[1 / (1 - newLlineFeq )]
```

Out[734]= $\dfrac{b\,(a+c+d+g)}{(a+c+d)\,(c+d+g)}$

```
In[736]:= r0Ll = FullSimplify[Factor[1 / (1 - newLlineLeq )]]
```

Out[736]= $\dfrac{b\left(\frac{a+c+d}{a+c+d+g}+\frac{a\,t}{c+d+g}\right)}{c+d+a\,t}$

```
In[737]:= r0Ml = FullSimplify[Factor[1 / (1 - newLlineMeq )]]
```

Out[737]= $\dfrac{b\left(1+\frac{a\,(a+2\,c+d+g)\,t}{(a+2\,c+d)\,(2\,c+d+g)}\right)}{2\,c+d+a\,t}$

Public health analysis for new drug

For the new drug scenario, it's trickier to do full analysis like for adjuvant mode. This is because depending on the parameters, various strain can become the fittest under front-line intervention. And both M and F can become the fittest under last-line intervention. However, we can in fact apply logical deduction to demonstrate the point that the strain selected by front-line intervention will have a lower fitness than the strain selected by the last-line intervention, both when F is fittest first and when M was fittest first.

- **If F was the fittest strain before intervention**

It follows the exact same logic as before:

The last-line intervention does not affect the fitness of the F strain (r0Fl = r0F), so under last-line intervention, that strain will remain the fittest.
The front-line intervention reduces the fitness of all strains or leave it equal (r0Xf <= r0X)
Specifically, we can show that r0Ff<r0F , r0Mf<r0M, and r0Lf<r0L whenever 0< t < 1, that is, whenever the new drug is used to some rate. The fitness of the S is unchanged (r0Sf = r0S)
Depending the other parameter, different strain may become the fittest (another strain than F can become fittest under front-line intervention, leading to strain replacement at equilibrium). But regardless, since the fitness of all strains get reduced under the front -line intervention, and F was the fittest before intervention, it necessarily follows that any strain selected under front-line will be of lower fitness than the strain selected under de last-line intervention, which is the front-line resistant one.

```
In[770]:= Reduce[r0Ff < r0F && 0 < t < 1 && a > 0 && b > 0 && c > 0 && d > 0 && g > 0]
Out[770]= g > 0 && 0 < t < 1 && d > 0 && c > 0 && b > 0 && a > 0

In[769]:= Reduce[r0Mf < r0M && 0 < t < 1 && a > 0 && b > 0 && c > 0 && d > 0 && g > 0]
Out[769]= g > 0 && 0 < t < 1 && d > 0 && c > 0 && b > 0 && a > 0

In[767]:= Reduce[r0Lf < r0L && 0 < t < 1 && a > 0 && b > 0 && c > 0 && d > 0 && g > 0]
Out[767]= g > 0 && 0 < t < 1 && d > 0 && c > 0 && b > 0 && a > 0

In[764]:= Reduce[r0Sf == r0S && 0 < t < 1 && a > 0 && b > 0 && c > 0 && d > 0 && g > 0]
Out[764]= 0 < t < 1 && a > 0 && b > 0 && c > 0 && d > 0 && g > 0
```

- **If M was the fittest strain before intervention**

It is a bit trickier to see, but some logic will work too.
Given three things to demonstrate, then the logic that follows shows that the strain selected by the front-line intervention will necessarily have a lower fitness than the strain selected by the last-line intervention.

(1) we showed in the first section that if M strain is the fittest before intervention, the only possible relative order of strain's fitness is M>F>L>S
(2) In addition, here, r0Mf < r0Ml as long as a < 2c+d (shown on evaluation below), which is the condition that we have seen is met (necessary for front-line drug to be used more)

(3) And here again, the last-line intervention does not change the fitness of the front-line resistant strain (r0F = r0Fl)

In[775]:=
```
Reduce[r0Mf < r0Ml && 0 < t < 1 &&
  a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && a < 2 c + d,]
```

Out[775]= $d > 0 \,\&\&\, c > 0 \,\&\&\, 0 < a < 2c + d \,\&\&\, 0 < t < 1 \,\&\&\, g > 0 \,\&\&\, b > 0$

If last-line intervention leads the M strain to be replaced, it will necessarily be by the F strain.
This is because we know that the only possible strain order if M is the fittest before the intervention is M>F>L>S
We know that the last-line interventions causes the fitness of M and L to drop, so L can only become even lower below F, and it does not affect S, so S will remain below F. Hence, the only possibility is that the M strain drops below F under last-line intervention, and that strain then becomes the fittest, with the same fitness as it had before intervention, r0F

Now, what will be the fitness of the strains under front-line interventions compared to this F strain under last-line intervention?

We know that r0Mf < r0Ml as long as a < 2c+d , so if M strain is replaced under last-line intervention, implying that r0Ml < r0Fl, then necessarily, r0Mf < r0Ml < r0Fl.

For the other strains, we must recall that we know that originally M>F>L>S
Under front-line intervention, all strains fitness drop. Hence, Ff < F0, and Lf<L0<F0, and Sf<S0<F0.
Hence, all strains F, L and S are necessarily less fit than F0, and since Fl = F0, those three strains are necessarily less fit than the strain selected by last-line intervention.

Hence, if the last-line intervention leads to replacement of the M strain by the F strain, then regardless of wether the front-line intervention (i) leaves M fittest or (ii) leads to replacement by any of the other three strains, the fitness of the strain selected by the front-line intervention will have a lower fitness than the strain selected by the last-line intervention.

In[780]:=
```
Reduce[r0Ml < r0M && 0 < t < 1 &&
  a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && a < 2 c + d]
```

Out[780]= $d > 0 \,\&\&\, c > 0 \,\&\&\, 0 < a < 2c + d \,\&\&\, 0 < t < 1 \,\&\&\, g > 0 \,\&\&\, b > 0$

In[785]:=
```
Reduce[r0Ll < r0L && 0 < t < 1 &&
  a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && a < 2 c + d]
```

Out[785]= $d > 0 \,\&\&\, c > 0 \,\&\&\, 0 < a < 2c + d \,\&\&\, 0 < t < 1 \,\&\&\, g > 0 \,\&\&\, b > 0$

In[782]:=
```
Reduce[r0Fl == r0F ]
```

Out[782]= True

In[784]:=
```
Reduce[r0Sl == r0S ]
```

Out[784]= True

```
In[788]:= Reduce[r0Mf < r0M && 0 < t < 1 &&
            a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && a < 2 c + d]
Out[788]= d > 0 && c > 0 && 0 < a < 2 c + d && 0 < t < 1 && g > 0 && b > 0

In[789]:= Reduce[r0Ff < r0F && 0 < t < 1 &&
            a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && a < 2 c + d]
Out[789]= d > 0 && c > 0 && 0 < a < 2 c + d && 0 < t < 1 && g > 0 && b > 0

In[790]:= Reduce[r0Lf < r0L && 0 < t < 1 &&
            a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && a < 2 c + d]
Out[790]= d > 0 && c > 0 && 0 < a < 2 c + d && 0 < t < 1 && g > 0 && b > 0

In[791]:= Reduce[r0Mf < r0M && 0 < t < 1 &&
            a > 0 && b > 0 && c > 0 && d > 0 && g > 0 && a < 2 c + d]
Out[791]= d > 0 && c > 0 && 0 < a < 2 c + d && 0 < t < 1 && g > 0 && b > 0
```

If last-line intervention leaves the M strain to be the fittest. Then we must examine the case where the front-line intervention also leaves the M strain the fittest, and the case where front-line intervention leads to strain replacement.

- If *both* interventions leave M to be the fittest, we show that Mf<Ml, as long as a<2c+d, which is a condition met here for front-line drug to be used more. So in this case front-line intervention better

- If last-line intervention leaves M the fittest *but front-line intervention leads to strain replacement*: Whatever strains replaces the M strain under the front-line intervention, we know that this strain will have a fitness below that of Fl, since all strains fitness get reduced under the front-line intervention, and originally M>F>L>S, all strains but M will necessarily have a lower fitness than F0 = Fl. And M remaining fittest under last-line intervention implies is has to be higher than Fl, hence whichever strain replaces the M strain under front-line intervention will necessarily have a lower fitness than the M strain under last-line intervention.