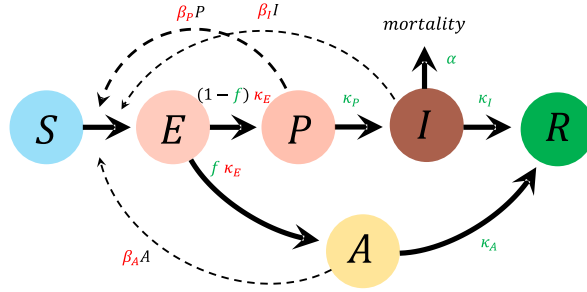


## Supplementary Material: “On the Evolutionary Epidemiology of SARS-CoV-2”

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### ■ Analysis of model with genetic variation (wildtype and mutant subtypes)

Based on Figure 2:



We develop ordinary differential equations for both the wildtype (w) and the mutant (m):

$$\begin{aligned} dSdt &= -((\beta_I * I_w + \beta_A * A_w + \beta_P * P_w) + (\beta_{Im} * I_m + \beta_{Am} * A_m + \beta_P * P_m)) * S; \\ dEwdt &= (\beta_I * I_w + \beta_A * A_w + \beta_P * P_w) * S - \kappa_E * E_w; \\ dPwdt &= (1-f) * \kappa_E * E_w - \kappa_P * P_w; \\ dIwdt &= \kappa_P * P_w - \alpha * I_w - \kappa_I * I_w; \\ dAwdt &= f * \kappa_E * E_w - \kappa_A * A_w; \\ dEmdt &= (\beta_{Im} * I_m + \beta_{Am} * A_m + \beta_P * P_m) * S - \kappa_{Em} * E_m; \\ dPmdt &= (1-f_m) * \kappa_{Em} * E_m - \kappa_{Pm} * P_m; \\ dImdt &= \kappa_{Pm} * P_m - \alpha_m * I_m - \kappa_{Im} * I_m; \\ dAmdt &= f_m * \kappa_{Em} * E_m - \kappa_{Am} * A_m; \end{aligned}$$

We assume that the disease is fairly rare and study its growth by analysing the properties of the local stability matrix:

$$\text{start} = \{E_w \rightarrow 0, A_w \rightarrow 0, P_w \rightarrow 0, I_w \rightarrow 0, E_m \rightarrow 0, A_m \rightarrow 0, P_m \rightarrow 0, I_m \rightarrow 0\};$$

$$\begin{aligned} \text{stabmat} &= \{ \{ D[dSdt, S], D[dSdt, E_w], D[dSdt, P_w], \\ &\quad D[dSdt, I_w], D[dSdt, A_w], D[dSdt, E_m], D[dSdt, P_m], D[dSdt, I_m], D[dSdt, A_m] \}, \\ &\{ D[dEwdt, S], D[dEwdt, E_w], D[dEwdt, P_w], D[dEwdt, I_w], D[dEwdt, A_w], \\ &\quad D[dEwdt, E_m], D[dEwdt, P_m], D[dEwdt, I_m], D[dEwdt, A_m] \}, \\ &\{ D[dPwdt, S], D[dPwdt, E_w], D[dPwdt, P_w], D[dPwdt, I_w], D[dPwdt, A_w], \\ &\quad D[dPwdt, E_m], D[dPwdt, P_m], D[dPwdt, I_m], D[dPwdt, A_m] \}, \\ &\{ D[dIwdt, S], D[dIwdt, E_w], D[dIwdt, P_w], D[dIwdt, I_w], D[dIwdt, A_w], D[dIwdt, E_m], \\ &\quad D[dIwdt, P_m], D[dIwdt, I_m], D[dIwdt, A_m] \}, \{ D[dAwdt, S], D[dAwdt, E_w], D[dAwdt, P_w], \\ &\quad D[dAwdt, I_w], D[dAwdt, A_w], D[dAwdt, E_m], D[dAwdt, P_m], D[dAwdt, I_m], D[dAwdt, A_m] \}, \\ &\{ D[dEmdt, S], D[dEmdt, E_w], D[dEmdt, P_w], D[dEmdt, I_w], D[dEmdt, A_w], \\ &\quad D[dEmdt, E_m], D[dEmdt, P_m], D[dEmdt, I_m], D[dEmdt, A_m] \}, \\ &\{ D[dPmdt, S], D[dPmdt, E_w], D[dPmdt, P_w], D[dPmdt, I_w], D[dPmdt, A_w], \\ &\quad D[dPmdt, E_m], D[dPmdt, P_m], D[dPmdt, I_m], D[dPmdt, A_m] \}, \\ &\{ D[dImdt, S], D[dImdt, E_w], D[dImdt, P_w], D[dImdt, I_w], D[dImdt, A_w], \\ &\quad D[dImdt, E_m], D[dImdt, P_m], D[dImdt, I_m], D[dImdt, A_m] \}, \\ &\{ D[dAmdt, S], D[dAmdt, E_w], D[dAmdt, P_w], D[dAmdt, I_w], D[dAmdt, A_w], \\ &\quad D[dAmdt, E_m], D[dAmdt, P_m], D[dAmdt, I_m], D[dAmdt, A_m] \} \} /. \text{start}; \end{aligned}$$

In the special case where the exposed class is highly transitory and most infections occur during the pre-symptomatic phase, we have the simpler equations:

$$\begin{aligned} dPwdt &= (1-f) * \beta_P * P_w - \kappa_P * P_w \\ dPmdt &= (1-f_m) * \beta_{Pm} * P_m - \kappa_{Pm} * P_m; \end{aligned}$$

The change in allele frequency,  $p = \frac{P_m}{P_m + P_w}$ , is thus given by  $\frac{dp}{dt} = \frac{d\left(\frac{P_m}{P_m + P_w}\right)}{dt}$ , which is:

$$D\left[\frac{Pm[t]}{Pw[t] + Pm[t]}, t\right] /. Pm'[t] \rightarrow (1 - fm) * \beta Pm + S Pm - \kappa Pm * Pm /. Pw'[t] \rightarrow (1 - f) * \beta P * S * Pw - \kappa P * Pw /. Pm[t] \rightarrow Pm /. Pw[t] \rightarrow Pw /. fm \rightarrow f + \Delta f /. \beta Pm \rightarrow \beta P + \Delta \beta /. \kappa Pm \rightarrow \kappa P + \Delta \kappa /. \{Pm \rightarrow p (Pm + Pw), Pw \rightarrow (1 - p) (Pm + Pw)\} // Factor$$

$$(-1 + p) p (S \beta P \Delta f - S \Delta \beta + f S \Delta \beta + S \Delta f \Delta \beta + \Delta \kappa)$$

Assuming that  $\Delta f \Delta \beta$  is small, relative to the other terms (weak selection), gives equations (1) and (2).

Returning to the generic model:

**stabmat // MatrixForm**

$$\begin{pmatrix} 0 & 0 & -S \beta P & -S \beta I & -S \beta A & 0 & -S \beta P & -S \beta Im & -S \beta Am \\ 0 & -\kappa E & S \beta P & S \beta I & S \beta A & 0 & 0 & 0 & 0 \\ 0 & (1 - f) \kappa E & -\kappa P & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & \kappa P & -\alpha - \kappa I & 0 & 0 & 0 & 0 & 0 \\ 0 & f \kappa E & 0 & 0 & -\kappa A & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -\kappa Em & S \beta Pm & S \beta Im & S \beta Am \\ 0 & 0 & 0 & 0 & 0 & (1 - fm) \kappa Em & -\kappa Pm & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & \kappa Pm & -\alpha m - \kappa Im & 0 \\ 0 & 0 & 0 & 0 & 0 & fm \kappa Em & 0 & 0 & -\kappa Am \end{pmatrix}$$

The eigenvalues,  $\lambda$ , are determined by the roots of the following characteristic polynomial:

**charpoly = Det[ $\lambda$  IdentityMatrix[9] - stabmat] // Factor**

$$\lambda \left( -S \alpha \beta P \kappa A \kappa E + f S \alpha \beta P \kappa A \kappa E - S \beta P \kappa A \kappa E \kappa I + f S \beta P \kappa A \kappa E \kappa I - f S \alpha \beta A \kappa E \kappa P + \alpha \kappa A \kappa E \kappa P - S \beta I \kappa A \kappa E \kappa P + f S \beta I \kappa A \kappa E \kappa P - f S \beta A \kappa E \kappa I \kappa P + \kappa A \kappa E \kappa I \kappa P - f S \alpha \beta A \kappa E \lambda - S \alpha \beta P \kappa E \lambda + f S \alpha \beta P \kappa E \lambda + \alpha \kappa A \kappa E \lambda - S \beta P \kappa A \kappa E \lambda + f S \beta P \kappa A \kappa E \lambda - f S \beta A \kappa E \kappa I \lambda - S \beta P \kappa E \kappa I \lambda + f S \beta P \kappa E \kappa I \lambda + \kappa A \kappa E \kappa I \lambda + \alpha \kappa A \kappa P \lambda + \alpha \kappa E \kappa P \lambda - f S \beta A \kappa E \kappa P \lambda - S \beta I \kappa E \kappa P \lambda + f S \beta I \kappa E \kappa P \lambda + \kappa A \kappa E \kappa P \lambda + \kappa A \kappa I \kappa P \lambda + \kappa E \kappa I \kappa P \lambda + \alpha \kappa A \lambda^2 + \alpha \kappa E \lambda^2 - f S \beta A \kappa E \lambda^2 - S \beta P \kappa E \lambda^2 + f S \beta P \kappa E \lambda^2 + \kappa A \kappa E \lambda^2 + \kappa A \kappa I \lambda^2 + \kappa E \kappa I \lambda^2 + \alpha \kappa P \lambda^2 + \kappa A \kappa P \lambda^2 + \kappa E \kappa P \lambda^2 + \kappa I \kappa P \lambda^2 + \alpha \lambda^3 + \kappa A \lambda^3 + \kappa E \lambda^3 + \kappa I \lambda^3 + \kappa P \lambda^3 + \lambda^4 \right) \\ (-S \alpha m \beta Pm \kappa Am \kappa Em + fm S \alpha m \beta Pm \kappa Am \kappa Em - S \beta Pm \kappa Am \kappa Em \kappa Im + fm S \beta Pm \kappa Am \kappa Em \kappa Im - fm S \alpha m \beta Am \kappa Em \kappa Pm + \alpha m \kappa Am \kappa Em \kappa Pm - S \beta Im \kappa Am \kappa Em \kappa Pm + fm S \beta Im \kappa Am \kappa Em \kappa Pm - fm S \beta Am \kappa Em \kappa Im \kappa Pm + \kappa Am \kappa Em \kappa Im \kappa Pm - fm S \alpha m \beta Am \kappa Em \lambda - S \alpha m \beta Pm \kappa Em \lambda + fm S \alpha m \beta Pm \kappa Em \lambda + \alpha m \kappa Am \kappa Em \lambda - S \beta Pm \kappa Am \kappa Em \lambda + fm S \beta Pm \kappa Am \kappa Em \lambda - fm S \beta Am \kappa Em \kappa Im \lambda - S \beta Pm \kappa Em \kappa Im \lambda + fm S \beta Pm \kappa Em \kappa Im \lambda + \kappa Am \kappa Em \kappa Im \lambda + \alpha m \kappa Am \kappa Pm \lambda + \alpha m \kappa Em \kappa Pm \lambda - fm S \beta Am \kappa Em \kappa Pm \lambda - S \beta Im \kappa Em \kappa Pm \lambda + fm S \beta Im \kappa Em \kappa Pm \lambda + \kappa Am \kappa Em \kappa Pm \lambda + \kappa Am \kappa Im \kappa Pm \lambda + \kappa Em \kappa Im \kappa Pm \lambda + \alpha m \kappa Am \lambda^2 + \alpha m \kappa Em \lambda^2 - fm S \beta Am \kappa Em \lambda^2 - S \beta Pm \kappa Em \lambda^2 + fm S \beta Pm \kappa Em \lambda^2 + \kappa Am \kappa Em \lambda^2 + \kappa Am \kappa Im \lambda^2 + \kappa Em \kappa Im \lambda^2 + \alpha m \kappa Pm \lambda^2 + \kappa Am \kappa Pm \lambda^2 + \kappa Em \kappa Pm \lambda^2 + \kappa Im \kappa Pm \lambda^2 + \alpha m \lambda^3 + \kappa Am \lambda^3 + \kappa Em \lambda^3 + \kappa Im \lambda^3 + \kappa Pm \lambda^3 + \lambda^4)$$

This separates into a characteristic polynomial describing the growth of the resident:

**poly = Collect[ charpoly[[2]],  $\lambda$ , Factor]**

$$\kappa E (-S \alpha \beta P \kappa A + f S \alpha \beta P \kappa A - S \beta P \kappa A \kappa I + f S \beta P \kappa A \kappa I - f S \alpha \beta A \kappa P + \alpha \kappa A \kappa P - S \beta I \kappa A \kappa P + f S \beta I \kappa A \kappa P - f S \beta A \kappa I \kappa P + \kappa A \kappa I \kappa P) + (-f S \alpha \beta A \kappa E - S \alpha \beta P \kappa E + f S \alpha \beta P \kappa E + \alpha \kappa A \kappa E - S \beta P \kappa A \kappa E + f S \beta P \kappa A \kappa E - f S \beta A \kappa E \kappa I - S \beta P \kappa E \kappa I + f S \beta P \kappa E \kappa I + \kappa A \kappa E \kappa I + \alpha \kappa A \kappa P - S \beta I \kappa A \kappa P - f S \beta I \kappa A \kappa P + f S \beta I \kappa E \kappa P + \kappa A \kappa E \kappa P + \kappa A \kappa I \kappa P + \kappa E \kappa I \kappa P) \lambda + (\alpha \kappa A + \alpha \kappa E - f S \beta A \kappa E - S \beta P \kappa E + f S \beta P \kappa E + \kappa A \kappa E + \kappa A \kappa I + \kappa E \kappa I + \alpha \kappa P + \kappa A \kappa P + \kappa E \kappa P + \kappa I \kappa P) \lambda^2 + (\alpha + \kappa A + \kappa E + \kappa I + \kappa P) \lambda^3 + \lambda^4$$

**poly /.  $\beta I \rightarrow 0$  /.  $\beta A \rightarrow 0$  // Factor**

$$(\kappa A + \lambda) (\alpha + \kappa I + \lambda) (-S \beta P \kappa E + f S \beta P \kappa E + \kappa E \kappa P + \kappa E \lambda + \kappa P \lambda + \lambda^2)$$

And a characteristic polynomial describing the growth of the mutant:

**polym = Collect[ charpoly[[3]],  $\lambda$ , Factor] /.  $\lambda \rightarrow \lambda m$**

$$\kappa Em (-S \alpha m \beta Pm \kappa Am + fm S \alpha m \beta Pm \kappa Am - S \beta Pm \kappa Am \kappa Im + fm S \beta Pm \kappa Am \kappa Im - fm S \alpha m \beta Am \kappa Pm + \alpha m \kappa Am \kappa Pm - S \beta Im \kappa Am \kappa Pm + fm S \beta Im \kappa Am \kappa Pm - fm S \beta Am \kappa Im \kappa Pm + \kappa Am \kappa Im \kappa Pm) + (-fm S \alpha m \beta Am \kappa Em - S \alpha m \beta Pm \kappa Em + fm S \alpha m \beta Pm \kappa Em + \alpha m \kappa Am \kappa Em - S \beta Pm \kappa Am \kappa Em + fm S \beta Pm \kappa Am \kappa Em - fm S \beta Am \kappa Em \kappa Im - S \beta Pm \kappa Em \kappa Im + fm S \beta Pm \kappa Em \kappa Im + \kappa Am \kappa Em \kappa Im + \alpha m \kappa Am \kappa Pm + \alpha m \kappa Em \kappa Pm - fm S \beta Am \kappa Em \kappa Pm - S \beta Im \kappa Em \kappa Pm + fm S \beta Im \kappa Em \kappa Pm + \kappa Am \kappa Em \kappa Pm + \kappa Am \kappa Im \kappa Pm + \kappa Em \kappa Im \kappa Pm) \lambda m + (\alpha m \kappa Am + \alpha m \kappa Em - fm S \beta Am \kappa Em - S \beta Pm \kappa Em + fm S \beta Pm \kappa Em + \kappa Am \kappa Em + \kappa Am \kappa Im + \kappa Em \kappa Im + \alpha m \kappa Pm + \kappa Am \kappa Pm + \kappa Em \kappa Pm + \kappa Im \kappa Pm) \lambda m^2 + (\alpha m + \kappa Am + \kappa Em + \kappa Im + \kappa Pm) \lambda m^3 + \lambda m^4$$

As expected, when most individuals are susceptible, mutations spread independently and the one with the largest eigenvalue will spread fastest. To determine the difference in the leading eigenvalue, we assume that the mutational effects are small (all of the “m” terms above are near the wildtype rate, with the difference of order  $\epsilon$ ). We can then calculate  $\Delta \lambda m = \lambda m - \lambda$ , by taking the Taylor series and solving the characteristic polynomial for  $\Delta \lambda m$ .

**smallmutant = { $\alpha m \rightarrow \alpha + \epsilon * \Delta \alpha$ ,  $fm \rightarrow f + \epsilon * \Delta f$ ,  $\kappa Im \rightarrow \kappa I + \epsilon * \Delta \kappa I$ ,  $\kappa Em \rightarrow \kappa E + \epsilon * \Delta \kappa E$ ,  $\kappa Am \rightarrow \kappa A + \epsilon * \Delta \kappa A$ ,  $\kappa Pm \rightarrow \kappa P + \epsilon * \Delta \kappa P$ ,  $\beta Am \rightarrow \beta A + \epsilon * \Delta \beta A$ ,  $\beta Pm \rightarrow \beta P + \epsilon * \Delta \beta P$ ,  $\beta Im \rightarrow \beta I + \epsilon * \Delta \beta I$ };**  
**smallterms = { $\Delta \alpha$ ,  $\Delta f$ ,  $\Delta \kappa I$ ,  $\Delta \kappa E$ ,  $\Delta \kappa A$ ,  $\Delta \kappa P$ ,  $\Delta \beta A$ ,  $\Delta \beta P$ ,  $\Delta \beta I$ };**

As expected, polym is zero to O(1) (reduces to poly for the wildtype, which is zero by definition of the eigenvalues):

**Factor[Normal[Series[polym /.  $\lambda m \rightarrow \lambda + \epsilon * \Delta \lambda m$  /. smallmutant, { $\epsilon$ , 0, 0}]]]**

$$-S \alpha \beta P \kappa A \kappa E + f S \alpha \beta P \kappa A \kappa E - S \beta P \kappa A \kappa E \kappa I + f S \beta P \kappa A \kappa E \kappa I - f S \alpha \beta A \kappa E \kappa P + \alpha \kappa A \kappa E \kappa P - S \beta I \kappa A \kappa E \kappa P + f S \beta I \kappa A \kappa E \kappa P - f S \beta A \kappa E \kappa I \kappa P + \kappa A \kappa E \kappa I \kappa P - f S \alpha \beta A \kappa E \lambda - S \alpha \beta P \kappa E \lambda + f S \alpha \beta P \kappa E \lambda + \alpha \kappa A \kappa E \lambda - S \beta P \kappa A \kappa E \lambda + f S \beta P \kappa A \kappa E \lambda - f S \beta A \kappa E \kappa I \lambda - S \beta P \kappa E \kappa I \lambda + f S \beta P \kappa E \kappa I \lambda + \kappa A \kappa E \kappa I \lambda + \alpha \kappa A \kappa P \lambda + \alpha \kappa E \kappa P \lambda - f S \beta A \kappa E \kappa P \lambda - S \beta I \kappa E \kappa P \lambda + f S \beta I \kappa E \kappa P \lambda + \kappa A \kappa E \kappa P \lambda + \kappa A \kappa I \kappa P \lambda + \kappa E \kappa I \kappa P \lambda + \alpha \kappa A \lambda^2 + \alpha \kappa E \lambda^2 - f S \beta A \kappa E \lambda^2 - S \beta P \kappa E \lambda^2 + f S \beta P \kappa E \lambda^2 + \kappa A \kappa E \lambda^2 + \kappa A \kappa I \lambda^2 + \kappa E \kappa I \lambda^2 + \alpha \kappa P \lambda^2 + \kappa A \kappa P \lambda^2 + \kappa E \kappa P \lambda^2 + \kappa I \kappa P \lambda^2 + \alpha \lambda^3 + \kappa A \lambda^3 + \kappa E \lambda^3 + \kappa I \lambda^3 + \kappa P \lambda^3 + \lambda^4$$

**Factor [% - poly]**

0

To order  $\epsilon$ , we can find effect of the mutation on the rate of growth,  $\Delta\lambda m$ :

**Factor[SeriesCoefficient[Series[poly /.  $\lambda m \rightarrow \lambda + \epsilon * \Delta\lambda m$  /. smallmutant, { $\epsilon$ , 0, 1}], 1]];**  
**Factor[Flatten[Solve[% == 0,  $\Delta\lambda m$ ]]]**

$$\left\{ \Delta\lambda m \rightarrow \begin{aligned} & - \left( S \alpha \beta P \Delta k E \kappa A - f S \alpha \beta P \Delta k E \kappa A + S \alpha \beta P \Delta k A \kappa E - f S \alpha \beta P \Delta k A \kappa E + f S \alpha \beta A \Delta k P \kappa E - S \alpha \beta P \Delta f \kappa A \kappa E + S \beta P \Delta \alpha \kappa A \kappa E - f S \beta P \Delta \alpha \kappa A \right. \\ & \quad \kappa E + S \alpha \Delta \beta P \kappa A \kappa E - f S \alpha \Delta \beta P \kappa A \kappa E + S \beta P \Delta \kappa I \kappa A \kappa E - f S \beta P \Delta \kappa I \kappa A \kappa E - \alpha \Delta \kappa P \kappa A \kappa E + S \beta I \Delta \kappa P \kappa A \kappa E - f S \beta I \Delta \kappa P \kappa A \kappa E + \\ & \quad S \beta P \Delta k E \kappa A \kappa I - f S \beta P \Delta k E \kappa A \kappa I + S \beta P \Delta k A \kappa E \kappa I - f S \beta P \Delta k A \kappa E \kappa I + f S \beta A \Delta k P \kappa E \kappa I - S \beta P \Delta f \kappa A \kappa E \kappa I + \\ & \quad S \Delta \beta P \kappa A \kappa E \kappa I - f S \Delta \beta P \kappa A \kappa E \kappa I - \Delta \kappa P \kappa A \kappa E \kappa I + f S \alpha \beta A \Delta k E \kappa P - \alpha \Delta k E \kappa A \kappa P + S \beta I \Delta k E \kappa A \kappa P - f S \beta I \Delta k E \kappa A \kappa P + \\ & \quad S \alpha \beta A \Delta f \kappa E \kappa P + f S \beta A \Delta \alpha \kappa E \kappa P - \alpha \Delta k A \kappa E \kappa P + S \beta I \Delta k A \kappa E \kappa P - f S \beta I \Delta k A \kappa E \kappa P + f S \beta A \Delta \kappa I \kappa E \kappa P - \\ & \quad S \beta I \Delta f \kappa A \kappa E \kappa P - \Delta \alpha \kappa A \kappa E \kappa P + S \Delta \beta I \kappa A \kappa E \kappa P - f S \Delta \beta I \kappa A \kappa E \kappa P - \Delta \kappa I \kappa A \kappa E \kappa P + f S \beta A \Delta k E \kappa I \kappa P - \Delta k E \kappa A \kappa I \kappa P + \\ & \quad S \beta A \Delta f \kappa E \kappa I \kappa P + f S \Delta \beta A \kappa E \kappa I \kappa P - \Delta k A \kappa E \kappa I \kappa P + f S \alpha \beta A \Delta k E \lambda + S \alpha \beta P \Delta k E \lambda - f S \alpha \beta P \Delta k E \lambda - \alpha \Delta k E \kappa A \lambda + S \beta P \Delta k E \kappa A \lambda - \\ & \quad f S \beta P \Delta k E \kappa A \lambda - \alpha \Delta \kappa P \kappa A \lambda + S \alpha \beta A \Delta f \kappa E \lambda - S \alpha \beta P \Delta f \kappa E \lambda + f S \beta A \Delta \alpha \kappa E \lambda + S \beta P \Delta \alpha \kappa E \lambda - f S \beta P \Delta \alpha \kappa E \lambda + f S \alpha \Delta \beta A \kappa E \lambda + \\ & \quad S \alpha \Delta \beta P \kappa E \lambda - f S \alpha \Delta \beta P \kappa E \lambda - \alpha \Delta k A \kappa E \lambda + S \beta P \Delta k A \kappa E \lambda - f S \beta P \Delta k A \kappa E \lambda + f S \beta A \Delta \kappa I \kappa E \lambda + S \beta P \Delta \kappa I \kappa E \lambda - f S \beta P \Delta \kappa I \kappa E \lambda - \\ & \quad \alpha \Delta \kappa P \kappa E \lambda + f S \beta A \Delta \kappa P \kappa E \lambda + S \beta I \Delta \kappa P \kappa E \lambda - f S \beta I \Delta \kappa P \kappa E \lambda - S \beta P \Delta f \kappa A \kappa E \lambda - \Delta \alpha \kappa A \kappa E \lambda + S \Delta \beta P \kappa A \kappa E \lambda - f S \Delta \beta P \kappa A \kappa E \lambda - \\ & \quad \Delta \kappa I \kappa A \kappa E \lambda - \Delta \kappa P \kappa A \kappa E \lambda + f S \beta A \Delta k E \kappa I \lambda + S \beta P \Delta k E \kappa I \lambda - f S \beta P \Delta k E \kappa I \lambda - \Delta k E \kappa A \kappa I \lambda - \Delta \kappa P \kappa A \kappa I \lambda + S \beta A \Delta f \kappa E \kappa I \lambda - \\ & \quad S \beta P \Delta f \kappa E \kappa I \lambda + f S \Delta \beta A \kappa E \kappa I \lambda + S \Delta \beta P \kappa E \kappa I \lambda - f S \Delta \beta P \kappa E \kappa I \lambda - \Delta k A \kappa E \kappa I \lambda - \Delta \kappa P \kappa E \kappa I \lambda - \alpha \Delta k A \kappa P \lambda - \alpha \Delta k E \kappa P \lambda + \\ & \quad f S \beta A \Delta k E \kappa P \lambda + S \beta I \Delta k E \kappa P \lambda - f S \beta I \Delta k E \kappa P \lambda - \Delta \alpha \kappa A \kappa P \lambda - \Delta k E \kappa A \kappa P \lambda - \Delta \kappa I \kappa A \kappa P \lambda + S \beta A \Delta f \kappa E \kappa P \lambda - S \beta I \Delta f \kappa E \kappa P \lambda - \\ & \quad \Delta \alpha \kappa E \kappa P \lambda + f S \Delta \beta A \kappa E \kappa P \lambda + S \Delta \beta I \kappa E \kappa P \lambda - f S \Delta \beta I \kappa E \kappa P \lambda - \Delta k A \kappa E \kappa P \lambda - \Delta \kappa I \kappa E \kappa P \lambda - \Delta k A \kappa I \kappa P \lambda - \Delta k E \kappa I \kappa P \lambda - \\ & \quad \alpha \Delta k A \lambda^2 - \alpha \Delta k E \lambda^2 + f S \beta A \Delta k E \lambda^2 + S \beta P \Delta k E \lambda^2 - f S \beta P \Delta k E \lambda^2 - \alpha \Delta \kappa P \lambda^2 - \Delta \alpha \kappa A \lambda^2 - \Delta k E \kappa A \lambda^2 - \Delta \kappa I \kappa A \lambda^2 - \Delta \kappa P \kappa A \lambda^2 + \\ & \quad S \beta A \Delta f \kappa E \lambda^2 - S \beta P \Delta f \kappa E \lambda^2 - \Delta \alpha \kappa E \lambda^2 + f S \Delta \beta A \kappa E \lambda^2 + S \Delta \beta P \kappa E \lambda^2 - f S \Delta \beta P \kappa E \lambda^2 - \Delta k A \kappa E \lambda^2 - \Delta \kappa I \kappa E \lambda^2 - \Delta \kappa P \kappa E \lambda^2 - \\ & \quad \Delta k A \kappa I \lambda^2 - \Delta k E \kappa I \lambda^2 - \Delta \alpha \kappa P \lambda^2 - \Delta k A \kappa P \lambda^2 - \Delta k E \kappa P \lambda^2 - \Delta \kappa I \kappa P \lambda^2 - \Delta \alpha \lambda^3 - \Delta k A \lambda^3 - \Delta k E \lambda^3 - \Delta \kappa I \lambda^3 - \Delta \kappa P \lambda^3 \Big) / \\ & \left( f S \alpha \beta A \kappa E + S \alpha \beta P \kappa E - f S \alpha \beta P \kappa E - \alpha \kappa A \kappa E + S \beta P \kappa A \kappa E - f S \beta P \kappa A \kappa E + f S \beta A \kappa E \kappa I + S \beta P \kappa E \kappa I - \right. \\ & \quad f S \beta P \kappa E \kappa I - \kappa A \kappa E \kappa I - \alpha \kappa A \kappa P - \alpha \kappa E \kappa P + f S \beta A \kappa E \kappa P + S \beta I \kappa E \kappa P - f S \beta I \kappa E \kappa P - \kappa A \kappa E \kappa P - \kappa A \kappa I \kappa P - \\ & \quad \kappa E \kappa I \kappa P - 2 \alpha \kappa A \lambda - 2 \alpha \kappa E \lambda + 2 f S \beta A \kappa E \lambda + 2 S \beta P \kappa E \lambda - 2 f S \beta P \kappa E \lambda - 2 \kappa A \kappa E \lambda - 2 \kappa A \kappa I \lambda - \\ & \quad \left. 2 \kappa E \kappa I \lambda - 2 \alpha \kappa P \lambda - 2 \kappa A \kappa P \lambda - 2 \kappa E \kappa P \lambda - 2 \kappa I \kappa P \lambda - 3 \alpha \lambda^2 - 3 \kappa A \lambda^2 - 3 \kappa E \lambda^2 - 3 \kappa I \lambda^2 - 3 \kappa P \lambda^2 - 4 \lambda^3 \right) \} \end{aligned}$$

The denominator is shared and equals the slope of the characteristic polynomial at the leading eigenvalue (positive given the form of the cubic):

**denom = D[poly,  $\lambda$ ] // Factor**

$$\begin{aligned} & - f S \alpha \beta A \kappa E - S \alpha \beta P \kappa E + f S \alpha \beta P \kappa E + \alpha \kappa A \kappa E - S \beta P \kappa A \kappa E + f S \beta P \kappa A \kappa E - f S \beta A \kappa E \kappa I - \\ & S \beta P \kappa E \kappa I + f S \beta P \kappa E \kappa I + \kappa A \kappa E \kappa I + \alpha \kappa A \kappa P + \alpha \kappa E \kappa P - f S \beta A \kappa E \kappa P - S \beta I \kappa E \kappa P + f S \beta I \kappa E \kappa P + \kappa A \kappa E \kappa P + \\ & \kappa A \kappa I \kappa P + \kappa E \kappa I \kappa P + 2 \alpha \kappa A \lambda + 2 \alpha \kappa E \lambda - 2 f S \beta A \kappa E \lambda - 2 S \beta P \kappa E \lambda + 2 f S \beta P \kappa E \lambda + 2 \kappa A \kappa E \lambda + 2 \kappa A \kappa I \lambda + \\ & 2 \kappa E \kappa I \lambda + 2 \alpha \kappa P \lambda + 2 \kappa A \kappa P \lambda + 2 \kappa E \kappa P \lambda + 2 \kappa I \kappa P \lambda + 3 \alpha \lambda^2 + 3 \kappa A \lambda^2 + 3 \kappa E \lambda^2 + 3 \kappa I \lambda^2 + 3 \kappa P \lambda^2 + 4 \lambda^3 \end{aligned}$$

**selection = Collect[denom  $\Delta\lambda m$  / slope /. %, smallterms, Factor]**

$$\begin{aligned} & - \frac{(-1 + f) S \Delta \beta I \kappa E \kappa P (\kappa A + \lambda)}{\text{slope}} - \frac{(-1 + f) S \Delta \beta P \kappa E (\kappa A + \lambda) (\alpha + \kappa I + \lambda)}{\text{slope}} + \frac{f S \Delta \beta A \kappa E (\alpha + \kappa I + \lambda) (\kappa P + \lambda)}{\text{slope}} - \frac{1}{\text{slope}} S \Delta f \kappa E \\ & \left( \alpha \beta P \kappa A + \beta P \kappa A \kappa I - \alpha \beta A \kappa P + \beta I \kappa A \kappa P - \beta A \kappa I \kappa P - \alpha \beta A \lambda + \alpha \beta P \lambda + \beta P \kappa A \lambda - \beta A \kappa I \lambda + \beta P \kappa I \lambda - \beta A \kappa P \lambda + \beta I \kappa P \lambda - \beta A \lambda^2 + \beta P \lambda^2 \right) + \\ & \frac{1}{\text{slope}} \Delta \kappa P \left( f S \alpha \beta A \kappa E - \alpha \kappa A \kappa E + S \beta I \kappa A \kappa E - f S \beta I \kappa A \kappa E + f S \beta A \kappa E \kappa I - \kappa A \kappa E \kappa I - \alpha \kappa A \lambda - \alpha \kappa E \lambda + \right. \\ & \quad \left. f S \beta A \kappa E \lambda + S \beta I \kappa E \lambda - f S \beta I \kappa E \lambda - \kappa A \kappa E \lambda - \kappa A \kappa I \lambda - \kappa E \kappa I \lambda - \alpha \lambda^2 - \kappa A \lambda^2 - \kappa E \lambda^2 - \kappa I \lambda^2 - \lambda^3 \right) + \\ & \frac{1}{\text{slope}} \Delta \alpha \left( S \beta P \kappa A \kappa E - f S \beta P \kappa A \kappa E + f S \beta A \kappa E \kappa P - \kappa A \kappa E \kappa P + f S \beta A \kappa E \lambda + S \beta P \kappa E \lambda - f S \beta P \kappa E \lambda - \kappa A \kappa E \lambda - \right. \\ & \quad \left. \kappa A \kappa P \lambda - \kappa E \kappa P \lambda - \kappa A \lambda^2 - \kappa E \lambda^2 - \kappa P \lambda^2 - \lambda^3 \right) + \frac{1}{\text{slope}} \Delta \kappa I \left( S \beta P \kappa A \kappa E - f S \beta P \kappa A \kappa E + f S \beta A \kappa E \kappa P - \right. \\ & \quad \left. \kappa A \kappa E \kappa P + f S \beta A \kappa E \lambda + S \beta P \kappa E \lambda - f S \beta P \kappa E \lambda - \kappa A \kappa E \lambda - \kappa A \kappa P \lambda - \kappa E \kappa P \lambda - \kappa A \lambda^2 - \kappa E \lambda^2 - \kappa P \lambda^2 - \lambda^3 \right) + \\ & \frac{1}{\text{slope}} \Delta \kappa E \left( S \alpha \beta P \kappa A - f S \alpha \beta P \kappa A + S \beta P \kappa A \kappa I - f S \beta P \kappa A \kappa I + f S \alpha \beta A \kappa P - \alpha \kappa A \kappa P + S \beta I \kappa A \kappa P - f S \beta I \kappa A \kappa P + f S \beta A \kappa I \kappa P - \right. \\ & \quad \left. \kappa A \kappa I \kappa P + f S \alpha \beta A \lambda + S \alpha \beta P \lambda - f S \alpha \beta P \lambda - \alpha \kappa A \lambda + S \beta P \kappa A \lambda - f S \beta P \kappa A \lambda + f S \beta A \kappa I \lambda + S \beta P \kappa I \lambda - f S \beta P \kappa I \lambda - \kappa A \kappa I \lambda - \right. \\ & \quad \left. \alpha \kappa P \lambda + f S \beta A \kappa P \lambda + S \beta I \kappa P \lambda - f S \beta I \kappa P \lambda - \kappa A \kappa P \lambda - \kappa I \kappa P \lambda - \alpha \lambda^2 + f S \beta A \lambda^2 + S \beta P \lambda^2 - f S \beta P \lambda^2 - \kappa A \lambda^2 - \kappa I \lambda^2 - \kappa P \lambda^2 - \lambda^3 \right) - \\ & \frac{1}{\text{slope}} \Delta \kappa A \left( - S \alpha \beta P \kappa E + f S \alpha \beta P \kappa E - S \beta P \kappa E \kappa I + f S \beta P \kappa E \kappa I + \alpha \kappa E \kappa P - S \beta I \kappa E \kappa P + f S \beta I \kappa E \kappa P + \kappa E \kappa I \kappa P + \right. \\ & \quad \left. \alpha \kappa E \lambda - S \beta P \kappa E \lambda + f S \beta P \kappa E \lambda + \kappa E \kappa I \lambda + \alpha \kappa P \lambda + \kappa E \kappa P \lambda + \kappa I \kappa P \lambda + \alpha \lambda^2 + \kappa E \lambda^2 + \kappa I \lambda^2 + \kappa P \lambda^2 + \lambda^3 \right) \end{aligned}$$

We can also understand selection on mutants by using the method in Box 10.2 of Otto and Day, calculating selection as

$$\frac{d\lambda}{dz} = \frac{v^T \frac{dM}{dz} u}{v^T u}, \text{ where } z \text{ represents some underlying trait that the mutation affects (e.g., replication rate) and } v^T \text{ and } u \text{ are}$$

the left and right eigenvectors of  $M$ , the matrix describing movement between the infected classes for the resident:

```
submat = stabmat[[2 ;; 5, 2 ;; 5]];
% // MatrixForm
```

$$\begin{pmatrix} -\kappa E & S \beta P & S \beta I & S \beta A \\ (1-f) \kappa E & -\kappa P & 0 & 0 \\ 0 & \kappa P & -\alpha - \kappa I & 0 \\ f \kappa E & 0 & 0 & -\kappa A \end{pmatrix}$$

and for the mutant:

```
submatm = stabmat[[6 ;; 9, 6 ;; 9]];
% // MatrixForm
```

$$\begin{pmatrix} -\kappa Em & S \beta Pm & S \beta Im & S \beta Am \\ (1-fm) \kappa Em & -\kappa Pm & 0 & 0 \\ 0 & \kappa Pm & -\alpha m - \kappa Im & 0 \\ fm \kappa Em & 0 & 0 & -\kappa Am \end{pmatrix}$$

Calculating the relative reproductive values (the left eigenvector):

```
left = {vE, vP, vI, vA};
```

```
left.submat - λ left
```

```
{f vA κE - vE κE + (1 - f) vP κE - vE λ, S vE βP + vI κP - vP κP - vP λ, S vE βI + vI (-α - κI) - vI λ, S vE βA - vA κA - vA λ}
```

```
leftvector = left /. Flatten[Solve[(%[[2 ;; 4]]) == 0, Table[left[[i]], {i, 2, 4}]]] // Simplify
```

$$\left\{ vE, \frac{S vE (\alpha \beta P + \beta I \kappa P + \beta P (\kappa I + \lambda))}{(\alpha + \kappa I + \lambda) (\kappa P + \lambda)}, \frac{S vE \beta I}{\alpha + \kappa I + \lambda}, \frac{S vE \beta A}{\kappa A + \lambda} \right\}$$

In addition, the fact that the characteristic polynomial is zero guarantees that the first term in  $v M - v \lambda$  is also zero:

```
((left.submat - λ left)[[1]] /. Table[left[[i]] → leftvector[[i]], {i, 1, 4}]) // Factor) /. Factor[poly] → 0
```

```
0
```

Calculating the proportion in each class (the right eigenvector):

```
right = {uE, uP, uI, uA};
```

```
submat.right - λ right
```

```
{S uA βA + S uI βI + S uP βP - uE κE - uE λ, (1 - f) uE κE - uP κP - uP λ, uI (-α - κI) + uP κP - uI λ, -uA κA + f uE κE - uA λ}
```

```
rightvector = right /. Flatten[Solve[(%[[2 ;; 4]]) == 0, Table[right[[i]], {i, 2, 4}]]] // Simplify
```

$$\left\{ uE, -\frac{(-1+f) uE \kappa E}{\kappa P + \lambda}, -\frac{(-1+f) uE \kappa E \kappa P}{(\alpha + \kappa I + \lambda) (\kappa P + \lambda)}, \frac{f uE \kappa E}{\kappa A + \lambda} \right\}$$

In addition, the fact that the characteristic polynomial is zero guarantees that the first term in  $v M - v \lambda$  is also zero:

```
((submat.right - λ right)[[1]] /. Table[right[[i]] → rightvector[[i]], {i, 1, 4}]) // Factor) /. Factor[poly] → 0
```

```
0
```

Note that the elements of both left and right eigenvectors are positive in a growing population ( $\lambda > 0$ ). Although the length of these eigenvectors is arbitrary, we constrain them so that  $v^T u$  in the denominator of  $\frac{d\lambda}{dz} = \frac{v^T \frac{dM}{dz} u}{v^T u}$  is one by rescaling the right eigenvector (choosing this one keeps the left eigenvector easier to read):

$$\text{rightvector} = \frac{\text{rightvector}}{\text{leftvector} \cdot \text{rightvector}};$$

$\frac{dM}{dz}$  represents the mutational effect on the transition matrix for a viral genotype:

```
mutmat = Factor[Normal[Series[submatm - submat /. smallmutant, {ε, 0, 1}]] /. ε → 1];
MatrixForm[%]
```

$$\begin{pmatrix} -\Delta \kappa E & S \Delta \beta P & S \Delta \beta I & S \Delta \beta A \\ \Delta \kappa E - f \Delta \kappa E - \Delta f \kappa E & -\Delta \kappa P & 0 & 0 \\ 0 & \Delta \kappa P & -\Delta \alpha - \Delta \kappa I & 0 \\ f \Delta \kappa E + \Delta f \kappa E & 0 & 0 & -\Delta \kappa A \end{pmatrix}$$

This gives us an equivalent way to write the selection coefficient on the mutation, using the fact that the characteristic polynomial is zero:

```
Factor[leftvector.mutmat.rightvector - (selection /. slope -> denom)] /. Factor[poly] → 0
```

```
0
```

Selection is thus proportional to:

```
Collect[Table[left[[i]], {i, 1, 4}].mutmat.Table[right[[i]], {i, 1, 4}], smallterms, Factor]
```

```
-uI vI Δα + S uA vE ΔβA + S uI vE ΔβI + S uP vE ΔβP - uA vA ΔκA +  
uE (f vA - vE + vP - f vP) ΔκE - uI vI ΔκI + uP (vI - vP) ΔκP + uE (vA - vP) Δf κE
```

```
S vE (uA ΔβA + uI ΔβI + uP ΔβP) - uI vI Δα + uE ((1-f)vP + f vA - vE) ΔκE + uE (vA - vP) Δf κE - uI vI ΔκI - uP (vP - vI) ΔκP - uA vA ΔκA
```

This way of calculating selection makes it clearer what selection acts upon when a disease is spreading ( $\lambda > 0$ ):

- \* Always favors increased transmission [ $\Delta\beta A$ ,  $\Delta\beta P$ ,  $\Delta\beta I$ ]
- \* Always favors lower virulence [ $\Delta\alpha$ ] and slower recovery [ $\Delta\kappa I$ ]
- \* Always favors faster progression from E  $\rightarrow$  A/P [ $\Delta\kappa E$ ] because  $(1-f)vP + f vA > vE$  [see Note 1]
- \* Favors slower progression from P  $\rightarrow$  I [ $\Delta\kappa P$ ] if  $vP > vI$  [always true if  $\beta I \leq \beta P (1 + 1/(D\lambda))$  - see Note 2]
- \* Favors more asymptomatic individuals [ $\Delta f$ ] only if  $vA > vP$  [true only with high enough  $\beta A$  - see Note 3]
- \* Never favors faster progression from A  $\rightarrow$  R [ $\Delta\kappa Am$ ]

[Note 1] In a spreading disease,  $(1-f)vP + f vA$  is always greater than  $vE$  because the next stage individuals (P&A) pass on the disease earlier than exposed individuals, contributing earlier to growth.

```
Factor[(1 - f) leftvector[[2]] + (f) leftvector[[4]] - leftvector[[1]] /. Solve[poly == 0, βP]]
```

$$\left\{ \frac{vE \lambda}{\kappa E} \right\}$$

[Note 2]  $vP$  is greater than  $vI$  as long as  $\beta I \leq \beta P (1 + (\alpha + \gamma)/(\lambda))$  because infected individuals have less time to pass on the disease than pre-asymptomatics.

```
Factor[leftvector[[3]] - leftvector[[2]]]
```

$$\frac{S vE (-\alpha \beta P - \beta P \kappa I + \beta I \lambda - \beta P \lambda)}{(\alpha + \kappa I + \lambda) (\kappa P + \lambda)}$$

```
Solve[% == 0, βI] // Simplify
```

$$\left\{ \left\{ \beta I \rightarrow \frac{\beta P (\alpha + \kappa I + \lambda)}{\lambda} \right\} \right\}$$

[Note 3]  $vP$  is greater than  $vA$  as long as presymptomatics are expected to give rise to enough more cases than asymptomatics that  $\frac{\beta P}{\kappa P + \lambda} \geq \frac{\beta A}{\kappa A + \lambda}$  (symptomatic infectious individuals make this condition even easier to satisfy).

```
Collect[leftvector[[4]] - leftvector[[2]], {βP, βI, βA}, Factor]
```

$$\frac{S vE \beta A}{\kappa A + \lambda} - \frac{S vE \beta P}{\kappa P + \lambda} - \frac{S vE \beta I \kappa P}{(\alpha + \kappa I + \lambda) (\kappa P + \lambda)}$$

### ■ Figure 3 - Numerical analyses

#### ■ Code

Common settings

```
Clear["Global`*"]  
  
Off[General::spell1]  
Off[General::spell]  
Off[NDSolve::nlnum]  
  
tfinal = 500;  
  
tfig = 500;  
  
label = {"Time (days)", "Frequency"};  
label = None;
```

```
parvec = {β, βm, α, am, xYP, xYPm, f, fm, xYE, xYI, xYA, c1, c2, c3, mut};
```

```
Clear[finalfreq, NSolution]
```

```
finalfreq[vec_] :=
```

```
finalfreq[vec] = Block[{β = vec[[1]], βm = vec[[2]], α = vec[[3]], am = vec[[4]], xYP = vec[[5]],  
xYPm = vec[[6]], f = vec[[7]], fm = vec[[8]], xYE = vec[[9]], xYI = vec[[10]],  
xYA = vec[[11]], c1 = vec[[12]], c2 = vec[[13]], c3 = vec[[14]], mut = vec[[15]]},
```

```
(*REMAINING PARAMETERS*)
```

```
βYA = β / 10; βYP = β; βYI = β / 3;
```

```
xYAm = xYA; xYIm = xYI;
```

```

βyAm = βm / 10; βyPm = βm; βyIm = βm / 3;

(* E: Exposed (non-infectious) cases *)
(* A: asymptomatic cases *)
(* P: pre-symptomatic cases *)
(* S: symptomatic cases *)
(* f: proportion of fsymptomatic hosts *)
(* c: amount of distancing applied *)

(*INOCULATION*)
start = 10-5;

t = .;
c = .;

c[t_] := Evaluate[If[t < t1min, 0,
  If[t < t1max, c1, If[t < t2min, 0, If[t < t2max, c2, If[t < t3min, 0, If[t < t3max, c3, 0]]]]]];
h[t] = (1 - c[t]) (βyA yA[t] + βyP yP[t] + βyI yI[t]);
hm[t] = (1 - c[t]) (βyAm yAm[t] + βyPm yPm[t] + βyIm yIm[t]);

sys = {S'[t] == -(h[t] + hm[t]) S[t],
  yE'[t] == h[t] S[t] - κyE yE[t],
  yA'[t] == f κyE yE[t] - κyA yA[t],
  yP'[t] == (1 - f) κyE yE[t] - κyP yP[t],
  yI'[t] == κyP yP[t] - (κyI + α) yI[t],
  yR'[t] == κyA yA[t] + κyI yI[t],
  yD'[t] == α yI[t]}; (*yD serves as a counter of the cumulative number of deaths*)

sysm = {
  yEm'[t] == hm[t] S[t] - κyE yEm[t],
  yAm'[t] == fm κyE yEm[t] - κyAm yAm[t],
  yPm'[t] == (1 - fm) κyE yEm[t] - κyPm yPm[t],
  yIm'[t] == κyPm yPm[t] - (κyIm + αm) yIm[t],
  yRm'[t] == κyAm yAm[t] + κyIm yIm[t],
  yDm'[t] == αm yIm[t]}; (*yDm serves as a counter of the cumulative number of deaths*)

(*FIRST BOUT OF CONTROL*)
t1min = 75;
t1max = 150;
(*SECOND BOUT OF CONTROL*)
t2min = 225;
t2max = 300;
(*THIRD BOUT OF CONTROL*)
t3min = 375;
t3max = 450;

init = {S[0] == 1, yE[0] == start (1 - mut), yA[0] == 0, yP[0] == 0, yI[0] == 0, yR[0] == 0, yD[0] == 0};
initm = {yEm[0] == start (mut), yAm[0] == 0, yPm[0] == 0, yIm[0] == 0, yRm[0] == 0, yDm[0] == 0};

var = {S, yE, yA, yP, yI, yR, yD};
varm = {yEm, yAm, yPm, yIm, yRm, yDm};

NSolution[vec] =
  NDSolve[
    Flatten[{sys, sysm, init, initm}], Flatten[{var, varm}], {t, 0, tfinal}, AccuracyGoal → 100];

(*R0*)
Print["R0 of the wild type = ",  $\frac{\beta yA f}{\kappa yA} + \frac{(1 - f) (\beta yP (\alpha + \kappa yI) + \beta yI \kappa yP)}{(\alpha + \kappa yI) \kappa yP}$ ];

(*Rm*)
Print["R0 of the mutant type = ",  $\frac{\beta yAm f}{\kappa yAm} + \frac{(1 - f) (\beta yPm (\alpha m + \kappa yIm) + \beta yIm \kappa yPm)}{(\alpha m + \kappa yIm) \kappa yPm}$ ];

(*CASE MORTALITY*)
Print["Case mortality = ",  $(1 - f) \frac{\alpha}{\kappa yI + \alpha}$ ];
Print["Case mortality (mutant) = ",  $(1 - fm) \frac{\alpha m}{\kappa yI + \alpha m}$ ];

(*CUMULATIVE MORTALITY*)
Print["Cumulative mortality (total) = ", yD[tfinal] + yDm[tfinal] /. Flatten[NSolution[vec]]];
Print["Cumulative mortality (mutant) = ", yDm[tfinal] /. Flatten[NSolution[vec]]];

```

■ Figure 3a: Evolution of transmission  $\beta$ , no control measures

```

pars = {β -> 1, βm -> 1.2, (*TRANSMISSION OF THE MUTANT*)
  α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
  κyP -> 1, κyPm -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

  f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
  κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
  κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
  κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

  (*Strength of control measures*)
  c1 -> 0, c2 -> 0, c3 -> 0
};

```

The doubling time of the disease when rare, as calculated from the eigenvalue ("poly") of the stability matrix:

```

Sort[Solve[
  (κE (-S α βP κA + f S α βP κA - S βP κA κI + f S βP κA κI - f S α βA κP + α κA κP - S βI κA κP + f S βI κA κP - f S βA κI κP + κA κI κP) +
    (-f S α βA κE - S α βP κE + f S α βP κE + α κA κE - S βP κA κE + f S βP κA κE - f S βA κE κI - S βP κE κI + f S βP κE κI +
      κA κE κI + α κA κP + α κE κP - f S βA κE κP - S βI κE κP + f S βI κE κP + κA κE κP + κA κI κP + κE κI κP) λ +
    (α κA + α κE - f S βA κE - S βP κE + f S βP κE + κA κE + κA κI + κE κI + α κP + κA κP + κE κP + κI κP) λ2 +
    (α + κA + κE + κI + κP) λ3 + λ4 /. S -> 1 /. βA -> β / 10 /. βP -> β /.
    βI -> β / 3 /. κA -> κyA /. κE -> κyE /. κP -> κyP /. κI -> κyI /. pars) == 0, λ]]

Solve[
  (Exp[
    λ
    t] ==
    2) /.
  Last[
    %],
  t]

{{λ -> -1.145}, {λ -> -0.431496}, {λ -> -0.115364}, {λ -> 0.126863}}

{{t -> 5.46374}}

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];
R0 of the wild type = 2.28263
R0 of the mutant type = 2.73916
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0167685
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut -> 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange -> {{0, tfig}, {10-7, 1}}, PlotStyle -> {{Thickness[0.005], Red}}, AspectRatio -> 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t -> tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange -> {{0, tfig}, {0, 1}},
  PlotStyle -> {{Thickness[0.008], Black}}, AspectRatio -> 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Blue}, AspectRatio -> 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling -> Axis, FillingStyle -> LightGray,
  PlotStyle -> None, Frame -> True, PlotRange -> {{0, tfig}, {0, 1}}, AspectRatio -> 0.75, Frame -> True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% ("], ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

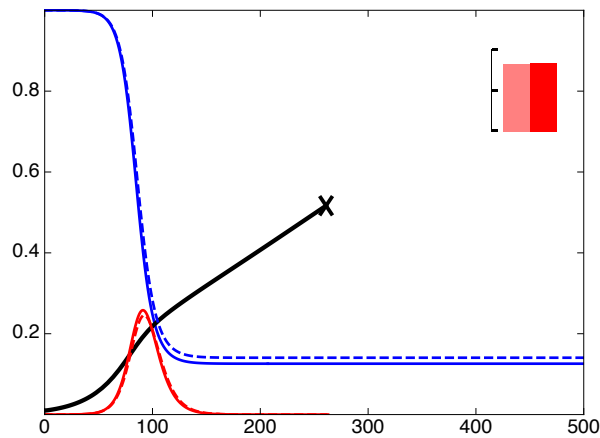
DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP1 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame -> True,
  TicksStyle -> Directive[Black, FontFamily -> "Helvetica", 11],
  LabelStyle -> Directive[12, FontFamily -> "Helvetica", Black],
  FrameTicks -> {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle -> {{Directive[FontSize -> 12], Directive[FontOpacity -> 0, FontSize -> 0]},
    {Directive[FontSize -> 12], Directive[FontOpacity -> 0, FontSize -> 0]}}
]

R0 of the wild type = 2.28263
R0 of the mutant type = 2.73916
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0170565
Cumulative mortality (mutant) = 0.00329928
261
{0.516598}

```





■ Figure 3b: Evolution of asymptomatic fraction  $f$ , no control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1$  -> 0,  $c_2$  -> 0,  $c_3$  -> 0
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.28263
R0 of the mutant type = 2.28263
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0167685
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

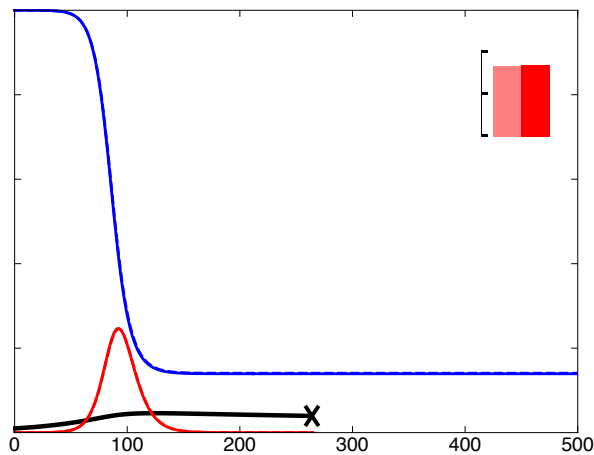
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% ("], ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP2 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.28263
R0 of the mutant type = 2.28263
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0168822
Cumulative mortality (mutant) = 0.000797917
264
{0.039494}

```



■ Figure 3c: Evolution of pre-symptomatic phase  $\kappa$ , no control measures

```

pars = {β -> 1, βm -> 1, (*TRANSMISSION OF THE MUTANT*)
  α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
  κyP -> 1, κyPm -> 2 / 3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

  f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
  κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
  κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
  κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

  (*Strength of control measures*)
  c1 -> 0, c2 -> 0, c3 -> 0
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.28263
R0 of the mutant type = 2.68263
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0167685
Cumulative mortality (mutant) = 0.
265

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

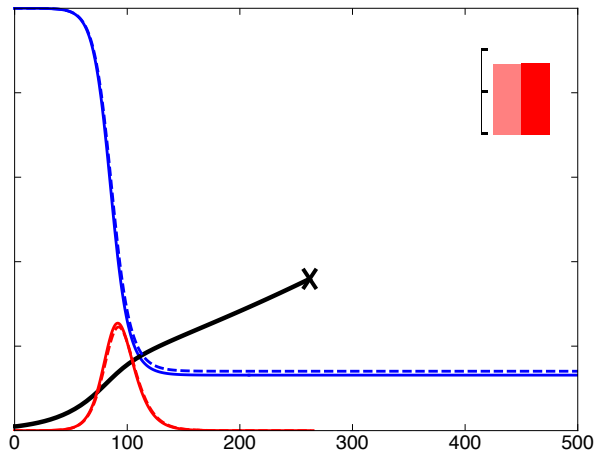
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% ("], ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP3 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.28263
R0 of the mutant type = 2.68263
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0169484
Cumulative mortality (mutant) = 0.00228206
262
{0.359268}

```



■ Figure 3d: Evolution of virulence  $\alpha$ , no control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.0, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1 -> 0, c2 -> 0, c3 -> 0
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.28263
R0 of the mutant type = 2.31515
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0167685
Cumulative mortality (mutant) = 0.
265

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

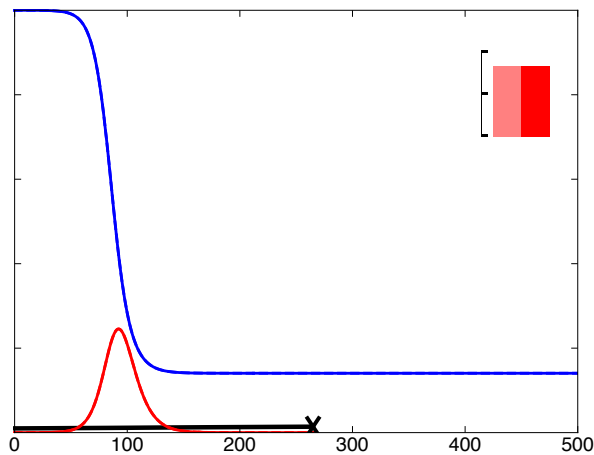
linel = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% ("], ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP4 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, linel, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.28263
R0 of the mutant type = 2.31515
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0165804
Cumulative mortality (mutant) = 0.
265
{0.0140646}

```



■ Figure 3e: Evolution of transmission  $\beta$ , control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1.2, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1 -> 0.6, c2 -> 0.6, c3 -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.28263
R0 of the mutant type = 2.73916
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0115874
Cumulative mortality (mutant) = 0.
449

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

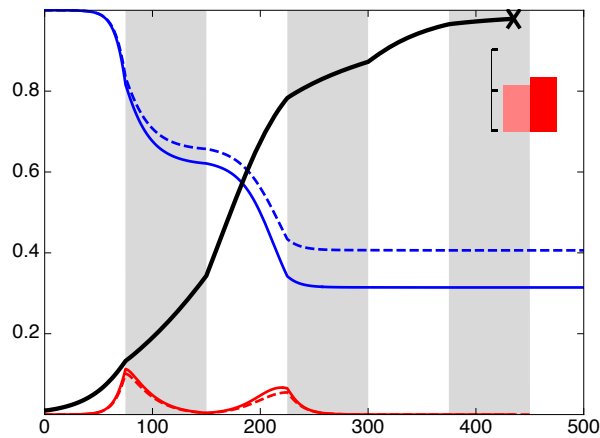
DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT1 = Show[fcontrol, fS, fSDashed, FIGfreq, fnoevol, fevol, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

R0 of the wild type = 2.28263
R0 of the mutant type = 2.73916
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0133774
Cumulative mortality (mutant) = 0.00545342
435
{0.979012}

```





■ Figure 3f: Evolution of asymptomatic fraction  $f$ , control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1$  -> 0.6,  $c_2$  -> 0.6,  $c_3$  -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.28263
R0 of the mutant type = 2.28263
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0115874
Cumulative mortality (mutant) = 0.
449

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

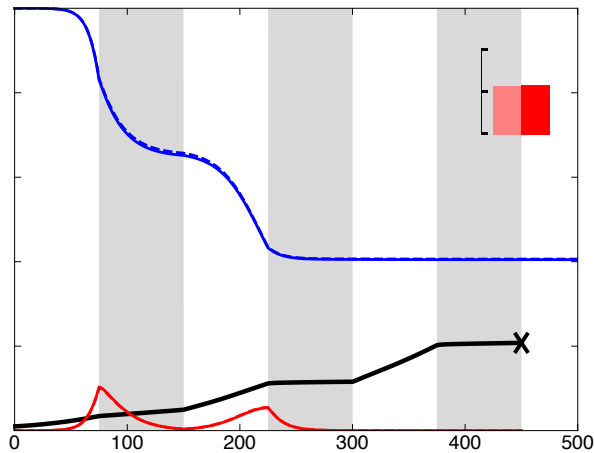
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT2 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

R0 of the wild type = 2.28263
R0 of the mutant type = 2.28263
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0117056
Cumulative mortality (mutant) = 0.000832288
450
{0.207847}

```



■ Figure 3g: Evolution of pre-symptomatic phase  $\kappa$ , control measures

```

pars = {β -> 1, βm -> 1, (*TRANSMISSION OF THE MUTANT*)
  α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
  κyP -> 1, κyPm -> 2 / 3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

  f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
  κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
  κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
  κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

  (*Strength of control measures*)
  c1 -> 0.6, c2 -> 0.6, c3 -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.28263
R0 of the mutant type = 2.68263
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0115874
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray, PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

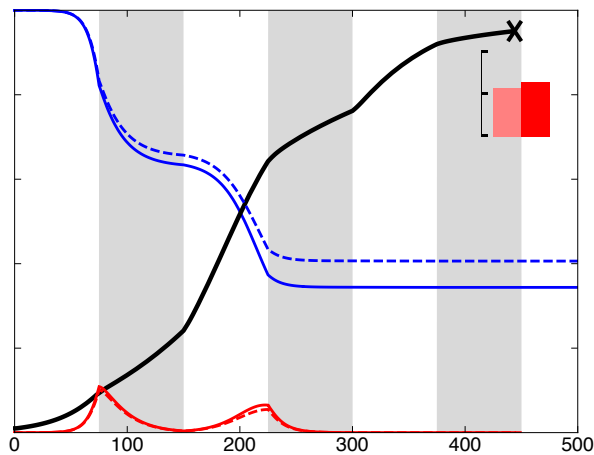
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}], Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT3 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True, TicksStyle → Directive[Black, FontFamily → "Helvetica", 11], LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}}, FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]}, {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}]
]

R0 of the wild type = 2.28263
R0 of the mutant type = 2.68263
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0128022
Cumulative mortality (mutant) = 0.00397109
444
{0.950803}

```



■ Figure 3h: Evolution of virulence  $\alpha$ , control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.00, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1$  -> 0.6,  $c_2$  -> 0.6,  $c_3$  -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.28263
R0 of the mutant type = 2.31515
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0115874
Cumulative mortality (mutant) = 0.
449

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

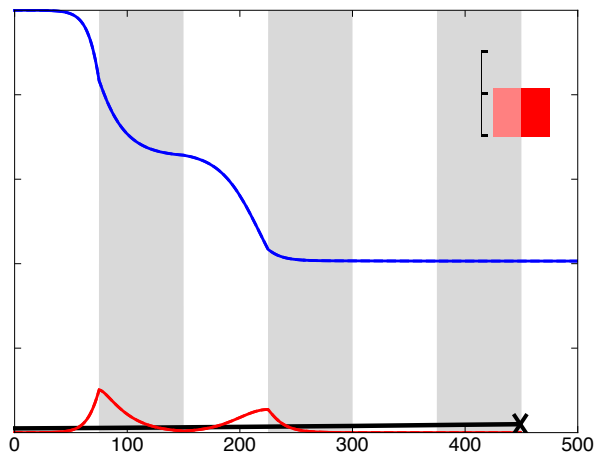
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT4 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

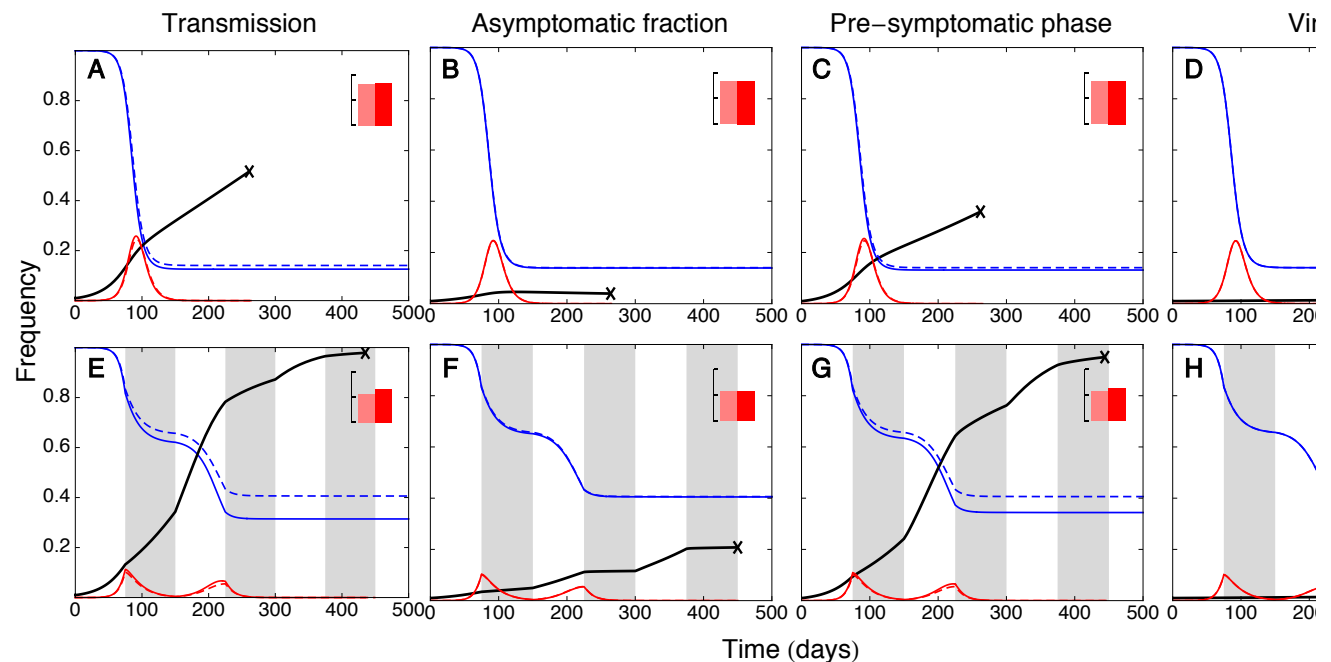
R0 of the wild type = 2.28263
R0 of the mutant type = 2.31515
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0114448
Cumulative mortality (mutant) = 0.
449
{0.0199521}

```



### ■ Altogether

```
Show[
GraphicsGrid[{{FigTOP1, FigTOP2, FigTOP3, FigTOP4}, {FigBOT1, FigBOT2, FigBOT3, FigBOT4}},
FrameLabel -> label, Spacings -> {-10, 10}],
Graphics[Text[Style["A", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {45, -33}]],
Graphics[Text[Style["B", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {379, -33}]],
Graphics[Text[Style["C", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {729, -33}]],
Graphics[Text[Style["D", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {1080, -33}]],
Graphics[Text[Style["E", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {45, -315}]],
Graphics[Text[Style["F", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {379, -315}]],
Graphics[Text[Style["G", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {729, -315}]],
Graphics[Text[Style["H", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {1080, -315}]],
Graphics[Text[Style["Transmission", 16, FontFamily -> "Helvetica"], {180, 10}]],
Graphics[Text[Style["Asymptomatic fraction", 16, FontFamily -> "Helvetica"], {520, 10}]],
Graphics[Text[Style["Pre-symptomatic phase", 16, FontFamily -> "Helvetica"], {870, 10}]],
Graphics[Text[Style["Virulence", 16, FontFamily -> "Helvetica"], {1220, 10}]],
Graphics[Text[Style["Time (days)", 16, FontFamily -> "Helvetica"], {700, -580}]],
Graphics[Rotate[Text[Style["Frequency", 16, FontFamily -> "Helvetica"], {-20, -270}], Pi / 2]]
]
```



### ■ Figure 4 - Numerical analyses

#### ■ Code

Common settings

```

Clear["Global`*"]

Off[General::spell1]
Off[General::spell]
Off[NDSolve::nlnum]

tfinal = 500;

tfig = 500;

label = {"Time (days)", "Frequency"};
label = None;

parvec = {β, βm, α, αm, x̄yP, x̄yPm, f, fm, x̄yE, x̄yI, x̄yA, c1, c2, c3, mut};

Clear[finalfreq, NSolution]
finalfreq[vec_] :=
finalfreq[vec] = Block[{β = vec[[1]], βm = vec[[2]], α = vec[[3]], αm = vec[[4]], x̄yP = vec[[5]],
  x̄yPm = vec[[6]], f = vec[[7]], fm = vec[[8]], x̄yE = vec[[9]], x̄yI = vec[[10]],
  x̄yA = vec[[11]], c1 = vec[[12]], c2 = vec[[13]], c3 = vec[[14]], mut = vec[[15]]},

  (*REMAINING PARAMETERS*)
  βyA = β / 10; βyP = β; βyI = β / 3;
  x̄yAm = x̄yA; x̄yIm = x̄yI;
  βyAm = βm / 10; βyPm = βm; βyIm = βm / 3;

  (* E: Exposed (non-infectious) cases *)
  (* A: asymptomatic cases *)
  (* P: pre-symptomatic cases *)
  (* S: symptomatic cases *)
  (* f: proportion of fsymptomatic hosts *)
  (* c: amount of distancing applied *)

  (*INOCULATION*)
  start = 10-5;

  t = .;
  c = .;

  c[t_] := Evaluate[If[t < t1min, 0,
    If[t < t1max, c1, If[t < t2min, 0, If[t < t2max, c2, If[t < t3min, 0, If[t < t3max, c3, 0]]]]]];
  h[t] = (1 - c[t]) (βyA yA[t] + βyP yP[t] + βyI yI[t]);
  hm[t] = (1 - c[t]) (βyAm yAm[t] + βyPm yPm[t] + βyIm yIm[t]);

  sys = {S'[t] == - (h[t] + hm[t]) S[t],
    yE'[t] == h[t] S[t] - x̄yE yE[t],
    yA'[t] == f x̄yE yE[t] - x̄yA yA[t],
    yP'[t] == (1 - f) x̄yE yE[t] - x̄yP yP[t],
    yI'[t] == x̄yP yP[t] - (x̄yI + α) yI[t],
    yR'[t] == x̄yA yA[t] + x̄yI yI[t],
    yD'[t] == α yI[t]}; (*yD serves as a counter of the cumulative number of deaths*)

  sysm = {
    yEm'[t] == hm[t] S[t] - x̄yE yEm[t],
    yAm'[t] == fm x̄yE yEm[t] - x̄yAm yAm[t],
    yPm'[t] == (1 - fm) x̄yE yEm[t] - x̄yPm yPm[t],
    yIm'[t] == x̄yPm yPm[t] - (x̄yIm + αm) yIm[t],
    yRm'[t] == x̄yAm yAm[t] + x̄yIm yIm[t],
    yDm'[t] == αm yIm[t]}; (*yDm serves as a counter of the cumulative number of deaths*)

  (*FIRST BOUT OF CONTROL*)
  t1min = 75;
  t1max = 150;
  (*SECOND BOUT OF CONTROL*)
  t2min = 225;
  t2max = 300;
  (*THIRD BOUT OF CONTROL*)
  t3min = 375;
  t3max = 450;

  init = {S[0] == 1, yE[0] == start (1 - mut), yA[0] == 0, yP[0] == 0, yI[0] == 0, yR[0] == 0, yD[0] == 0};
  initm = {yEm[0] == start (mut), yAm[0] == 0, yPm[0] == 0, yIm[0] == 0, yRm[0] == 0, yDm[0] == 0};

  var = {S, yE, yA, yP, yI, yR, yD};
  varm = {yEm, yAm, yPm, yIm, yRm, yDm};

  NSolution[vec] =
  NDSolve[
    Flatten[{sys, sysm, init, initm}], Flatten[{var, varm}], {t, 0, tfinal}, AccuracyGoal → 100];

```



```

(*R0*)
Print["R0 of the wild type = ",  $\frac{\beta y_A f}{\kappa y_A} + \frac{(1-f)(\beta y_P(\alpha + \kappa y_I) + \beta y_I \kappa y_P)}{(\alpha + \kappa y_I) \kappa y_P}$ ];

(*Rm*)
Print["R0 of the mutant type = ",  $\frac{\beta y_{Am} f}{\kappa y_{Am}} + \frac{(1-f)(\beta y_{Pm}(\alpha_m + \kappa y_{Im}) + \beta y_{Im} \kappa y_{Pm})}{(\alpha_m + \kappa y_{Im}) \kappa y_{Pm}}$ ];

(*CASE MORTALITY*)
Print["Case mortality = ",  $(1-f) \frac{\alpha}{\kappa y_I + \alpha}$ ];
Print["Case mortality (mutant) = ",  $(1-f_m) \frac{\alpha_m}{\kappa y_I + \alpha_m}$ ];

(*CUMULATIVE MORTALITY*)
Print["Cumulative mortality (total) = ", yD[tfinal] + yDm[tfinal] /. Flatten[NSolution[vec]]];
Print["Cumulative mortality (mutant) = ", yDm[tfinal] /. Flatten[NSolution[vec]]];
]

```

■ Figure 4a: Evolution with positive pleiotropy between transmission  $\beta$  and virulence  $\alpha$ , no control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1.2, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.01, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1 -> 0, c2 -> 0, c3 -> 0
};

Print["Case mortality = ",  $\frac{\alpha}{\kappa y_I + \alpha}$  /. pars];
Print["Case mortality (mutant) = ",  $\frac{\alpha_m}{\kappa y_I + \alpha_m}$  /. pars];

Case mortality = 0.0243902
Case mortality (mutant) = 0.047619

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.28263
R0 of the mutant type = 2.70199
Case mortality = 0.0195122
Case mortality (mutant) = 0.0380952
Cumulative mortality (total) = 0.0167685
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut -> 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange -> {{0, tfig}, {10^-7, 1}}, PlotStyle -> {{Thickness[0.005], Red}}, AspectRatio -> 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t -> tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {{Thickness[0.008], Black}}, AspectRatio -> 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig}, PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Blue}, AspectRatio -> 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling -> Axis, FillingStyle -> LightGray, PlotStyle -> None, Frame -> True, PlotRange -> {{0, tfig}, {0, 1}}, AspectRatio -> 0.75, Frame -> True];

line1 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10^-1]]], "% ("], ToString[N[Round[100 (mortalityevol), 10^-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}], Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP1 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame -> True, TicksStyle -> Directive[Black, FontFamily -> "Helvetica", 11], LabelStyle -> Directive[12, FontFamily -> "Helvetica", Black], FrameTicks -> {{N[{0, 0.2, 0.4, 0.6, 0.8, 1}], None}, {{0, 100, 200, 300, 400, 500}, None}}, FrameLabel -> {None, None}]

```

R0 of the wild type = 2.28263

R0 of the mutant type = 2.70199

Case mortality = 0.0195122

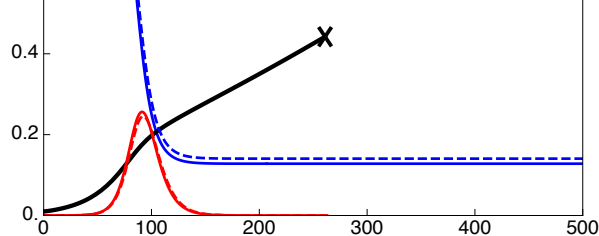
Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0198733

Cumulative mortality (mutant) = 0.00586488

261

{0.442172}



■ Figure 4b: Evolution with negative pleiotropy between transmission  $\beta$  and virulence  $\alpha$ , no control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1.2, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.000, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1 -> 0, c2 -> 0, c3 -> 0
};

Print["Case mortality = ",  $\frac{\alpha}{\kappa y_I + \alpha}$  /. pars];

Print["Case mortality (mutant) = ",  $\frac{\alpha_m}{\kappa y_I + \alpha_m}$  /. pars];

Case mortality = 0.0243902
Case mortality (mutant) = 0.

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.28263
R0 of the mutant type = 2.77818
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0167685
Cumulative mortality (mutant) = 0.
265

```

```

parset = parvec /. pars /. mut -> 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 1, tfig, 1}]], # > 10^-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange -> {{0, tfig}, {10^-7, 1}}, PlotStyle -> {{Thickness[0.005], Red}}, AspectRatio -> 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t -> tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {{Thickness[0.008], Black}}, AspectRatio -> 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig}, PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Blue}, AspectRatio -> 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling -> Axis, FillingStyle -> LightGray, PlotStyle -> None, Frame -> True, PlotRange -> {{0, tfig}, {0, 1}}, AspectRatio -> 0.75, Frame -> True];

line1 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10^-1]]], "% ("], ToString[N[Round[100 (mortalityevol), 10^-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

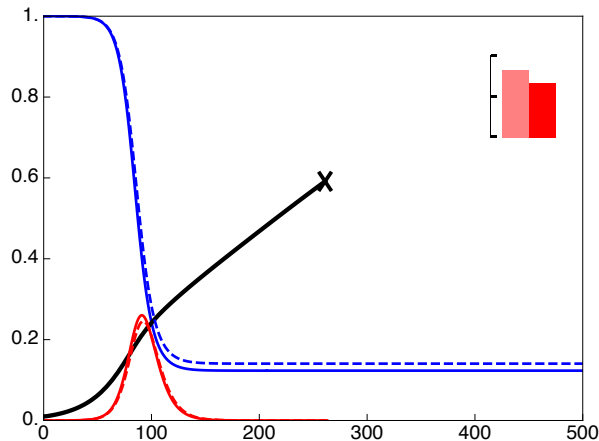
DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}], Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP2 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame -> True, TicksStyle -> Directive[Black, FontFamily -> "Helvetica", 11], LabelStyle -> Directive[12, FontFamily -> "Helvetica", Black], FrameTicks -> {{N[{0, 0.2, 0.4, 0.6, 0.8, 1}], None}, {{0, 100, 200, 300, 400, 500}, None}}, FrameLabel -> {None, None}]

R0 of the wild type = 2.28263
R0 of the mutant type = 2.77818
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0134869
Cumulative mortality (mutant) = 0.

261
{0.591416}

```



■ Figure 4c: Evolution with positive pleiotropy between transmission  $\beta$  and virulence  $\alpha$ , control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1.2, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.01, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1 -> 0.6, c2 -> 0.6, c3 -> 0.6
};

Print["Case mortality = ",  $\frac{\alpha}{\kappa y_I + \alpha}$  /. pars];

Print["Case mortality (mutant) = ",  $\frac{\alpha_m}{\kappa y_I + \alpha_m}$  /. pars];

Case mortality = 0.0243902
Case mortality (mutant) = 0.047619

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.28263
R0 of the mutant type = 2.70199
Case mortality = 0.0195122
Case mortality (mutant) = 0.0380952
Cumulative mortality (total) = 0.0115874
Cumulative mortality (mutant) = 0.
449

```



If we increase the pleiotropic effect on the length of the pre-symptomatic phase, however, the mutant allele no longer rises in frequency if  $\kappa P_m >$

```
tab = Table[Flatten[{ $\kappa$ , finalfreq[parvec /.  $\kappa P_m \rightarrow \kappa$  /. pars /. mut  $\rightarrow$  0.01];
  Evaluate[(yEm[tfig] + yAm[tfig] + yPm[tfig] + yIm[tfig]) /
    (yE[tfig] + yA[tfig] + yP[tfig] + yI[tfig] + yEm[tfig] + yAm[tfig] + yPm[tfig] + yIm[tfig])] /.
    Flatten[NSolution[parvec /.  $\kappa P_m \rightarrow \kappa$  /. pars /. mut  $\rightarrow$  0.01]]]], { $\kappa$ , 1, 2, 0.05}];
```

```
ReplaceAll::reps: {NSolution[{1, 1.2, 0.005, 0.01, 1, 1., 0.2, 0.2, 0.25, 0.2, 0.11, 0.6, 0.6, 0.6, 0.01}]}
  is neither a list of replacement rules nor a valid dispatch table, and so cannot be used for replacing. >>
```

R0 of the wild type = 2.28263

R0 of the mutant type = 2.70199

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0176922

Cumulative mortality (mutant) = 0.0094659

```
ReplaceAll::reps: {NSolution[{1, 1.2, 0.005, 0.01, 1, 1.05, 0.2, 0.2, 0.25, 0.2, 0.11, 0.6, 0.6, 0.6, 0.01}]}
  is neither a list of replacement rules nor a valid dispatch table, and so cannot be used for replacing. >>
```

R0 of the wild type = 2.28263

R0 of the mutant type = 2.65628

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.016212

Cumulative mortality (mutant) = 0.00731841

```
ReplaceAll::reps: {NSolution[{1, 1.2, 0.005, 0.01, 1, 1.1, 0.2, 0.2, 0.25, 0.2, 0.11, 0.6, 0.6, 0.6, 0.01}]}
  is neither a list of replacement rules nor a valid dispatch table, and so cannot be used for replacing. >>
```

General::stop: Further output of ReplaceAll::reps will be suppressed during this calculation. >>

R0 of the wild type = 2.28263

R0 of the mutant type = 2.61472

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0149464

Cumulative mortality (mutant) = 0.00546339

R0 of the wild type = 2.28263

R0 of the mutant type = 2.57677

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0139649

Cumulative mortality (mutant) = 0.0039964

R0 of the wild type = 2.28263

R0 of the mutant type = 2.54199

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0132536

Cumulative mortality (mutant) = 0.002905

R0 of the wild type = 2.28263

R0 of the mutant type = 2.50999

Case mortality = 0.0195122

Case mortality (mutant) = 0.0380952

Cumulative mortality (total) = 0.0127587

Cumulative mortality (mutant) = 0.00212146

R0 of the wild type = 2.28263  
R0 of the mutant type = 2.48045  
Case mortality = 0.0195122  
Case mortality (mutant) = 0.0380952  
Cumulative mortality (total) = 0.0124211  
Cumulative mortality (mutant) = 0.0015676  
R0 of the wild type = 2.28263  
R0 of the mutant type = 2.4531  
Case mortality = 0.0195122  
Case mortality (mutant) = 0.0380952  
Cumulative mortality (total) = 0.0121919  
Cumulative mortality (mutant) = 0.00117673  
R0 of the wild type = 2.28263  
R0 of the mutant type = 2.42771  
Case mortality = 0.0195122  
Case mortality (mutant) = 0.0380952  
Cumulative mortality (total) = 0.0120355  
Cumulative mortality (mutant) = 0.000898881  
R0 of the wild type = 2.28263  
R0 of the mutant type = 2.40406  
Case mortality = 0.0195122  
Case mortality (mutant) = 0.0380952  
Cumulative mortality (total) = 0.0119277  
Cumulative mortality (mutant) = 0.000698954  
R0 of the wild type = 2.28263  
R0 of the mutant type = 2.38199  
Case mortality = 0.0195122  
Case mortality (mutant) = 0.0380952  
Cumulative mortality (total) = 0.0118524  
Cumulative mortality (mutant) = 0.000552961  
R0 of the wild type = 2.28263  
R0 of the mutant type = 2.36135  
Case mortality = 0.0195122  
Case mortality (mutant) = 0.0380952  
Cumulative mortality (total) = 0.0117991  
Cumulative mortality (mutant) = 0.000444664  
R0 of the wild type = 2.28263  
R0 of the mutant type = 2.34199  
Case mortality = 0.0195122  
Case mortality (mutant) = 0.0380952  
Cumulative mortality (total) = 0.0117607  
Cumulative mortality (mutant) = 0.000363051  
R0 of the wild type = 2.28263  
R0 of the mutant type = 2.32381  
Case mortality = 0.0195122  
Case mortality (mutant) = 0.0380952

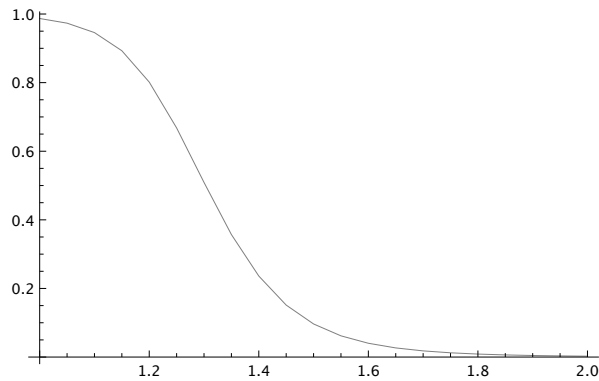


Cumulative mortality (total) = 0.0117327  
 Cumulative mortality (mutant) = 0.000300597  
 R0 of the wild type = 2.28263  
 R0 of the mutant type = 2.3067  
 Case mortality = 0.0195122  
 Case mortality (mutant) = 0.0380952  
 Cumulative mortality (total) = 0.0117119  
 Cumulative mortality (mutant) = 0.0002521  
 R0 of the wild type = 2.28263  
 R0 of the mutant type = 2.29056  
 Case mortality = 0.0195122  
 Case mortality (mutant) = 0.0380952  
 Cumulative mortality (total) = 0.0116962  
 Cumulative mortality (mutant) = 0.000213919  
 R0 of the wild type = 2.28263  
 R0 of the mutant type = 2.27532  
 Case mortality = 0.0195122  
 Case mortality (mutant) = 0.0380952  
 Cumulative mortality (total) = 0.0116843  
 Cumulative mortality (mutant) = 0.00018347  
 R0 of the wild type = 2.28263  
 R0 of the mutant type = 2.26091  
 Case mortality = 0.0195122  
 Case mortality (mutant) = 0.0380952  
 Cumulative mortality (total) = 0.0116752  
 Cumulative mortality (mutant) = 0.000158896  
 R0 of the wild type = 2.28263  
 R0 of the mutant type = 2.24725  
 Case mortality = 0.0195122  
 Case mortality (mutant) = 0.0380952  
 Cumulative mortality (total) = 0.011668  
 Cumulative mortality (mutant) = 0.000138841  
 R0 of the wild type = 2.28263  
 R0 of the mutant type = 2.2343  
 Case mortality = 0.0195122  
 Case mortality (mutant) = 0.0380952  
 Cumulative mortality (total) = 0.0116623  
 Cumulative mortality (mutant) = 0.000122305  
 R0 of the wild type = 2.28263  
 R0 of the mutant type = 2.22199  
 Case mortality = 0.0195122  
 Case mortality (mutant) = 0.0380952  
 Cumulative mortality (total) = 0.0116578  
 Cumulative mortality (mutant) = 0.000108541

tab

```
{1., 0.986936}, {1.05, 0.973369}, {1.1, 0.945886}, {1.15, 0.892974}, {1.2, 0.801584}, {1.25, 0.667858},
{1.3, 0.509017}, {1.35, 0.357082}, {1.4, 0.236172}, {1.45, 0.151524}, {1.5, 0.0964691},
{1.55, 0.0618317}, {1.6, 0.0402133}, {1.65, 0.0266361}, {1.7, 0.0179921}, {1.75, 0.012394},
{1.8, 0.00870141}, {1.85, 0.00622027}, {1.9, 0.00452286}, {1.95, 0.00334145}, {2., 0.00250564}
```

plot1 = ListPlot[tab, Joined → True, PlotStyle → Gray]



■ Figure 4d: Evolution with negative pleiotropy between transmission  $\beta$  and virulence  $\alpha$ , control measures

```
pars = {β -> 1, βm -> 1.2, (*TRANSMISSION OF THE MUTANT*)
α -> 0.005, αm -> 0.000, (*VIRULENCE OF THE MUTANT*)
κyP -> 1, κyPm -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1 -> 0.6, c2 -> 0.6, c3 -> 0.6
};

Print["Case mortality = ",  $\frac{\alpha}{\kappa y I + \alpha}$  /. pars];

Print["Case mortality (mutant) = ",  $\frac{\alpha m}{\kappa y I + \alpha m}$  /. pars];

Case mortality = 0.0243902
Case mortality (mutant) = 0.

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.28263
R0 of the mutant type = 2.77818
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0115874
Cumulative mortality (mutant) = 0.
```

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```

parset = parvec /. pars /. mut -> 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t,
  0, tevolNC}], PlotRange -> {{0, tfig}, {10-7, 1}}, PlotStyle -> {{Thickness[0.005], Red}}, AspectRatio -> 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t -> tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]], {t, 0, tevolNC}], PlotRange -> {{0, tfig}, {0, 1}},
  PlotStyle -> {{Thickness[0.008], Black}}, AspectRatio -> 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Blue}, AspectRatio -> 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling -> Axis, FillingStyle -> LightGray,
  PlotStyle -> None, Frame -> True, PlotRange -> {{0, tfig}, {0, 1}}, AspectRatio -> 0.75, Frame -> True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT2 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame -> True,
  TicksStyle -> Directive[Black, FontFamily -> "Helvetica", 11],
  LabelStyle -> Directive[12, FontFamily -> "Helvetica", Black], FrameTicks ->
    {{N[{0, 0.2, 0.4, 0.6, 0.8, 1}], None}, {{0, 100, 200, 300, 400, 500}, None}}, FrameLabel -> {None, None}}

```

R0 of the wild type = 2.28263

R0 of the mutant type = 2.77818

Case mortality = 0.0195122

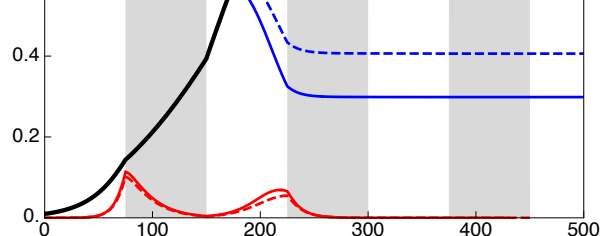
Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.00762998

Cumulative mortality (mutant) = 0.

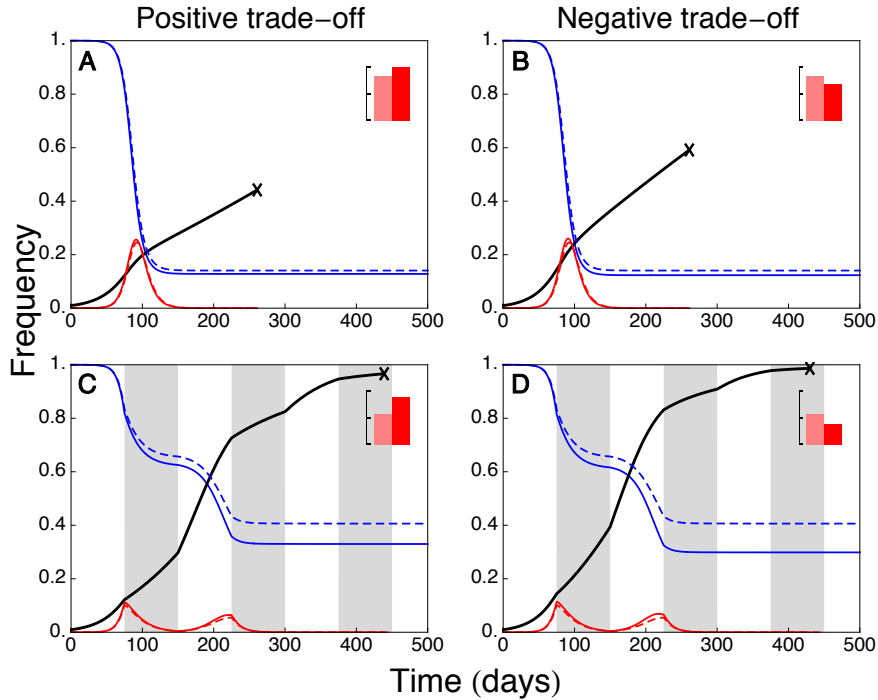
430

{0.986768}



## ■ Altogether

```
Show[
GraphicsGrid[{{FigTOP1, FigTOP2}, {FigBOT1, FigBOT2}}, FrameLabel -> label],
Graphics[Text[Style["A", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {55, -38}]],
Graphics[Text[Style["B", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {440, -38}]],
Graphics[Text[Style["C", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {55, -325}]],
Graphics[Text[Style["D", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {440, -325}]],
Graphics[Text[Style["Positive trade-off", 18, FontFamily -> "Helvetica"], {200, 0}]],
Graphics[Text[Style["Negative trade-off", 18, FontFamily -> "Helvetica"], {580, 0}]],
Graphics[Text[Style["Time (days)", 20, FontFamily -> "Helvetica"], {400, -590}]],
Graphics[Rotate[Text[Style["Frequency", 20, FontFamily -> "Helvetica"], {0, -250}], Pi / 2]]
]
```



## ■ Figure 3alt - Main change is a longer presymptomatic phase ( $\kappa_P=1/2.5$ )

$\beta$  adjusted to keep  $R_0$  and doubling time of the disease within range observed.

## ■ Code

Common settings

```
Clear["Global`*"]

Off[General::spell1]
Off[General::spell]
Off[NDSolve::nlnum]

tfinal = 500;
tfig = 500;

label = {"Time (days)", "Frequency"};
label = None;

parvec = {β, βm, α, αm, κP, κPm, f, fm, κE, κI, κA, c1, c2, c3, mut};

Clear[finalfreq, NSolution]
finalfreq[vec_] :=
finalfreq[vec] = Block[{β = vec[[1]], βm = vec[[2]], α = vec[[3]], αm = vec[[4]], κP = vec[[5]],
κPm = vec[[6]], f = vec[[7]], fm = vec[[8]], κE = vec[[9]], κI = vec[[10]],
κA = vec[[11]], c1 = vec[[12]], c2 = vec[[13]], c3 = vec[[14]], mut = vec[[15]]},

(*REMAINING PARAMETERS*)
βyA = β / 10; βyP = β; βyI = β / 3;
κyAm = κyA; κyIm = κyI;
βyAm = βm / 10; βyPm = βm; βyIm = βm / 3;

(* E: Exposed (non-infectious) cases *)
(* A: asymptomatic cases *)
```

```

(* P: pre-symptomatic cases *)
(* S: symptomatic cases *)
(* f: proportion of fsymptomatic hosts *)
(* c: amount of distancing applied *)

(*INOCULATION*)
start = 10-5;

t = .;
c = .;

c[t_] := Evaluate[If[t < t1min, 0,
  If[t < t1max, c1, If[t < t2min, 0, If[t < t2max, c2, If[t < t3min, 0, If[t < t3max, c3, 0]]]]]];
h[t] = (1 - c[t]) (βyA yA[t] + βyP yP[t] + βyI yI[t]);
hm[t] = (1 - c[t]) (βyAm yAm[t] + βyPm yPm[t] + βyIm yIm[t]);

sys = {S'[t] == - (h[t] + hm[t]) S[t],
  yE'[t] == h[t] S[t] - κyE yE[t],
  yA'[t] == f κyE yE[t] - κyA yA[t],
  yP'[t] == (1 - f) κyE yE[t] - κyP yP[t],
  yI'[t] == κyP yP[t] - (κyI + α) yI[t],
  yR'[t] == κyA yA[t] + κyI yI[t],
  yD'[t] == α yI[t]}; (*yD serves as a counter of the cumulative number of deaths*)

sysm = {
  yEm'[t] == hm[t] S[t] - κyE yEm[t],
  yAm'[t] == fm κyE yEm[t] - κyAm yAm[t],
  yPm'[t] == (1 - fm) κyE yEm[t] - κyPm yPm[t],
  yIm'[t] == κyPm yPm[t] - (κyIm + αm) yIm[t],
  yRm'[t] == κyAm yAm[t] + κyIm yIm[t],
  yDm'[t] == αm yIm[t]}; (*yDm serves as a counter of the cumulative number of deaths*)

(*FIRST BOUT OF CONTROL*)
t1min = 75;
t1max = 150;
(*SECOND BOUT OF CONTROL*)
t2min = 225;
t2max = 300;
(*THIRD BOUT OF CONTROL*)
t3min = 375;
t3max = 450;

init = {S[0] == 1, yE[0] == start (1 - mut), yA[0] == 0, yP[0] == 0, yI[0] == 0, yR[0] == 0, yD[0] == 0};
initm = {yEm[0] == start (mut), yAm[0] == 0, yPm[0] == 0, yIm[0] == 0, yRm[0] == 0, yDm[0] == 0};

var = {S, yE, yA, yP, yI, yR, yD};
varm = {yEm, yAm, yPm, yIm, yRm, yDm};

NSolution[vec] =
  NDSolve[
    Flatten[{sys, sysm, init, initm}], Flatten[{var, varm}], {t, 0, tfinal}, AccuracyGoal → 100];

(*R0*)
Print["R0 of the wild type = ",  $\frac{\beta yA f}{\kappa yA} + \frac{(1 - f) (\beta yP (\alpha + \kappa yI) + \beta yI \kappa yP)}{(\alpha + \kappa yI) \kappa yP}$ ];

(*Rm*)
Print["R0 of the mutant type = ",  $\frac{\beta yAm f}{\kappa yAm} + \frac{(1 - f) (\beta yPm (\alpha m + \kappa yIm) + \beta yIm \kappa yPm)}{(\alpha m + \kappa yIm) \kappa yPm}$ ];

(*CASE MORTALITY*)
Print["Case mortality = ",  $(1 - f) \frac{\alpha}{\kappa yI + \alpha}$ ];
Print["Case mortality (mutant) = ",  $(1 - fm) \frac{\alpha m}{\kappa yI + \alpha m}$ ];

(*CUMULATIVE MORTALITY*)
Print["Cumulative mortality (total) = ", yD[tfinal] + yDm[tfinal] /. Flatten[NSolution[vec]]];
Print["Cumulative mortality (mutant) = ", yDm[tfinal] /. Flatten[NSolution[vec]]];

```

■ Figure 3a: Evolution of transmission  $\beta$ , no control measures

```

pars = {β → 0.7, βm → 0.7 × 1.2, (*TRANSMISSION OF THE MUTANT*)
α → 0.005, αm → 0.005, (*VIRULENCE OF THE MUTANT*)
κyP → 1 / 2.5, κyPm → 1 / 2.5, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f → 0.2, fm → 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
κyE → 0.25, (* 1/TIME IN EXPOSED CLASS *)
κyI → 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
κyA → 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1 → 0, c2 → 0, c3 → 0
};

```

The doubling time of the disease when rare, as calculated from the eigenvalue ("poly") of the stability matrix:

```

Sort[Solve[
  (κE (-S α βP κA + f S α βP κA - S βP κA κI + f S βP κA κI - f S α βA κP + α κA κP - S βI κA κP + f S βI κA κP - f S βA κI κP + κA κI κP) +
    (-f S α βA κE - S α βP κE + f S α βP κE + α κA κE - S βP κA κE + f S βP κA κE - f S βA κE κI - S βP κE κI + f S βP κE κI +
      κA κE κI + α κA κP + α κE κP - f S βA κE κP - S βI κE κP + f S βI κE κP + κA κE κP + κA κI κP + κE κI κP) λ +
    (α κA + α κE - f S βA κE - S βP κE + f S βP κE + κA κE + κA κI + κE κI + α κP + κA κP + κE κP + κI κP) λ2 +
    (α + κA + κE + κI + κP) λ3 + λ4 / . S → 1 / . βA → β / 10 / . βP → β / .
    βI → β / 3 / . κA → κyA / . κE → κyE / . κP → κyP / . κI → κyI / . pars) == 0, λ]]

Solve[
  (Exp[
    λ
    t] =
    2) / .
  Last[
    %],
  t]
{{λ → -0.649407}, {λ → -0.334169}, {λ → -0.113297}, {λ → 0.131873}}
{{t → 5.25617}}

parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
  {t, 0, tNOevolNC}, PlotRange → {{0, tfig}, {10-7, 1}},
  PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];
R0 of the wild type = 2.43784
R0 of the mutant type = 2.92541
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0172518
Cumulative mortality (mutant) = 0.
254

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

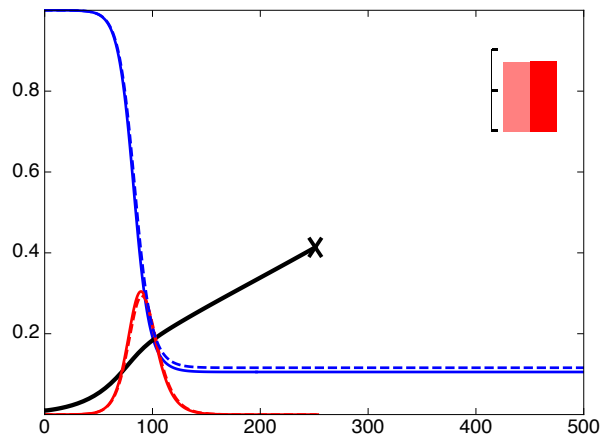
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% ("], ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP1 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

R0 of the wild type = 2.43784
R0 of the mutant type = 2.92541
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.017457
Cumulative mortality (mutant) = 0.00278104
251
{0.413578}

```



■ Figure 3b: Evolution of asymptomatic fraction  $f$ , no control measures

```

pars = { $\beta \rightarrow 0.7$ ,  $\beta_m \rightarrow 0.7$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha \rightarrow 0.005$ ,  $\alpha_m \rightarrow 0.005$ , (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P \rightarrow 1/2.5$ ,  $\kappa y_{Pm} \rightarrow 1/2.5$ , (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f  $\rightarrow 0.2$ ,  $f_m \rightarrow 0.1$ , (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E \rightarrow 0.25$ , (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I \rightarrow 0.2$ , (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A \rightarrow 0.11$ , (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1 \rightarrow 0$ ,  $c_2 \rightarrow 0$ ,  $c_3 \rightarrow 0$ 
};

parset = parvec /. pars /. mut  $\rightarrow 0$ ;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange  $\rightarrow$  {{0, tfig}, {10-7, 1}},
  PlotStyle  $\rightarrow$  {{Thickness[0.005], Red, Dashed}}, AspectRatio  $\rightarrow$  0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange  $\rightarrow$  {{0, tfig}, {0, 1}}, PlotStyle  $\rightarrow$  {Thickness[0.005], Dashed, Blue}, AspectRatio  $\rightarrow$  0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.43784
R0 of the mutant type = 2.43784
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0172518
Cumulative mortality (mutant) = 0.

```



```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

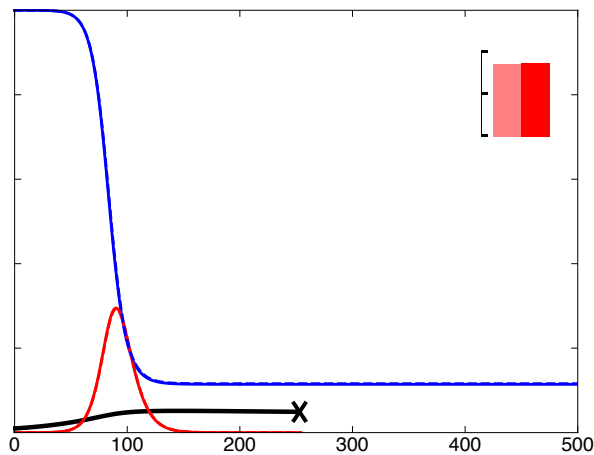
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP2 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.43784
R0 of the mutant type = 2.43784
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0173758
Cumulative mortality (mutant) = 0.0008657
253
{0.0491962}

```



■ Figure 3c: Evolution of pre-symptomatic phase  $\kappa$ , no control measures

```

pars = { $\beta \rightarrow 0.7$ ,  $\beta_m \rightarrow 0.7$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha \rightarrow 0.005$ ,  $\alpha_m \rightarrow 0.005$ , (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P \rightarrow 1/2.5$ ,  $\kappa y_{Pm} \rightarrow 1/4$ , (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f  $\rightarrow 0.2$ ,  $f_m \rightarrow 0.2$ , (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E \rightarrow 0.25$ , (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I \rightarrow 0.2$ , (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A \rightarrow 0.11$ , (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1 \rightarrow 0$ ,  $c_2 \rightarrow 0$ ,  $c_3 \rightarrow 0$ 
};

parset = parvec /. pars /. mut  $\rightarrow 0$ ;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange  $\rightarrow$  {{0, tfig}, {10-7, 1}},
  PlotStyle  $\rightarrow$  {{Thickness[0.005], Red, Dashed}}, AspectRatio  $\rightarrow$  0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange  $\rightarrow$  {{0, tfig}, {0, 1}}, PlotStyle  $\rightarrow$  {Thickness[0.005], Dashed, Blue}, AspectRatio  $\rightarrow$  0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.43784
R0 of the mutant type = 3.27784
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0172518
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

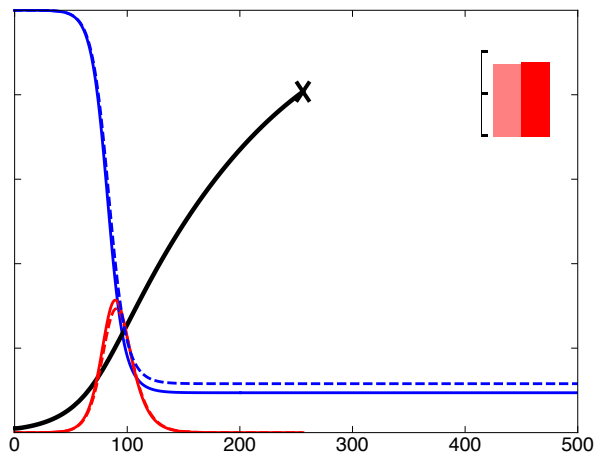
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% ("], ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP3 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.43784
R0 of the mutant type = 3.27784
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0176696
Cumulative mortality (mutant) = 0.00353411
256
{0.807354}

```



■ Figure 3d: Evolution of virulence  $\alpha$ , no control measures

```

pars = { $\beta \rightarrow 0.7$ ,  $\beta_m \rightarrow 0.7$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha \rightarrow 0.005$ ,  $\alpha_m \rightarrow 0$ , (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P \rightarrow 1/2.5$ ,  $\kappa y_{Pm} \rightarrow 1/2.5$ , (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f  $\rightarrow 0.2$ ,  $f_m \rightarrow 0.2$ , (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E \rightarrow 0.25$ , (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I \rightarrow 0.2$ , (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A \rightarrow 0.11$ , (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1 \rightarrow 0$ ,  $c_2 \rightarrow 0$ ,  $c_3 \rightarrow 0$ 
};

parset = parvec /. pars /. mut  $\rightarrow 0$ ;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange  $\rightarrow$  {{0, tfig}, {10-7, 1}},
  PlotStyle  $\rightarrow$  {{Thickness[0.005], Red, Dashed}}, AspectRatio  $\rightarrow$  0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange  $\rightarrow$  {{0, tfig}, {0, 1}}, PlotStyle  $\rightarrow$  {Thickness[0.005], Dashed, Blue}, AspectRatio  $\rightarrow$  0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.43784
R0 of the mutant type = 2.46061
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0172518
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

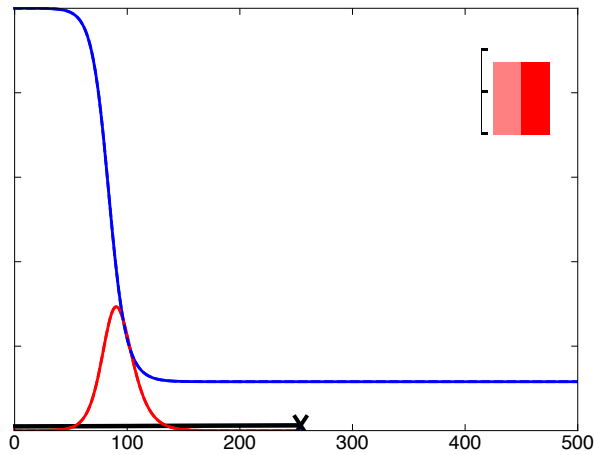
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP4 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.43784
R0 of the mutant type = 2.46061
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0170685
Cumulative mortality (mutant) = 0.
254
{0.0124554}

```



■ Figure 3e: Evolution of transmission  $\beta$ , control measures

```

pars = { $\beta \rightarrow 0.7$ ,  $\beta_m \rightarrow 0.7 \times 1.2$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha \rightarrow 0.005$ ,  $\alpha_m \rightarrow 0.005$ , (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P \rightarrow 1/2.5$ ,  $\kappa y_{Pm} \rightarrow 1/2.5$ , (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f  $\rightarrow 0.2$ ,  $f_m \rightarrow 0.2$ , (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E \rightarrow 0.25$ , (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I \rightarrow 0.2$ , (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A \rightarrow 0.11$ , (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1 \rightarrow 0.6$ ,  $c_2 \rightarrow 0.6$ ,  $c_3 \rightarrow 0.6$ 
};

parset = parvec /. pars /. mut  $\rightarrow 0$ ;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange  $\rightarrow$  {{0, tfig}, {10-7, 1}},
  PlotStyle  $\rightarrow$  {{Thickness[0.005], Red, Dashed}}, AspectRatio  $\rightarrow$  0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange  $\rightarrow$  {{0, tfig}, {0, 1}}, PlotStyle  $\rightarrow$  {Thickness[0.005], Dashed, Blue}, AspectRatio  $\rightarrow$  0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.43784
R0 of the mutant type = 2.92541
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0113614
Cumulative mortality (mutant) = 0.
500

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

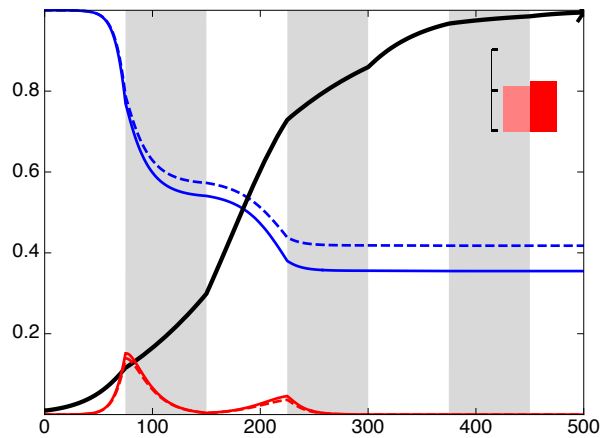
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT1 = Show[fcontrol, fS, fSDashed, FIGfreq, fnoevol, fevol, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

R0 of the wild type = 2.43784
R0 of the mutant type = 2.92541
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0125869
Cumulative mortality (mutant) = 0.00364809
500
{0.994766}

```



■ Figure 3f: Evolution of asymptomatic fraction  $f$ , control measures

```

pars = { $\beta \rightarrow 0.7$ ,  $\beta_m \rightarrow 0.7$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha \rightarrow 0.005$ ,  $\alpha_m \rightarrow 0.005$ , (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P \rightarrow 1/2.5$ ,  $\kappa y_{Pm} \rightarrow 1/2.5$ , (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f  $\rightarrow 0.2$ ,  $f_m \rightarrow 0.1$ , (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E \rightarrow 0.25$ , (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I \rightarrow 0.2$ , (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A \rightarrow 0.11$ , (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1 \rightarrow 0.6$ ,  $c_2 \rightarrow 0.6$ ,  $c_3 \rightarrow 0.6$ 
};

parset = parvec /. pars /. mut  $\rightarrow 0$ ;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange  $\rightarrow$  {{0, tfig}, {10-7, 1}},
  PlotStyle  $\rightarrow$  {{Thickness[0.005], Red, Dashed}}, AspectRatio  $\rightarrow$  0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange  $\rightarrow$  {{0, tfig}, {0, 1}}, PlotStyle  $\rightarrow$  {Thickness[0.005], Dashed, Blue}, AspectRatio  $\rightarrow$  0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.43784
R0 of the mutant type = 2.43784
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0113614
Cumulative mortality (mutant) = 0.

500

```



```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray, PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

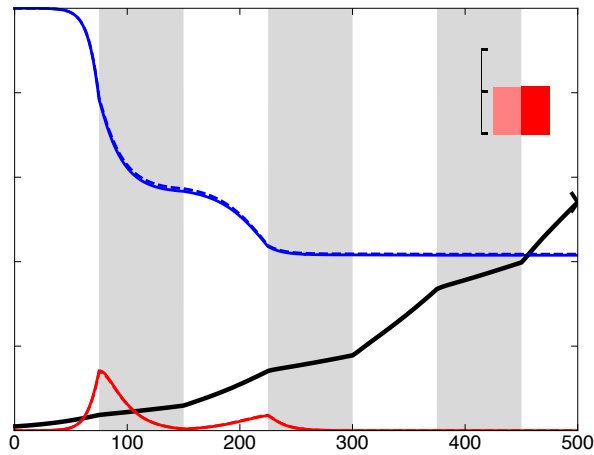
DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}], Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT2 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True, TicksStyle → Directive[Black, FontFamily → "Helvetica", 11], LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}}, FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]}, {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}]
]

R0 of the wild type = 2.43784
R0 of the mutant type = 2.43784
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.011499
Cumulative mortality (mutant) = 0.000804302

500
{0.540783}

```



■ Figure 3g: Evolution of pre-symptomatic phase  $\kappa$ , control measures

```

pars = { $\beta \rightarrow 0.7$ ,  $\beta_m \rightarrow 0.7$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha \rightarrow 0.005$ ,  $\alpha_m \rightarrow 0.005$ , (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P \rightarrow 1/2.5$ ,  $\kappa y_{Pm} \rightarrow 1/4$ , (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f  $\rightarrow 0.2$ ,  $f_m \rightarrow 0.2$ , (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E \rightarrow 0.25$ , (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I \rightarrow 0.2$ , (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A \rightarrow 0.11$ , (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1 \rightarrow 0.6$ ,  $c_2 \rightarrow 0.6$ ,  $c_3 \rightarrow 0.6$ 
};

parset = parvec /. pars /. mut  $\rightarrow 0$ ;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange  $\rightarrow$  {{0, tfig}, {10-7, 1}},
  PlotStyle  $\rightarrow$  {{Thickness[0.005], Red, Dashed}}, AspectRatio  $\rightarrow$  0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange  $\rightarrow$  {{0, tfig}, {0, 1}}, PlotStyle  $\rightarrow$  {Thickness[0.005], Dashed, Blue}, AspectRatio  $\rightarrow$  0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.43784
R0 of the mutant type = 3.27784
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0113614
Cumulative mortality (mutant) = 0.
500

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray, PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

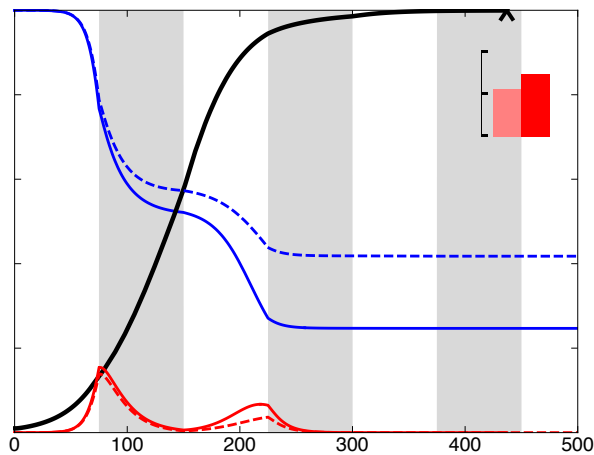
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}], Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT3 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True, TicksStyle → Directive[Black, FontFamily → "Helvetica", 11], LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}}, FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]}, {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}]
]

R0 of the wild type = 2.43784
R0 of the mutant type = 3.27784
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0146959
Cumulative mortality (mutant) = 0.00651372
437
{0.99953}

```



■ Figure 3h: Evolution of virulence  $\alpha$ , control measures

```

pars = { $\beta$  -> 0.7,  $\beta_m$  -> 0.7, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1 / 2.5,  $\kappa y_{Pm}$  -> 1 / 2.5, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1 -> 0.6, c2 -> 0.6, c3 -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.43784
R0 of the mutant type = 2.46061
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0113614
Cumulative mortality (mutant) = 0.
500

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray, PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

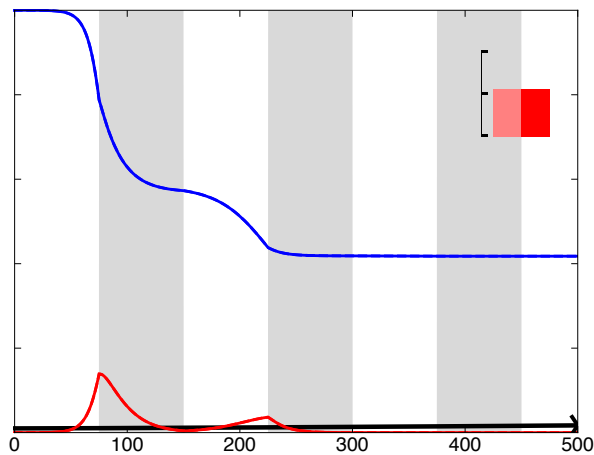
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}], Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT4 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True, TicksStyle → Directive[Black, FontFamily → "Helvetica", 11], LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}}, FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]}, {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}]
]

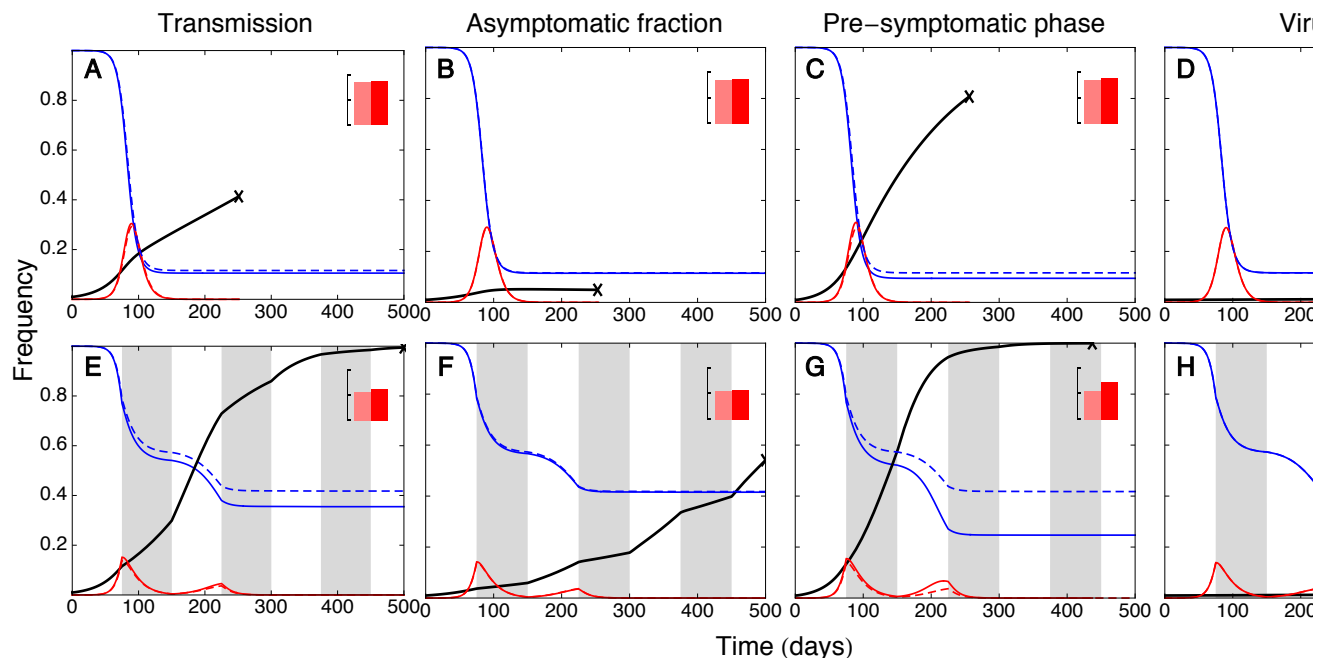
R0 of the wild type = 2.43784
R0 of the mutant type = 2.46061
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0112358
Cumulative mortality (mutant) = 0.
500
{0.0171055}

```



### ■ Altogether

```
Show[
GraphicsGrid[{{FigTOP1, FigTOP2, FigTOP3, FigTOP4}, {FigBOT1, FigBOT2, FigBOT3, FigBOT4}},
FrameLabel -> label, Spacings -> {-10, 10}],
Graphics[Text[Style["A", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {45, -33}]],
Graphics[Text[Style["B", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {379, -33}]],
Graphics[Text[Style["C", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {729, -33}]],
Graphics[Text[Style["D", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {1080, -33}]],
Graphics[Text[Style["E", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {45, -315}]],
Graphics[Text[Style["F", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {379, -315}]],
Graphics[Text[Style["G", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {729, -315}]],
Graphics[Text[Style["H", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {1080, -315}]],
Graphics[Text[Style["Transmission", 16, FontFamily -> "Helvetica"], {180, 10}]],
Graphics[Text[Style["Asymptomatic fraction", 16, FontFamily -> "Helvetica"], {520, 10}]],
Graphics[Text[Style["Pre-symptomatic phase", 16, FontFamily -> "Helvetica"], {870, 10}]],
Graphics[Text[Style["Virulence", 16, FontFamily -> "Helvetica"], {1220, 10}]],
Graphics[Text[Style["Time (days)", 16, FontFamily -> "Helvetica"], {700, -580}]],
Graphics[Rotate[Text[Style["Frequency", 16, FontFamily -> "Helvetica"], {-20, -270}], Pi / 2]]
]
```



### ■ Figure 3alt - Main change is a shorter asymptomatic phase ( $\kappa\gamma A=1/6$ )

$\beta$  adjusted to keep  $R_0$  and doubling time of the disease within range observed.

### ■ Code

Common settings

```

Clear["Global`*"]

Off[General::spell1]
Off[General::spell]
Off[NDSolve::nlnum]

tfinal = 500;

tfig = 500;

label = {"Time (days)", "Frequency"};
label = None;

parvec = { $\beta$ ,  $\beta_m$ ,  $\alpha$ ,  $\alpha_m$ ,  $\kappa y_P$ ,  $\kappa y_{Pm}$ ,  $f$ ,  $f_m$ ,  $\kappa y_E$ ,  $\kappa y_I$ ,  $\kappa y_A$ ,  $c_1$ ,  $c_2$ ,  $c_3$ ,  $\text{mut}$ };

Clear[finalfreq, NSolution]
finalfreq[vec_] :=
finalfreq[vec] = Block[{ $\beta$  = vec[[1]],  $\beta_m$  = vec[[2]],  $\alpha$  = vec[[3]],  $\alpha_m$  = vec[[4]],  $\kappa y_P$  = vec[[5]],
 $\kappa y_{Pm}$  = vec[[6]],  $f$  = vec[[7]],  $f_m$  = vec[[8]],  $\kappa y_E$  = vec[[9]],  $\kappa y_I$  = vec[[10]],
 $\kappa y_A$  = vec[[11]],  $c_1$  = vec[[12]],  $c_2$  = vec[[13]],  $c_3$  = vec[[14]],  $\text{mut}$  = vec[[15]]},

(*REMAINING PARAMETERS*)
 $\beta y_A$  =  $\beta$  / 10;  $\beta y_P$  =  $\beta$ ;  $\beta y_I$  =  $\beta$  / 3;
 $\kappa y_{Am}$  =  $\kappa y_A$ ;  $\kappa y_{Im}$  =  $\kappa y_I$ ;
 $\beta y_{Am}$  =  $\beta_m$  / 10;  $\beta y_{Pm}$  =  $\beta_m$ ;  $\beta y_{Im}$  =  $\beta_m$  / 3;

(* E: Exposed (non-infectious) cases *)
(* A: asymptomatic cases *)
(* P: pre-symptomatic cases *)
(* S: symptomatic cases *)
(* f: proportion of fsymptomatic hosts *)
(* c: amount of distancing applied *)

(*INOCULATION*)
start =  $10^{-5}$ ;

t = .;
c = .;

c[t_] := Evaluate[If[t < t1min, 0,
If[t < t1max, c1, If[t < t2min, 0, If[t < t2max, c2, If[t < t3min, 0, If[t < t3max, c3, 0]]]]]];
h[t] = (1 - c[t]) ( $\beta y_A y_A[t]$  +  $\beta y_P y_P[t]$  +  $\beta y_I y_I[t]$ );
hm[t] = (1 - c[t]) ( $\beta y_{Am} y_{Am}[t]$  +  $\beta y_{Pm} y_{Pm}[t]$  +  $\beta y_{Im} y_{Im}[t]$ );

sys = {S'[t] == - (h[t] + hm[t]) S[t],
yE'[t] == h[t] S[t] -  $\kappa y_E y_E[t]$ ,
yA'[t] == f  $\kappa y_E y_E[t]$  -  $\kappa y_A y_A[t]$ ,
yP'[t] == (1 - f)  $\kappa y_E y_E[t]$  -  $\kappa y_P y_P[t]$ ,
yI'[t] ==  $\kappa y_P y_P[t]$  - ( $\kappa y_I$  +  $\alpha$ ) yI[t],
yR'[t] ==  $\kappa y_A y_A[t]$  +  $\kappa y_I y_I[t]$ ,
yD'[t] ==  $\alpha y_I[t]$ }; (*yD serves as a counter of the cumulative number of deaths*)

sysm = {
yEm'[t] == hm[t] S[t] -  $\kappa y_E y_{Em}[t]$ ,
yAm'[t] == f_m  $\kappa y_E y_{Em}[t]$  -  $\kappa y_{Am} y_{Am}[t]$ ,
yPm'[t] == (1 - f_m)  $\kappa y_E y_{Em}[t]$  -  $\kappa y_{Pm} y_{Pm}[t]$ ,
yIm'[t] ==  $\kappa y_{Pm} y_{Pm}[t]$  - ( $\kappa y_{Im}$  +  $\alpha_m$ ) yIm[t],
yRm'[t] ==  $\kappa y_{Am} y_{Am}[t]$  +  $\kappa y_{Im} y_{Im}[t]$ ,
yDm'[t] ==  $\alpha_m y_{Im}[t]$ }; (*yDm serves as a counter of the cumulative number of deaths*)

(*FIRST BOUT OF CONTROL*)
t1min = 75;
t1max = 150;
(*SECOND BOUT OF CONTROL*)
t2min = 225;
t2max = 300;
(*THIRD BOUT OF CONTROL*)
t3min = 375;
t3max = 450;

init = {S[0] == 1, yE[0] == start (1 - mut), yA[0] == 0, yP[0] == 0, yI[0] == 0, yR[0] == 0, yD[0] == 0};
initm = {yEm[0] == start (mut), yAm[0] == 0, yPm[0] == 0, yIm[0] == 0, yRm[0] == 0, yDm[0] == 0};

var = {S, yE, yA, yP, yI, yR, yD};
varm = {yEm, yAm, yPm, yIm, yRm, yDm};

NSolution[vec] =
NDSolve[
Flatten[{sys, sysm, init, initm}], Flatten[{var, varm}], {t, 0, tfinal}, AccuracyGoal -> 100];

```

```

(*R0*)
Print["R0 of the wild type = ",  $\frac{\beta y_A f}{\kappa y_A} + \frac{(1-f)(\beta y_P(\alpha + \kappa y_I) + \beta y_I \kappa y_P)}{(\alpha + \kappa y_I) \kappa y_P}$ ];

(*Rm*)
Print["R0 of the mutant type = ",  $\frac{\beta y_{Am} f}{\kappa y_{Am}} + \frac{(1-f)(\beta y_{Pm}(\alpha m + \kappa y_{Im}) + \beta y_{Im} \kappa y_{Pm})}{(\alpha m + \kappa y_{Im}) \kappa y_{Pm}}$ ];

(*CASE MORTALITY*)
Print["Case mortality = ",  $(1-f) \frac{\alpha}{\kappa y_I + \alpha}$ ];
Print["Case mortality (mutant) = ",  $(1-fm) \frac{\alpha m}{\kappa y_I + \alpha m}$ ];

(*CUMULATIVE MORTALITY*)
Print["Cumulative mortality (total) = ", yD[tfinal] + yDm[tfinal] /. Flatten[NSolution[vec]]];
Print["Cumulative mortality (mutant) = ", yDm[tfinal] /. Flatten[NSolution[vec]]];
]

```

■ Figure 3a: Evolution of transmission  $\beta$ , no control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1.2, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 1/6, (* 1/TIME IN ASYMPTOMATIC CLASS = 1/6, EQUAL TO THE EXPECTED TIME IN P PLUS I *)

(*Strength of control measures*)
c1 -> 0, c2 -> 0, c3 -> 0
};

```

The doubling time of the disease when rare, as calculated from the eigenvalue ("poly") of the stability matrix:

```

Sort[Solve[
( $\kappa E(-S \alpha \beta P \kappa A + f S \alpha \beta P \kappa A - S \beta P \kappa A \kappa I + f S \beta P \kappa A \kappa I - f S \alpha \beta A \kappa P + \alpha \kappa A \kappa P - S \beta I \kappa A \kappa P + f S \beta I \kappa A \kappa P - f S \beta A \kappa I \kappa P + \kappa A \kappa I \kappa P) +$ 
 $(-f S \alpha \beta A \kappa E - S \alpha \beta P \kappa E + f S \alpha \beta P \kappa E + \alpha \kappa A \kappa E - S \beta P \kappa A \kappa E + f S \beta P \kappa A \kappa E - f S \beta A \kappa E \kappa I - S \beta P \kappa E \kappa I + f S \beta P \kappa E \kappa I +$ 
 $\kappa A \kappa E \kappa I + \alpha \kappa A \kappa P + \alpha \kappa E \kappa P - f S \beta A \kappa E \kappa P - S \beta I \kappa E \kappa P + f S \beta I \kappa E \kappa P + \kappa A \kappa E \kappa P + \kappa A \kappa I \kappa P + \kappa E \kappa I \kappa P) \lambda +$ 
 $(\alpha \kappa A + \alpha \kappa E - f S \beta A \kappa E - S \beta P \kappa E + f S \beta P \kappa E + \kappa A \kappa E + \kappa A \kappa I + \kappa E \kappa I + \alpha \kappa P + \kappa A \kappa P + \kappa E \kappa P + \kappa I \kappa P) \lambda^2 +$ 
 $(\alpha + \kappa A + \kappa E + \kappa I + \kappa P) \lambda^3 + \lambda^4 / . S \rightarrow 1 / . \beta A \rightarrow \beta / 10 / . \beta P \rightarrow \beta / .$ 
 $\beta I \rightarrow \beta / 3 / . \kappa A \rightarrow \kappa y_A / . \kappa E \rightarrow \kappa y_E / . \kappa P \rightarrow \kappa y_P / . \kappa I \rightarrow \kappa y_I / . pars) == 0, \lambda]]
Solve[
(Exp[
 $\lambda$ 
t] ==
2) /.
Last[
%],
t]
{{ $\lambda \rightarrow -1.14505$ }, { $\lambda \rightarrow -0.432584$ }, { $\lambda \rightarrow -0.168773$ }, { $\lambda \rightarrow 0.124737$ }}
{{t -> 5.55688}}

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
{t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
{t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];$ 
```



```

R0 of the wild type = 2.22081
R0 of the mutant type = 2.66498
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0165438
Cumulative mortality (mutant) = 0.

254

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t,
  0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

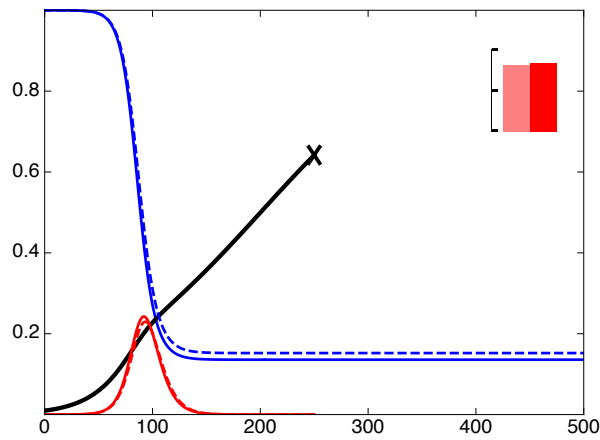
FigTOP1 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

R0 of the wild type = 2.22081
R0 of the mutant type = 2.66498
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0168639
Cumulative mortality (mutant) = 0.00341094

250

{0.641837}

```



■ Figure 3b: Evolution of asymptomatic fraction  $f$ , no control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 1/6, (* 1/TIME IN ASYMPTOMATIC CLASS = 1/6, EQUAL TO THE EXPECTED TIME IN P PLUS I *)

(*Strength of control measures*)
 $c_1$  -> 0,  $c_2$  -> 0,  $c_3$  -> 0
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.22081
R0 of the mutant type = 2.22081
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0165438
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

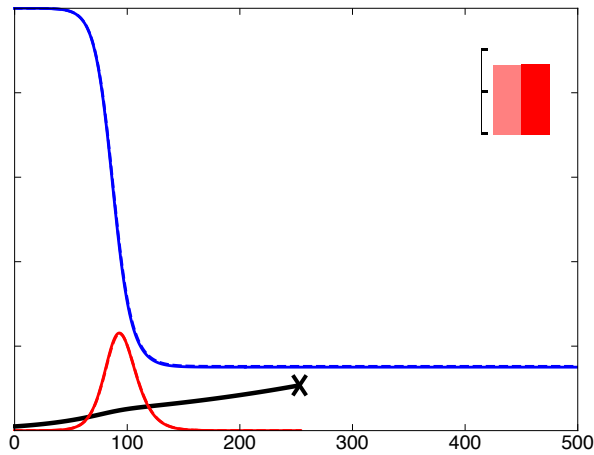
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP2 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.22081
R0 of the mutant type = 2.22081
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0166795
Cumulative mortality (mutant) = 0.000892206
253
{0.107256}

```



■ Figure 3c: Evolution of pre-symptomatic phase  $\kappa$ , no control measures

```

pars = {β -> 1, βm -> 1, (*TRANSMISSION OF THE MUTANT*)
  α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
  κyP -> 1, κyPm -> 2 / 3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

  f -> 0.2, fm -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
  κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
  κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
  κyA -> 1 / 6, (* 1/TIME IN ASYMPTOMATIC CLASS = 1/6, EQUAL TO THE EXPECTED TIME IN P PLUS I *)

  (*Strength of control measures*)
  c1 -> 0, c2 -> 0, c3 -> 0
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.22081
R0 of the mutant type = 2.62081
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0165438
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

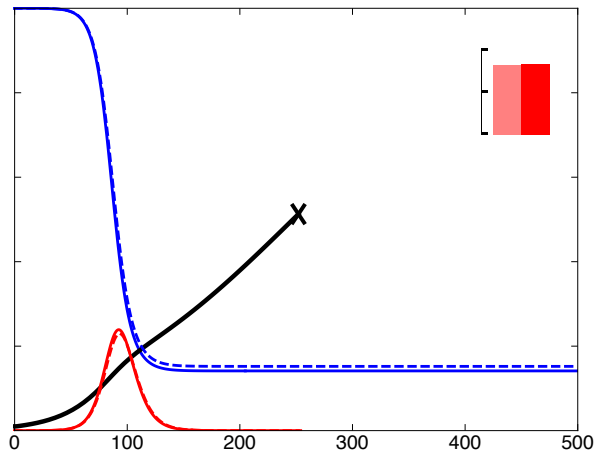
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP3 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.22081
R0 of the mutant type = 2.62081
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0167538
Cumulative mortality (mutant) = 0.00241291
252
{0.512691}

```



■ Figure 3d: Evolution of virulence  $\alpha$ , no control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.0, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 1/6, (* 1/TIME IN ASYMPTOMATIC CLASS = 1/6, EQUAL TO THE EXPECTED TIME IN P PLUS I *)

(*Strength of control measures*)
c1 -> 0, c2 -> 0, c3 -> 0
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.22081
R0 of the mutant type = 2.25333
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0165438
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

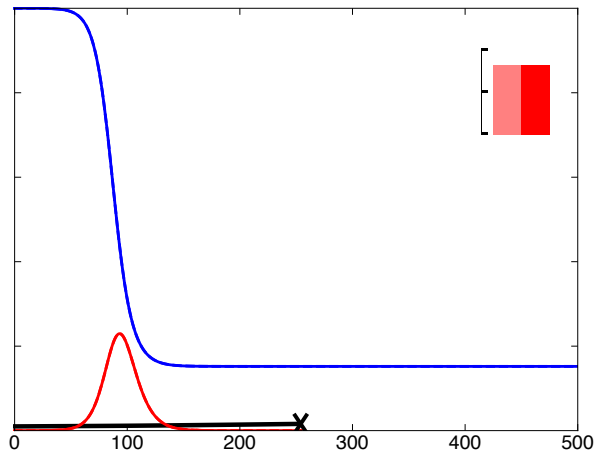
DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP4 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]
]

R0 of the wild type = 2.22081
R0 of the mutant type = 2.25333
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0163575
Cumulative mortality (mutant) = 0.

254
{0.0159552}

```



■ Figure 3e: Evolution of transmission  $\beta$ , control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1.2, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 1/6, (* 1/TIME IN ASYMPTOMATIC CLASS = 1/6, EQUAL TO THE EXPECTED TIME IN P PLUS I *)

(*Strength of control measures*)
c1 -> 0.6, c2 -> 0.6, c3 -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.22081
R0 of the mutant type = 2.66498
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0115353
Cumulative mortality (mutant) = 0.

```



```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

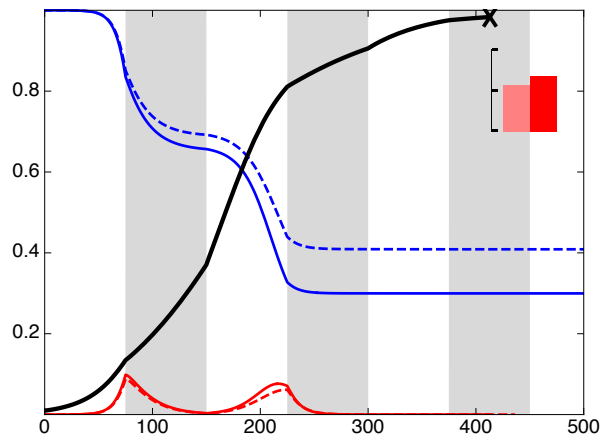
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT1 = Show[fcontrol, fS, fSDashed, FIGfreq, fnoevol, fevol, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

```

R0 of the wild type = 2.22081  
R0 of the mutant type = 2.66498  
Case mortality = 0.0195122  
Case mortality (mutant) = 0.0195122  
Cumulative mortality (total) = 0.0136644  
Cumulative mortality (mutant) = 0.00627264  
413  
{0.983372}



■ Figure 3f: Evolution of asymptomatic fraction  $f$ , control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 1/6, (* 1/TIME IN ASYMPTOMATIC CLASS = 1/6, EQUAL TO THE EXPECTED TIME IN P PLUS I *)

(*Strength of control measures*)
 $c_1$  -> 0.6,  $c_2$  -> 0.6,  $c_3$  -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.22081
R0 of the mutant type = 2.22081
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0115353
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray, PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

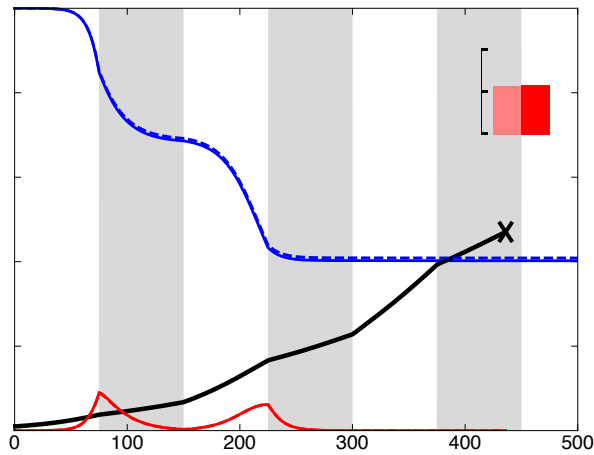
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}], Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT2 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True, TicksStyle → Directive[Black, FontFamily → "Helvetica", 11], LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}}, FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]}, {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}]
]

R0 of the wild type = 2.22081
R0 of the mutant type = 2.22081
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0117959
Cumulative mortality (mutant) = 0.00119438
436
{0.470476}

```



■ Figure 3g: Evolution of pre-symptomatic phase  $\kappa$ , control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 2 / 3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 1 / 6, (* 1/TIME IN ASYMPTOMATIC CLASS = 1/6, EQUAL TO THE EXPECTED TIME IN P PLUS I *)

(*Strength of control measures*)
 $c_1$  -> 0.6,  $c_2$  -> 0.6,  $c_3$  -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.22081
R0 of the mutant type = 2.62081
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0115353
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

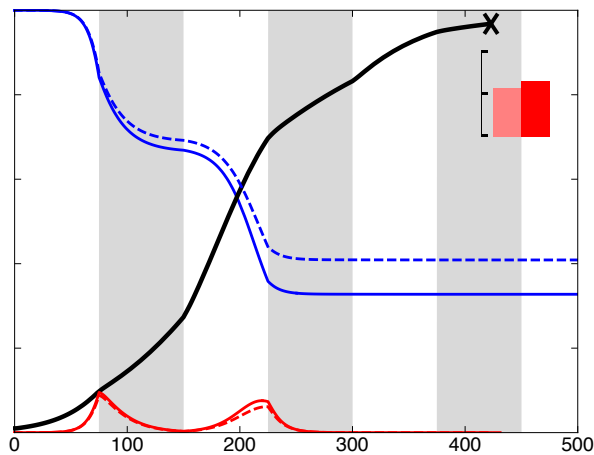
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT3 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

```

R0 of the wild type = 2.22081  
R0 of the mutant type = 2.62081  
Case mortality = 0.0195122  
Case mortality (mutant) = 0.0195122  
Cumulative mortality (total) = 0.0131208  
Cumulative mortality (mutant) = 0.00484045  
423  
{0.968044}



■ Figure 3h: Evolution of virulence  $\alpha$ , control measures

```

pars = { $\beta$  -> 1,  $\beta_m$  -> 1, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.00, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 1/6, (* 1/TIME IN ASYMPTOMATIC CLASS = 1/6, EQUAL TO THE EXPECTED TIME IN P PLUS I *)

(*Strength of control measures*)
c1 -> 0.6, c2 -> 0.6, c3 -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.22081
R0 of the mutant type = 2.25333
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0115353
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray, PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

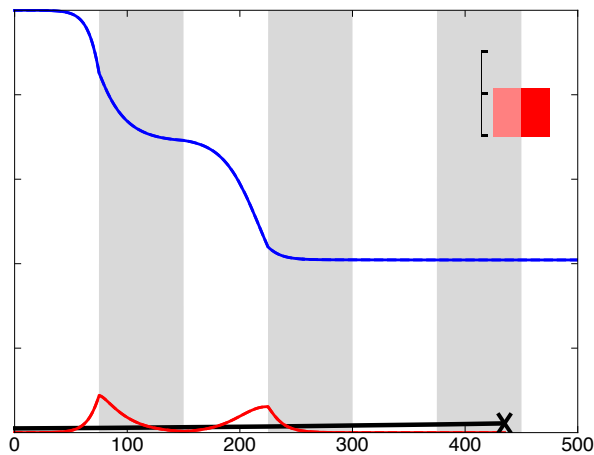
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}], Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT4 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True, TicksStyle → Directive[Black, FontFamily → "Helvetica", 11], LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}}, FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]}, {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}]
]

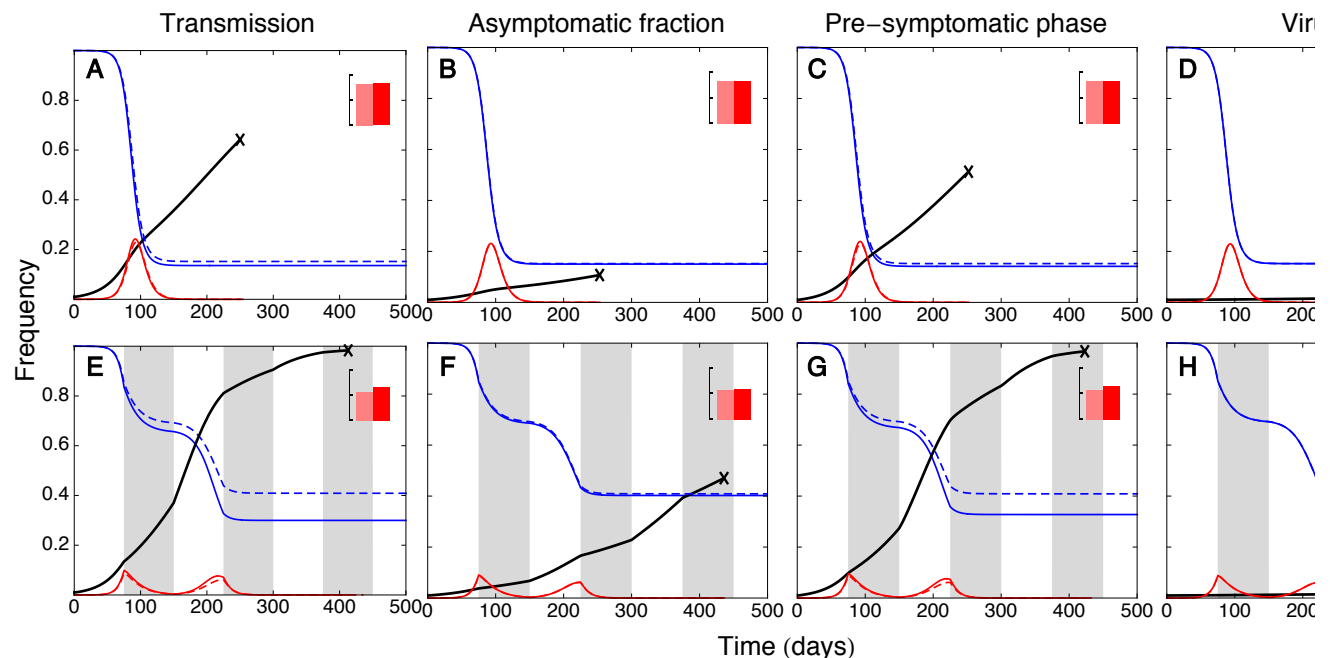
R0 of the wild type = 2.22081
R0 of the mutant type = 2.25333
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0113901
Cumulative mortality (mutant) = 0.
435
{0.0218945}

```



### Altogether

```
Show[
GraphicsGrid[{{FigTOP1, FigTOP2, FigTOP3, FigTOP4}, {FigBOT1, FigBOT2, FigBOT3, FigBOT4}},
FrameLabel -> label, Spacings -> {-10, 10}],
Graphics[Text[Style["A", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {45, -33}]],
Graphics[Text[Style["B", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {379, -33}]],
Graphics[Text[Style["C", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {729, -33}]],
Graphics[Text[Style["D", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {1080, -33}]],
Graphics[Text[Style["E", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {45, -315}]],
Graphics[Text[Style["F", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {379, -315}]],
Graphics[Text[Style["G", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {729, -315}]],
Graphics[Text[Style["H", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {1080, -315}]],
Graphics[Text[Style["Transmission", 16, FontFamily -> "Helvetica"], {180, 10}]],
Graphics[Text[Style["Asymptomatic fraction", 16, FontFamily -> "Helvetica"], {520, 10}]],
Graphics[Text[Style["Pre-symptomatic phase", 16, FontFamily -> "Helvetica"], {870, 10}]],
Graphics[Text[Style["Virulence", 16, FontFamily -> "Helvetica"], {1220, 10}]],
Graphics[Text[Style["Time (days)", 16, FontFamily -> "Helvetica"], {700, -580}]],
Graphics[Rotate[Text[Style["Frequency", 16, FontFamily -> "Helvetica"], {-20, -270}], Pi / 2]]
]
```



```
Export["Fig3.pdf", %];
```

### Figure 3alt - Main change is more asymptomatics ( $f=0.4$ )

$\beta$  adjusted to keep  $R_0$  and doubling time of the disease within range observed.

### Code

Common settings



```

Clear["Global`*"]

Off[General::spell1]
Off[General::spell]
Off[NDSolve::nlnum]

tfinal = 500;

tfig = 500;

label = {"Time (days)", "Frequency"};
label = None;

parvec = {β, βm, α, αm, x̄yP, x̄yPm, f, fm, x̄yE, x̄yI, x̄yA, c1, c2, c3, mut};

Clear[finalfreq, NSolution]
finalfreq[vec_] :=
finalfreq[vec] = Block[{β = vec[[1]], βm = vec[[2]], α = vec[[3]], αm = vec[[4]], x̄yP = vec[[5]],
  x̄yPm = vec[[6]], f = vec[[7]], fm = vec[[8]], x̄yE = vec[[9]], x̄yI = vec[[10]],
  x̄yA = vec[[11]], c1 = vec[[12]], c2 = vec[[13]], c3 = vec[[14]], mut = vec[[15]]},

  (*REMAINING PARAMETERS*)
  βyA = β / 10; βyP = β; βyI = β / 3;
  x̄yAm = x̄yA; x̄yIm = x̄yI;
  βyAm = βm / 10; βyPm = βm; βyIm = βm / 3;

  (* E: Exposed (non-infectious) cases *)
  (* A: asymptomatic cases *)
  (* P: pre-symptomatic cases *)
  (* S: symptomatic cases *)
  (* f: proportion of fsymptomatic hosts *)
  (* c: amount of distancing applied *)

  (*INOCULATION*)
  start = 10-5;

  t = .;
  c = .;

  c[t_] := Evaluate[If[t < t1min, 0,
    If[t < t1max, c1, If[t < t2min, 0, If[t < t2max, c2, If[t < t3min, 0, If[t < t3max, c3, 0]]]]]];
  h[t] = (1 - c[t]) (βyA yA[t] + βyP yP[t] + βyI yI[t]);
  hm[t] = (1 - c[t]) (βyAm yAm[t] + βyPm yPm[t] + βyIm yIm[t]);

  sys = {S'[t] == - (h[t] + hm[t]) S[t],
    yE'[t] == h[t] S[t] - x̄yE yE[t],
    yA'[t] == f x̄yE yE[t] - x̄yA yA[t],
    yP'[t] == (1 - f) x̄yE yE[t] - x̄yP yP[t],
    yI'[t] == x̄yP yP[t] - (x̄yI + α) yI[t],
    yR'[t] == x̄yA yA[t] + x̄yI yI[t],
    yD'[t] == α yI[t]}; (*yD serves as a counter of the cumulative number of deaths*)

  sysm = {
    yEm'[t] == hm[t] S[t] - x̄yE yEm[t],
    yAm'[t] == fm x̄yE yEm[t] - x̄yAm yAm[t],
    yPm'[t] == (1 - fm) x̄yE yEm[t] - x̄yPm yPm[t],
    yIm'[t] == x̄yPm yPm[t] - (x̄yIm + αm) yIm[t],
    yRm'[t] == x̄yAm yAm[t] + x̄yIm yIm[t],
    yDm'[t] == αm yIm[t]}; (*yDm serves as a counter of the cumulative number of deaths*)

  (*FIRST BOUT OF CONTROL*)
  t1min = 75;
  t1max = 150;
  (*SECOND BOUT OF CONTROL*)
  t2min = 225;
  t2max = 300;
  (*THIRD BOUT OF CONTROL*)
  t3min = 375;
  t3max = 450;

  init = {S[0] == 1, yE[0] == start (1 - mut), yA[0] == 0, yP[0] == 0, yI[0] == 0, yR[0] == 0, yD[0] == 0};
  initm = {yEm[0] == start (mut), yAm[0] == 0, yPm[0] == 0, yIm[0] == 0, yRm[0] == 0, yDm[0] == 0};

  var = {S, yE, yA, yP, yI, yR, yD};
  varm = {yEm, yAm, yPm, yIm, yRm, yDm};

  NSolution[vec] =
  NDSolve[
    Flatten[{sys, sysm, init, initm}], Flatten[{var, varm}], {t, 0, tfinal}, AccuracyGoal → 100];

```

```

(*R0*)
Print["R0 of the wild type = ",  $\frac{\beta y_A f}{\kappa y_A} + \frac{(1-f)(\beta y_P(\alpha + \kappa y_I) + \beta y_I \kappa y_P)}{(\alpha + \kappa y_I) \kappa y_P}$ ];

(*Rm*)
Print["R0 of the mutant type = ",  $\frac{\beta y_{Am} f}{\kappa y_{Am}} + \frac{(1-f)(\beta y_{Pm}(\alpha m + \kappa y_{Im}) + \beta y_{Im} \kappa y_{Pm})}{(\alpha m + \kappa y_{Im}) \kappa y_{Pm}}$ ];

(*CASE MORTALITY*)
Print["Case mortality = ",  $(1-f) \frac{\alpha}{\kappa y_I + \alpha}$ ];
Print["Case mortality (mutant) = ",  $(1-fm) \frac{\alpha m}{\kappa y_I + \alpha m}$ ];

(*CUMULATIVE MORTALITY*)
Print["Cumulative mortality (total) = ", yD[tfinal] + yDm[tfinal] /. Flatten[NSolution[vec]]];
Print["Cumulative mortality (mutant) = ", yDm[tfinal] /. Flatten[NSolution[vec]]];
]

```

■ Figure 3a: Evolution of transmission  $\beta$ , no control measures

```

pars = { $\beta \rightarrow 1.3$ ,  $\beta m \rightarrow 1.2 \times 1.3$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha \rightarrow 0.005$ ,  $\alpha m \rightarrow 0.005$ , (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P \rightarrow 1$ ,  $\kappa y_{Pm} \rightarrow 1$ , (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f  $\rightarrow 0.4$ ,  $f m \rightarrow 0.4$ , (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E \rightarrow 0.25$ , (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I \rightarrow 0.2$ , (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A \rightarrow 0.11$ , (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1  $\rightarrow 0$ , c2  $\rightarrow 0$ , c3  $\rightarrow 0$ 
};

```

The doubling time of the disease when rare, as calculated from the eigenvalue ("poly") of the stability matrix:

```

Sort[Solve[
( $\kappa E (-S \alpha \beta P \kappa A + f S \alpha \beta P \kappa A - S \beta P \kappa A \kappa I + f S \beta P \kappa A \kappa I - f S \alpha \beta A \kappa P + \alpha \kappa A \kappa P - S \beta I \kappa A \kappa P + f S \beta I \kappa A \kappa P - f S \beta A \kappa I \kappa P + \kappa A \kappa I \kappa P) +$ 
 $(-f S \alpha \beta A \kappa E - S \alpha \beta P \kappa E + f S \alpha \beta P \kappa E + \alpha \kappa A \kappa E - S \beta P \kappa A \kappa E + f S \beta P \kappa A \kappa E - f S \beta A \kappa E \kappa I - S \beta P \kappa E \kappa I + f S \beta P \kappa E \kappa I +$ 
 $\kappa A \kappa E \kappa I + \alpha \kappa A \kappa P + \alpha \kappa E \kappa P - f S \beta A \kappa E \kappa P - S \beta I \kappa E \kappa P + f S \beta I \kappa E \kappa P + \kappa A \kappa E \kappa P + \kappa A \kappa I \kappa P + \kappa E \kappa I \kappa P) \lambda +$ 
 $(\alpha \kappa A + \alpha \kappa E - f S \beta A \kappa E - S \beta P \kappa E + f S \beta P \kappa E + \kappa A \kappa E + \kappa A \kappa I + \kappa E \kappa I + \alpha \kappa P + \kappa A \kappa P + \kappa E \kappa P + \kappa I \kappa P) \lambda^2 +$ 
 $(\alpha + \kappa A + \kappa E + \kappa I + \kappa P) \lambda^3 + \lambda^4 / . S \rightarrow 1 / . \beta A \rightarrow \beta / 10 / . \beta P \rightarrow \beta / .$ 
 $\beta I \rightarrow \beta / 3 / . \kappa A \rightarrow \kappa y_A / . \kappa E \rightarrow \kappa y_E / . \kappa P \rightarrow \kappa y_P / . \kappa I \rightarrow \kappa y_I / . pars) == 0, \lambda]]

Solve[
(Exp[
 $\lambda$ 
t] ==
2) /.
Last[
%],
t]

{{ $\lambda \rightarrow -1.14279$ }, { $\lambda \rightarrow -0.438351$ }, { $\lambda \rightarrow -0.123009$ }, { $\lambda \rightarrow 0.139154$ }}

{{t  $\rightarrow 4.98116$ }}

parset = parvec /. pars /. mut  $\rightarrow 0$ ;
finalfreq[parset]

tNOevolNC = LengthWhile[
Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
{t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
{t, 0, tNOevolNC}, PlotRange  $\rightarrow \{\{0, tfig\}, \{10^{-7}, 1\}\}$ ,
PlotStyle  $\rightarrow \{\{Thickness[0.005], Red, Dashed\}\}$ , AspectRatio  $\rightarrow 0.75$ ];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
PlotRange  $\rightarrow \{\{0, tfig\}, \{0, 1\}\}$ , PlotStyle  $\rightarrow \{\{Thickness[0.005], Dashed, Blue\}\}$ , AspectRatio  $\rightarrow 0.75$ ];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];$ 
```

```

R0 of the wild type = 2.52102
R0 of the mutant type = 3.02522
Case mortality = 0.0146341
Case mortality (mutant) = 0.0146341
Cumulative mortality (total) = 0.013103
Cumulative mortality (mutant) = 0.

260

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% ("], ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]]];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

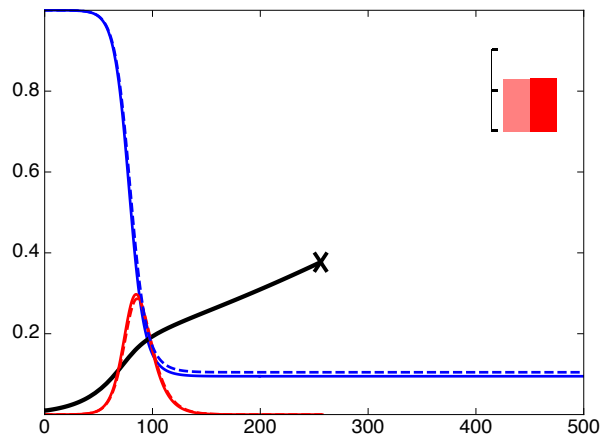
FigTOP1 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

R0 of the wild type = 2.52102
R0 of the mutant type = 3.02522
Case mortality = 0.0146341
Case mortality (mutant) = 0.0146341
Cumulative mortality (total) = 0.0132471
Cumulative mortality (mutant) = 0.00214751

256

{0.376943}

```



■ Figure 3b: Evolution of asymptomatic fraction  $f$ , no control measures

```

pars = { $\beta$  -> 1.3,  $\beta_m$  -> 1.3, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.4,  $f_m$  -> 0.3, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1$  -> 0,  $c_2$  -> 0,  $c_3$  -> 0
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.52102
R0 of the mutant type = 2.52102
Case mortality = 0.0146341
Case mortality (mutant) = 0.0170732
Cumulative mortality (total) = 0.013103
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

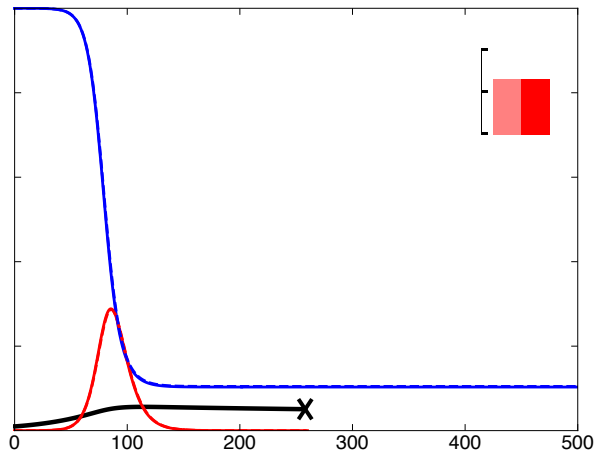
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP2 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.52102
R0 of the mutant type = 2.52102
Case mortality = 0.0146341
Case mortality (mutant) = 0.0170732
Cumulative mortality (total) = 0.0132374
Cumulative mortality (mutant) = 0.000791761
258
{0.0507279}

```



■ Figure 3c: Evolution of pre-symptomatic phase  $\kappa$ , no control measures

```

pars = {β -> 1.3, βm -> 1.3, (*TRANSMISSION OF THE MUTANT*)
  α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
  κyP -> 1, κyPm -> 2 / 3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

  f -> 0.4, fm -> 0.4, (* PROPORTION OF ASYMPTOMATIC CASES *)
  κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
  κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
  κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

  (*Strength of control measures*)
  c1 -> 0, c2 -> 0, c3 -> 0
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.52102
R0 of the mutant type = 2.91102
Case mortality = 0.0146341
Case mortality (mutant) = 0.0146341
Cumulative mortality (total) = 0.013103
Cumulative mortality (mutant) = 0.
260

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

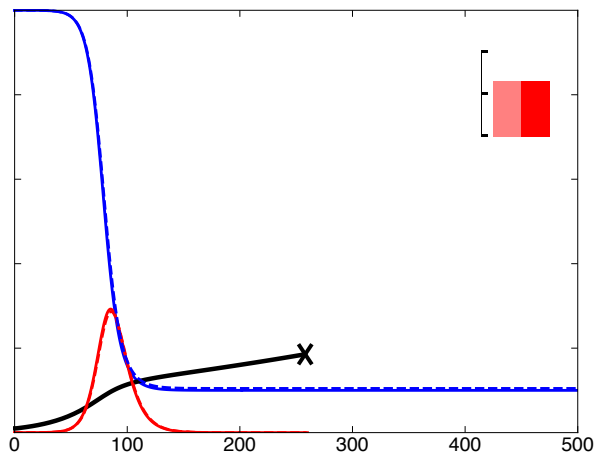
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP3 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.52102
R0 of the mutant type = 2.91102
Case mortality = 0.0146341
Case mortality (mutant) = 0.0146341
Cumulative mortality (total) = 0.01317
Cumulative mortality (mutant) = 0.00124589
258
{0.185488}

```



■ Figure 3d: Evolution of virulence  $\alpha$ , no control measures

```

pars = { $\beta$  -> 1.3,  $\beta_m$  -> 1.3, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.0, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.4,  $f_m$  -> 0.4, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1$  -> 0,  $c_2$  -> 0,  $c_3$  -> 0
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.52102
R0 of the mutant type = 2.55273
Case mortality = 0.0146341
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.013103
Cumulative mortality (mutant) = 0.

```



```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

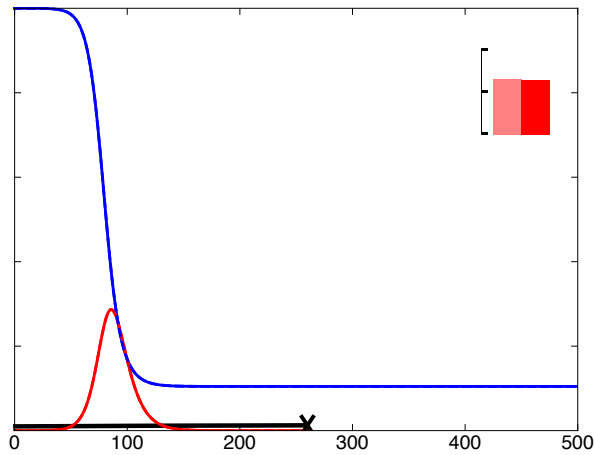
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP4 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.52102
R0 of the mutant type = 2.55273
Case mortality = 0.0146341
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0129592
Cumulative mortality (mutant) = 0.
260
{0.0125059}

```



■ Figure 3e: Evolution of transmission  $\beta$ , control measures

```

pars = { $\beta$  -> 1.3,  $\beta_m$  ->  $1.2 \times 1.3$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.4,  $f_m$  -> 0.4, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1$  -> 0.6,  $c_2$  -> 0.6,  $c_3$  -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.52102
R0 of the mutant type = 3.02522
Case mortality = 0.0146341
Case mortality (mutant) = 0.0146341
Cumulative mortality (total) = 0.008397
Cumulative mortality (mutant) = 0.

500

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

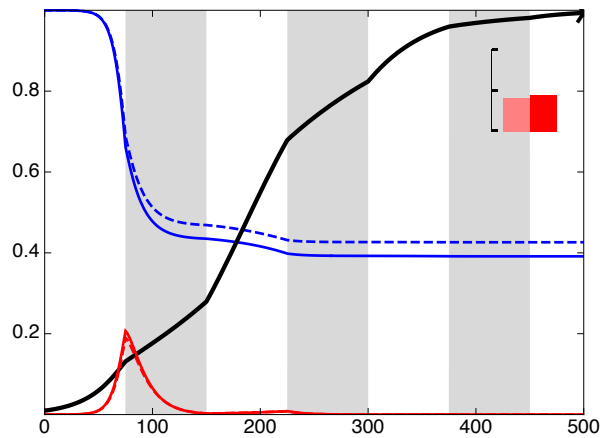
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT1 = Show[fcontrol, fS, fSDashed, FIGfreq, fnoevol, fevol, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

```

R0 of the wild type = 2.52102  
R0 of the mutant type = 3.02522  
Case mortality = 0.0146341  
Case mortality (mutant) = 0.0146341  
Cumulative mortality (total) = 0.00890626  
Cumulative mortality (mutant) = 0.00158136  
500  
{0.993585}



■ Figure 3f: Evolution of asymptomatic fraction  $f$ , control measures

```

pars = { $\beta$  -> 1.3,  $\beta_m$  -> 1.3, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.4,  $f_m$  -> 0.3, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1$  -> 0.6,  $c_2$  -> 0.6,  $c_3$  -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.52102
R0 of the mutant type = 2.52102
Case mortality = 0.0146341
Case mortality (mutant) = 0.0170732
Cumulative mortality (total) = 0.008397
Cumulative mortality (mutant) = 0.
500

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

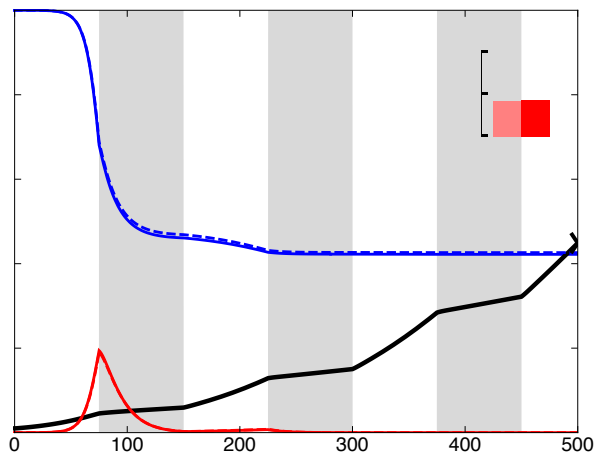
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT2 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

R0 of the wild type = 2.52102
R0 of the mutant type = 2.52102
Case mortality = 0.0146341
Case mortality (mutant) = 0.0170732
Cumulative mortality (total) = 0.00853032
Cumulative mortality (mutant) = 0.000512453
500
{0.448727}

```



■ Figure 3g: Evolution of pre-symptomatic phase  $\kappa$ , control measures

```

pars = {β -> 1.3, βm -> 1.3, (*TRANSMISSION OF THE MUTANT*)
  α -> 0.005, αm -> 0.005, (*VIRULENCE OF THE MUTANT*)
  κyP -> 1, κyPm -> 2 / 3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

  f -> 0.4, fm -> 0.4, (* PROPORTION OF ASYMPTOMATIC CASES *)
  κyE -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
  κyI -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
  κyA -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

  (*Strength of control measures*)
  c1 -> 0.6, c2 -> 0.6, c3 -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.52102
R0 of the mutant type = 2.91102
Case mortality = 0.0146341
Case mortality (mutant) = 0.0146341
Cumulative mortality (total) = 0.008397
Cumulative mortality (mutant) = 0.
500

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig}, PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray, PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}], Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

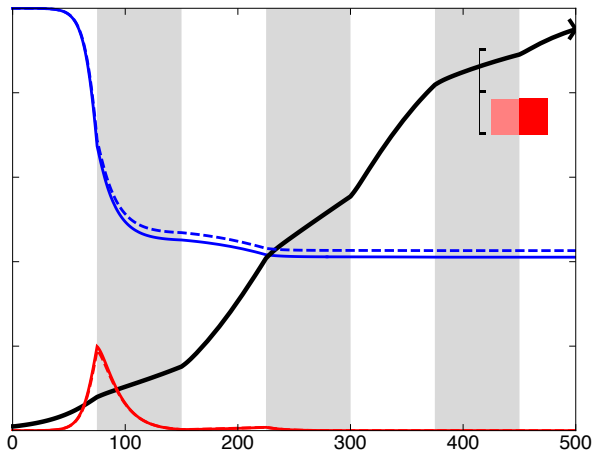
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}], Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}], Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT3 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True, TicksStyle → Directive[Black, FontFamily → "Helvetica", 11], LabelStyle → Directive[12, FontFamily → "Helvetica", Black], FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]}, {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}}, FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]}, {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}]
]

R0 of the wild type = 2.52102
R0 of the mutant type = 2.91102
Case mortality = 0.0146341
Case mortality (mutant) = 0.0146341
Cumulative mortality (total) = 0.00862458
Cumulative mortality (mutant) = 0.000886798
500
{0.950233}

```



■ **Figure 3h: Evolution of virulence  $\alpha$ , control measures**

```

pars = { $\beta$  -> 1.3,  $\beta_m$  -> 1.3, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.00, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.4,  $f_m$  -> 0.4, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1 -> 0.6, c2 -> 0.6, c3 -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.52102
R0 of the mutant type = 2.55273
Case mortality = 0.0146341
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.008397
Cumulative mortality (mutant) = 0.
500

```



```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

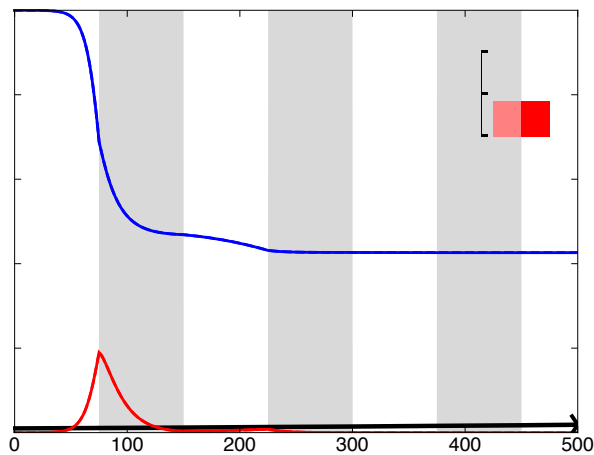
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT4 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

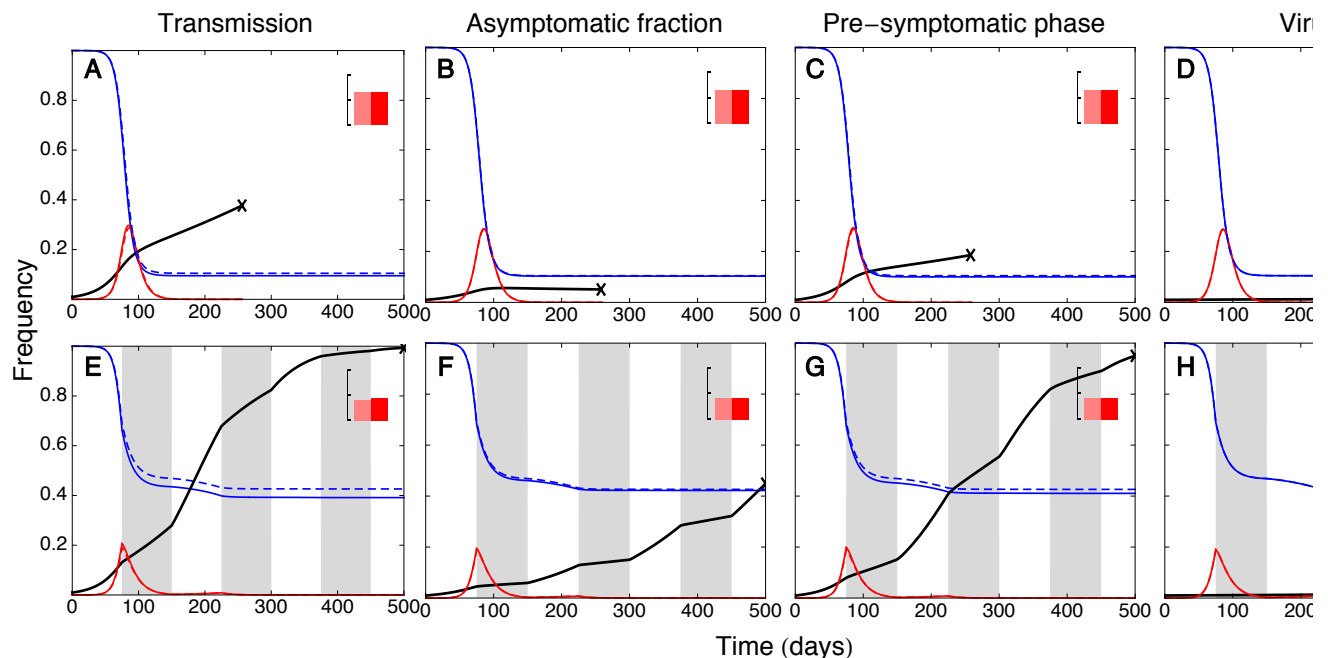
R0 of the wild type = 2.52102
R0 of the mutant type = 2.55273
Case mortality = 0.0146341
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.00830522
Cumulative mortality (mutant) = 0.
500
{0.0186469}

```



- **Altogether**

```
Show[
GraphicsGrid[{{FigTOP1, FigTOP2, FigTOP3, FigTOP4}, {FigBOT1, FigBOT2, FigBOT3, FigBOT4}},
FrameLabel -> label, Spacings -> {-10, 10}],
Graphics[Text[Style["A", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {45, -33}]],
Graphics[Text[Style["B", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {379, -33}]],
Graphics[Text[Style["C", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {729, -33}]],
Graphics[Text[Style["D", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {1080, -33}]],
Graphics[Text[Style["E", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {45, -315}]],
Graphics[Text[Style["F", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {379, -315}]],
Graphics[Text[Style["G", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {729, -315}]],
Graphics[Text[Style["H", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {1080, -315}]],
Graphics[Text[Style["Transmission", 16, FontFamily -> "Helvetica"], {180, 10}]],
Graphics[Text[Style["Asymptomatic fraction", 16, FontFamily -> "Helvetica"], {520, 10}]],
Graphics[Text[Style["Pre-symptomatic phase", 16, FontFamily -> "Helvetica"], {870, 10}]],
Graphics[Text[Style["Virulence", 16, FontFamily -> "Helvetica"], {1220, 10}]],
Graphics[Text[Style["Time (days)", 16, FontFamily -> "Helvetica"], {700, -580}]],
Graphics[Rotate[Text[Style["Frequency", 16, FontFamily -> "Helvetica"], {-20, -270}], Pi / 2]]
]
```



```
Export["Fig3.pdf", %];
```

- **Figure 3alt - Main change is more transmission in infectious stage ( $\beta_I = \beta_P$ )**

$\beta$  adjusted to keep R0 and doubling time of the disease within range observed, and mutant effect on  $\kappa P$  increased to visualize.

- **Code**

## Common settings

```

Clear["Global`*"]

Off[General::spell1]
Off[General::spell]
Off[NDSolve::nlnum]

tfinal = 500;

tfig = 500;

label = {"Time (days)", "Frequency"};
label = None;

parvec = { $\beta$ ,  $\beta_m$ ,  $\alpha$ ,  $\alpha_m$ ,  $\kappa y_P$ ,  $\kappa y_{Pm}$ ,  $f$ ,  $f_m$ ,  $\kappa y_E$ ,  $\kappa y_I$ ,  $\kappa y_A$ ,  $c_1$ ,  $c_2$ ,  $c_3$ ,  $\text{mut}$ };

Clear[finalfreq, NSolution]
finalfreq[vec_] :=
finalfreq[vec] = Block[{ $\beta$  = vec[[1]],  $\beta_m$  = vec[[2]],  $\alpha$  = vec[[3]],  $\alpha_m$  = vec[[4]],  $\kappa y_P$  = vec[[5]],
 $\kappa y_{Pm}$  = vec[[6]],  $f$  = vec[[7]],  $f_m$  = vec[[8]],  $\kappa y_E$  = vec[[9]],  $\kappa y_I$  = vec[[10]],
 $\kappa y_A$  = vec[[11]],  $c_1$  = vec[[12]],  $c_2$  = vec[[13]],  $c_3$  = vec[[14]],  $\text{mut}$  = vec[[15]]},

(*REMAINING PARAMETERS*)
 $\beta y_A$  =  $\beta$  / 10;  $\beta y_P$  =  $\beta$ ;  $\beta y_I$  =  $\beta$ ;
 $\kappa y_{Am}$  =  $\kappa y_A$ ;  $\kappa y_{Im}$  =  $\kappa y_I$ ;
 $\beta y_{Am}$  =  $\beta_m$  / 10;  $\beta y_{Pm}$  =  $\beta_m$ ;  $\beta y_{Im}$  =  $\beta_m$ ;

(* E: Exposed (non-infectious) cases *)
(* A: asymptomatic cases *)
(* P: pre-symptomatic cases *)
(* S: symptomatic cases *)
(* f: proportion of fsymptomatic hosts *)
(* c: amount of distancing applied *)

(*INOCULATION*)
start =  $10^{-5}$ ;

t = .;
c = .;

c[t_] := Evaluate[If[t < t1min, 0,
If[t < t1max, c1, If[t < t2min, 0, If[t < t2max, c2, If[t < t3min, 0, If[t < t3max, c3, 0]]]]]];
h[t] = (1 - c[t]) ( $\beta y_A y_A[t]$  +  $\beta y_P y_P[t]$  +  $\beta y_I y_I[t]$ );
hm[t] = (1 - c[t]) ( $\beta y_{Am} y_{Am}[t]$  +  $\beta y_{Pm} y_{Pm}[t]$  +  $\beta y_{Im} y_{Im}[t]$ );

sys = {S'[t] == - (h[t] + hm[t]) S[t],
yE'[t] == h[t] S[t] -  $\kappa y_E y_E[t]$ ,
yA'[t] == f  $\kappa y_E y_E[t]$  -  $\kappa y_A y_A[t]$ ,
yP'[t] == (1 - f)  $\kappa y_E y_E[t]$  -  $\kappa y_P y_P[t]$ ,
yI'[t] ==  $\kappa y_P y_P[t]$  - ( $\kappa y_I$  +  $\alpha$ ) yI[t],
yR'[t] ==  $\kappa y_A y_A[t]$  +  $\kappa y_I y_I[t]$ ,
yD'[t] ==  $\alpha y_I[t]$ }; (*yD serves as a counter of the cumulative number of deaths*)

sysm = {
yEm'[t] == hm[t] S[t] -  $\kappa y_E y_{Em}[t]$ ,
yAm'[t] == f_m  $\kappa y_E y_{Em}[t]$  -  $\kappa y_{Am} y_{Am}[t]$ ,
yPm'[t] == (1 - f_m)  $\kappa y_E y_{Em}[t]$  -  $\kappa y_{Pm} y_{Pm}[t]$ ,
yIm'[t] ==  $\kappa y_{Pm} y_{Pm}[t]$  - ( $\kappa y_{Im}$  +  $\alpha_m$ ) yIm[t],
yRm'[t] ==  $\kappa y_{Am} y_{Am}[t]$  +  $\kappa y_{Im} y_{Im}[t]$ ,
yDm'[t] ==  $\alpha_m y_{Im}[t]$ }; (*yDm serves as a counter of the cumulative number of deaths*)

(*FIRST BOUT OF CONTROL*)
t1min = 75;
t1max = 150;
(*SECOND BOUT OF CONTROL*)
t2min = 225;
t2max = 300;
(*THIRD BOUT OF CONTROL*)
t3min = 375;
t3max = 450;

init = {S[0] == 1, yE[0] == start (1 - mut), yA[0] == 0, yP[0] == 0, yI[0] == 0, yR[0] == 0, yD[0] == 0};
initm = {yEm[0] == start (mut), yAm[0] == 0, yPm[0] == 0, yIm[0] == 0, yRm[0] == 0, yDm[0] == 0};

var = {S, yE, yA, yP, yI, yR, yD};
varm = {yEm, yAm, yPm, yIm, yRm, yDm};

NSolution[vec] =
NDSolve[
Flatten[{sys, sysm, init, initm}], Flatten[{var, varm}], {t, 0, tfinal}, AccuracyGoal -> 100];

```

```

(*R0*)
Print["R0 of the wild type = ",  $\frac{\beta y_A f}{\kappa y_A} + \frac{(1-f)(\beta y_P(\alpha + \kappa y_I) + \beta y_I \kappa y_P)}{(\alpha + \kappa y_I) \kappa y_P}$ ];

(*Rm*)
Print["R0 of the mutant type = ",  $\frac{\beta y_{Am} f}{\kappa y_{Am}} + \frac{(1-f)(\beta y_{Pm}(\alpha m + \kappa y_{Im}) + \beta y_{Im} \kappa y_{Pm})}{(\alpha m + \kappa y_{Im}) \kappa y_{Pm}}$ ];

(*CASE MORTALITY*)
Print["Case mortality = ",  $(1-f) \frac{\alpha}{\kappa y_I + \alpha}$ ];
Print["Case mortality (mutant) = ",  $(1-fm) \frac{\alpha m}{\kappa y_I + \alpha m}$ ];

(*CUMULATIVE MORTALITY*)
Print["Cumulative mortality (total) = ", yD[tfinal] + yDm[tfinal] /. Flatten[NSolution[vec]]];
Print["Cumulative mortality (mutant) = ", yDm[tfinal] /. Flatten[NSolution[vec]]];
]

```

■ Figure 3a: Evolution of transmission  $\beta$ , no control measures

```

pars = { $\beta \rightarrow 0.53$ ,  $\beta m \rightarrow 1.2 \times 0.53$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha \rightarrow 0.005$ ,  $\alpha m \rightarrow 0.005$ , (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P \rightarrow 1$ ,  $\kappa y_{Pm} \rightarrow 1$ , (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f  $\rightarrow 0.2$ ,  $f m \rightarrow 0.2$ , (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E \rightarrow 0.25$ , (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I \rightarrow 0.2$ , (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A \rightarrow 0.11$ , (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1  $\rightarrow 0$ , c2  $\rightarrow 0$ , c3  $\rightarrow 0$ 
};

```

The doubling time of the disease when rare, as calculated from the eigenvalue ("poly") of the stability matrix:

```

Sort[Solve[
( $\kappa E(-S \alpha \beta P \kappa A + f S \alpha \beta P \kappa A - S \beta P \kappa A \kappa I + f S \beta P \kappa A \kappa I - f S \alpha \beta A \kappa P + \alpha \kappa A \kappa P - S \beta I \kappa A \kappa P + f S \beta I \kappa A \kappa P - f S \beta A \kappa I \kappa P + \kappa A \kappa I \kappa P) +$ 
 $(-f S \alpha \beta A \kappa E - S \alpha \beta P \kappa E + f S \alpha \beta P \kappa E + \alpha \kappa A \kappa E - S \beta P \kappa A \kappa E + f S \beta P \kappa A \kappa E - f S \beta A \kappa E \kappa I - S \beta P \kappa E \kappa I + f S \beta P \kappa E \kappa I +$ 
 $\kappa A \kappa E \kappa I + \alpha \kappa A \kappa P + \alpha \kappa E \kappa P - f S \beta A \kappa E \kappa P - S \beta I \kappa E \kappa P + f S \beta I \kappa E \kappa P + \kappa A \kappa E \kappa P + \kappa A \kappa I \kappa P + \kappa E \kappa I \kappa P) \lambda +$ 
 $(\alpha \kappa A + \alpha \kappa E - f S \beta A \kappa E - S \beta P \kappa E + f S \beta P \kappa E + \kappa A \kappa E + \kappa A \kappa I + \kappa E \kappa I + \alpha \kappa P + \kappa A \kappa P + \kappa E \kappa P + \kappa I \kappa P) \lambda^2 +$ 
 $(\alpha + \kappa A + \kappa E + \kappa I + \kappa P) \lambda^3 + \lambda^4 / . S \rightarrow 1 / . \beta A \rightarrow \beta / 10 / . \beta P \rightarrow \beta / .$ 
 $\beta I \rightarrow \beta / 3 / . \kappa A \rightarrow \kappa y_A / . \kappa E \rightarrow \kappa y_E / . \kappa P \rightarrow \kappa y_P / . \kappa I \rightarrow \kappa y_I / . pars) == 0, \lambda]]

Solve[
(Exp[
 $\lambda$ 
t] ==
2) /.
Last[
%],
t]

{{ $\lambda \rightarrow -1.07935$ }, { $\lambda \rightarrow -0.393555$ }, { $\lambda \rightarrow -0.116084$ }, { $\lambda \rightarrow 0.0239852$ }}

{{t  $\rightarrow 28.899$ }}

parset = parvec /. pars /. mut  $\rightarrow 0$ ;
finalfreq[parset]

tNOevolNC = LengthWhile[
Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
{t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
{t, 0, tNOevolNC}, PlotRange  $\rightarrow \{\{0, tfig\}, \{10^{-7}, 1\}\}$ ,
PlotStyle  $\rightarrow \{\{Thickness[0.005], Red, Dashed\}\}$ , AspectRatio  $\rightarrow 0.75$ ];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
PlotRange  $\rightarrow \{\{0, tfig\}, \{0, 1\}\}$ , PlotStyle  $\rightarrow \{\{Thickness[0.005], Dashed, Blue\}\}$ , AspectRatio  $\rightarrow 0.75$ ];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];$ 
```

```

R0 of the wild type = 2.58866
R0 of the mutant type = 3.10639
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0176311
Cumulative mortality (mutant) = 0.

249

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]]];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

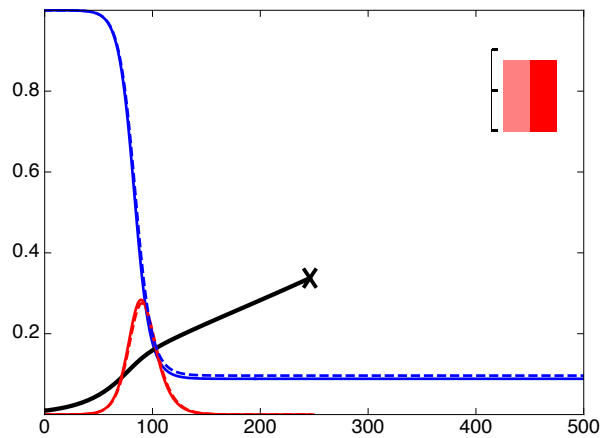
FigTOP1 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

R0 of the wild type = 2.58866
R0 of the mutant type = 3.10639
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0177853
Cumulative mortality (mutant) = 0.0024515

246

{0.33753}

```



■ Figure 3b: Evolution of asymptomatic fraction  $f$ , no control measures

```

pars = { $\beta$  -> 0.53,  $\beta_m$  -> 0.53, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1$  -> 0,  $c_2$  -> 0,  $c_3$  -> 0
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.58866
R0 of the mutant type = 2.58866
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0176311
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

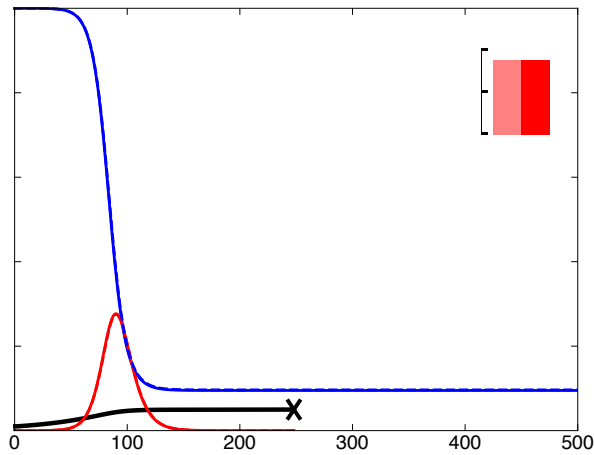
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP2 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.58866
R0 of the mutant type = 2.58866
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0177545
Cumulative mortality (mutant) = 0.000875875
248
{0.0498578}

```



■ Figure 3c: Evolution of pre-symptomatic phase  $\kappa$ , no control measures

```

pars = {β → 0.53, βm → 0.53, (*TRANSMISSION OF THE MUTANT*)
  α → 0.005, αm → 0.005, (*VIRULENCE OF THE MUTANT*)
  κyP → 1, κyPm → 1/3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

  f → 0.2, fm → 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
  κyE → 0.25, (* 1/TIME IN EXPOSED CLASS *)
  κyI → 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
  κyA → 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

  (*Strength of control measures*)
  c1 → 0, c2 → 0, c3 → 0
};

parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange → {{0, tfig}, {10-7, 1}},
  PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.58866
R0 of the mutant type = 3.43666
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0176311
Cumulative mortality (mutant) = 0.

```



```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

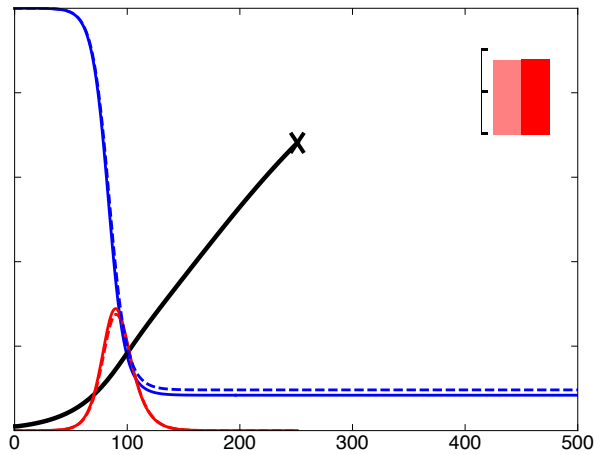
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP3 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.58866
R0 of the mutant type = 3.43666
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0178757
Cumulative mortality (mutant) = 0.00245761
251
{0.681379}

```



■ Figure 3d: Evolution of virulence  $\alpha$ , no control measures

```

pars = { $\beta$  -> 0.53,  $\beta_m$  -> 0.53, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.0, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1$  -> 0,  $c_2$  -> 0,  $c_3$  -> 0
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.58866
R0 of the mutant type = 2.64036
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0176311
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

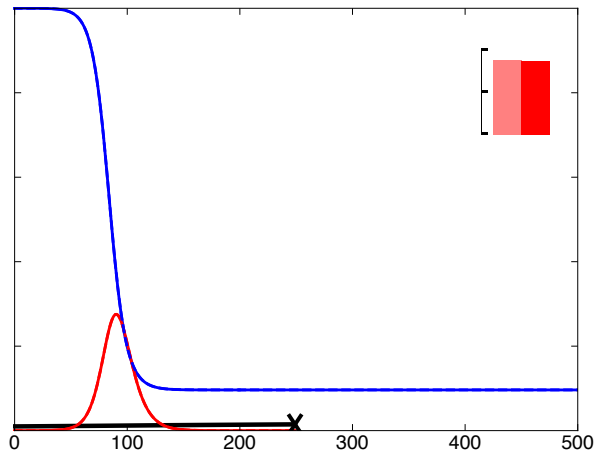
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP4 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.58866
R0 of the mutant type = 2.64036
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.017426
Cumulative mortality (mutant) = 0.
249
{0.0147944}

```



■ Figure 3e: Evolution of transmission  $\beta$ , control measures

```

pars = { $\beta \rightarrow 0.53$ ,  $\beta_m \rightarrow 0.53 \times 1.2$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha \rightarrow 0.005$ ,  $\alpha_m \rightarrow 0.005$ , (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P \rightarrow 1$ ,  $\kappa y_{Pm} \rightarrow 1$ , (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f  $\rightarrow 0.2$ ,  $f_m \rightarrow 0.2$ , (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E \rightarrow 0.25$ , (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I \rightarrow 0.2$ , (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A \rightarrow 0.11$ , (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1 \rightarrow 0.6$ ,  $c_2 \rightarrow 0.6$ ,  $c_3 \rightarrow 0.6$ 
};

parset = parvec /. pars /. mut  $\rightarrow 0$ ;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange  $\rightarrow$  {{0, tfig}, {10-7, 1}},
  PlotStyle  $\rightarrow$  {{Thickness[0.005], Red, Dashed}}, AspectRatio  $\rightarrow$  0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange  $\rightarrow$  {{0, tfig}, {0, 1}}, PlotStyle  $\rightarrow$  {Thickness[0.005], Dashed, Blue}, AspectRatio  $\rightarrow$  0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.58866
R0 of the mutant type = 3.10639
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0123517
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

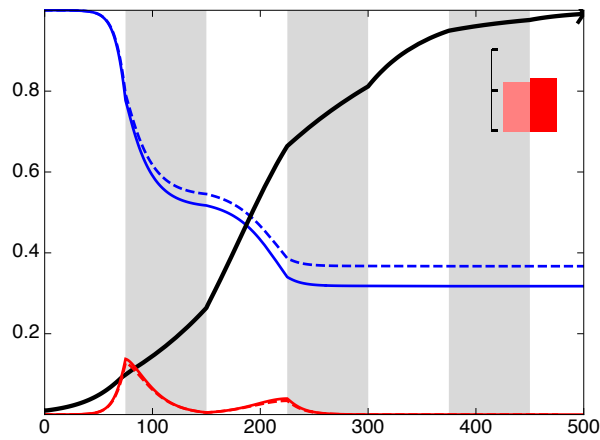
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT1 = Show[fcontrol, fS, fSDashed, FIGfreq, fnoevol, fevol, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

R0 of the wild type = 2.58866
R0 of the mutant type = 3.10639
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0133157
Cumulative mortality (mutant) = 0.00344839
500
{0.99107}

```



■ Figure 3f: Evolution of asymptomatic fraction  $f$ , control measures

```

pars = { $\beta$  -> 0.53,  $\beta_m$  -> 0.53, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1$  -> 0.6,  $c_2$  -> 0.6,  $c_3$  -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

475

Cumulative mortality (mutant) = 0.
Cumulative mortality (total) = 0.0123517
Case mortality (mutant) = 0.0219512
Case mortality = 0.0195122
R0 of the mutant type = 2.58866
R0 of the wild type = 2.58866
R0 of the wild type = 2.58866
R0 of the mutant type = 2.58866
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0123517
Cumulative mortality (mutant) = 0.
475

```

```

parset = parvec /. pars /. mut -> 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]], {t,
  0, tevolNC}], PlotRange -> {{0, tfig}, {10-7, 1}}, PlotStyle -> {{Thickness[0.005], Red}}, AspectRatio -> 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t -> tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]], {t, 0, tevolNC}], PlotRange -> {{0, tfig}, {0, 1}},
  PlotStyle -> {{Thickness[0.008], Black}}, AspectRatio -> 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Blue}, AspectRatio -> 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling -> Axis, FillingStyle -> LightGray,
  PlotStyle -> None, Frame -> True, PlotRange -> {{0, tfig}, {0, 1}}, AspectRatio -> 0.75, Frame -> True];

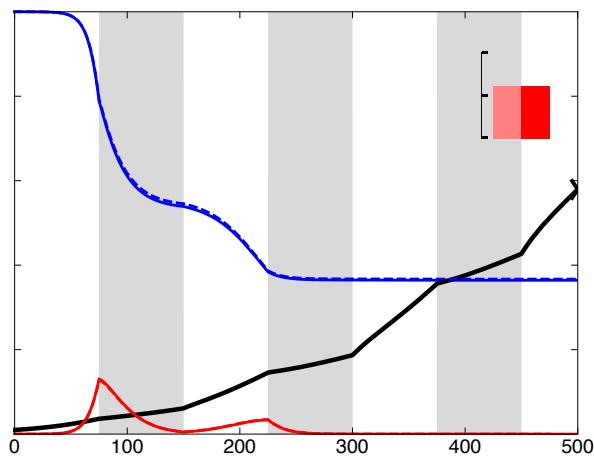
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalityevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT2 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame -> True,
  TicksStyle -> Directive[Black, FontFamily -> "Helvetica", 11],
  LabelStyle -> Directive[12, FontFamily -> "Helvetica", Black],
  FrameTicks -> {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle -> {{Directive[FontOpacity -> 0, FontSize -> 0], Directive[FontOpacity -> 0, FontSize -> 0]},
    {Directive[FontSize -> 12], Directive[FontOpacity -> 0, FontSize -> 0]}}
]
500
{0.579283}

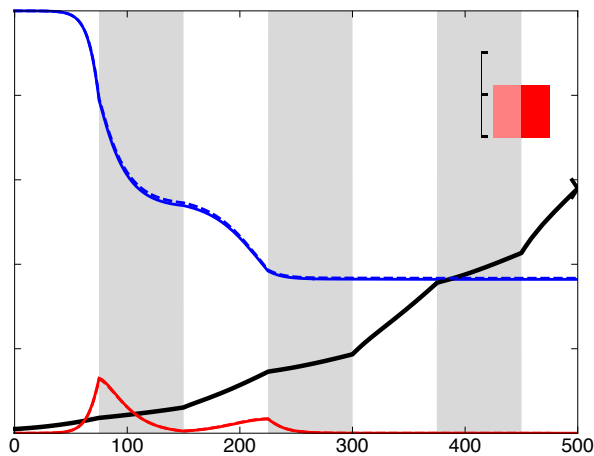
```



```

Cumulative mortality (mutant) = 0.000907129
Cumulative mortality (total) = 0.0125058
Case mortality (mutant) = 0.0219512
Case mortality = 0.0195122
R0 of the mutant type = 2.58866
R0 of the wild type = 2.58866
R0 of the wild type = 2.58866
R0 of the mutant type = 2.58866
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0125058
Cumulative mortality (mutant) = 0.000907129
500
{0.579283}

```



■ Figure 3g: Evolution of pre-symptomatic phase  $\kappa$ , control measures

```

pars = { $\beta$  -> 0.53,  $\beta_m$  -> 0.53, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa_P$  -> 1,  $\kappa_{Pm}$  -> 1 / 3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1 -> 0.6, c2 -> 0.6, c3 -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t]}} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

```



R0 of the wild type = 2.58866  
R0 of the mutant type = 3.43666  
Case mortality = 0.0195122  
Case mortality (mutant) = 0.0195122  
Cumulative mortality (total) = 0.0123517  
Cumulative mortality (mutant) = 0.  
475  
Cumulative mortality (mutant) = 0.  
Cumulative mortality (total) = 0.0123517  
Case mortality (mutant) = 0.0195122  
Case mortality = 0.0195122  
R0 of the mutant type = 3.43666  
R0 of the wild type = 2.58866  
R0 of the wild type = 2.58866  
R0 of the mutant type = 2.80066  
Case mortality = 0.0195122  
Case mortality (mutant) = 0.0195122  
Cumulative mortality (total) = 0.0123517  
Cumulative mortality (mutant) = 0.  
475

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

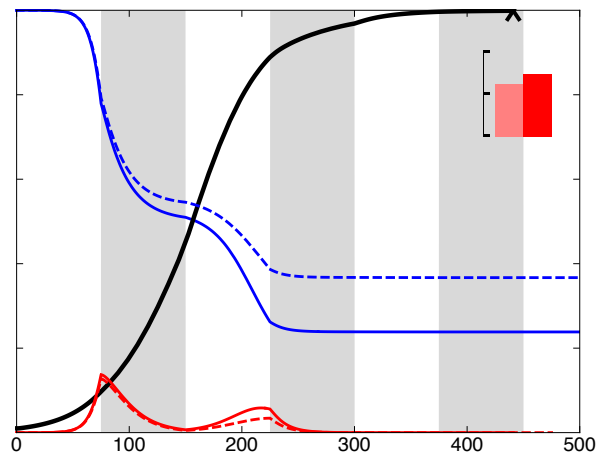
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT3 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

R0 of the wild type = 2.58866
R0 of the mutant type = 3.43666
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.014861
Cumulative mortality (mutant) = 0.00549454
441
{0.998914}

```



Cumulative mortality (mutant) = 0.00549454

Cumulative mortality (total) = 0.014861

Case mortality (mutant) = 0.0195122

Case mortality = 0.0195122

R0 of the mutant type = 3.43666

R0 of the wild type = 2.58866

R0 of the wild type = 2.58866

R0 of the mutant type = 2.80066

Case mortality = 0.0195122

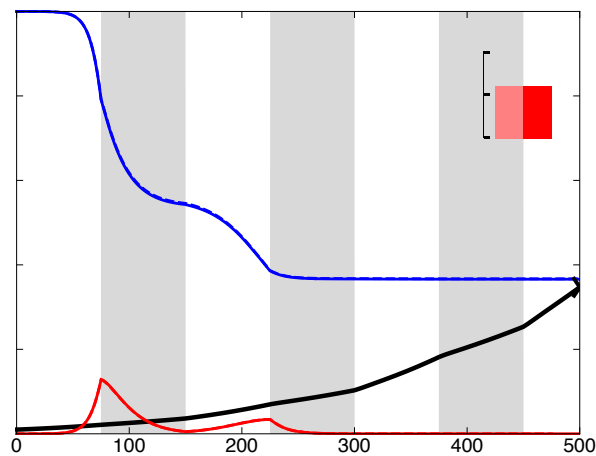
Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0123701

Cumulative mortality (mutant) = 0.000411584

500

{0.347002}



■ Figure 3h: Evolution of virulence  $\alpha$ , control measures

```
pars = { $\beta$  -> 0.53,  $\beta_m$  -> 0.53, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.00, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1$  -> 0.6,  $c_2$  -> 0.6,  $c_3$  -> 0.6
};
```

```

parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
  {t, 0, tNOevolNC}, PlotRange → {{0, tfig}, {10-7, 1}},
  PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.58866
R0 of the mutant type = 2.64036
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0123517
Cumulative mortality (mutant) = 0.
475

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT4 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

```

$R_0$  of the wild type = 2.58866

$R_0$  of the mutant type = 2.64036

Case mortality = 0.0195122

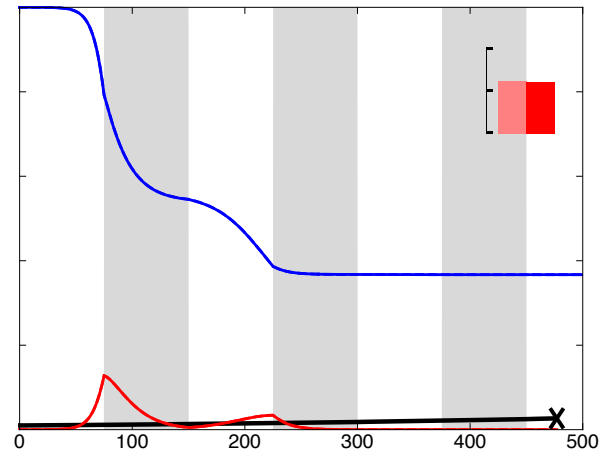
Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0121948

Cumulative mortality (mutant) = 0.

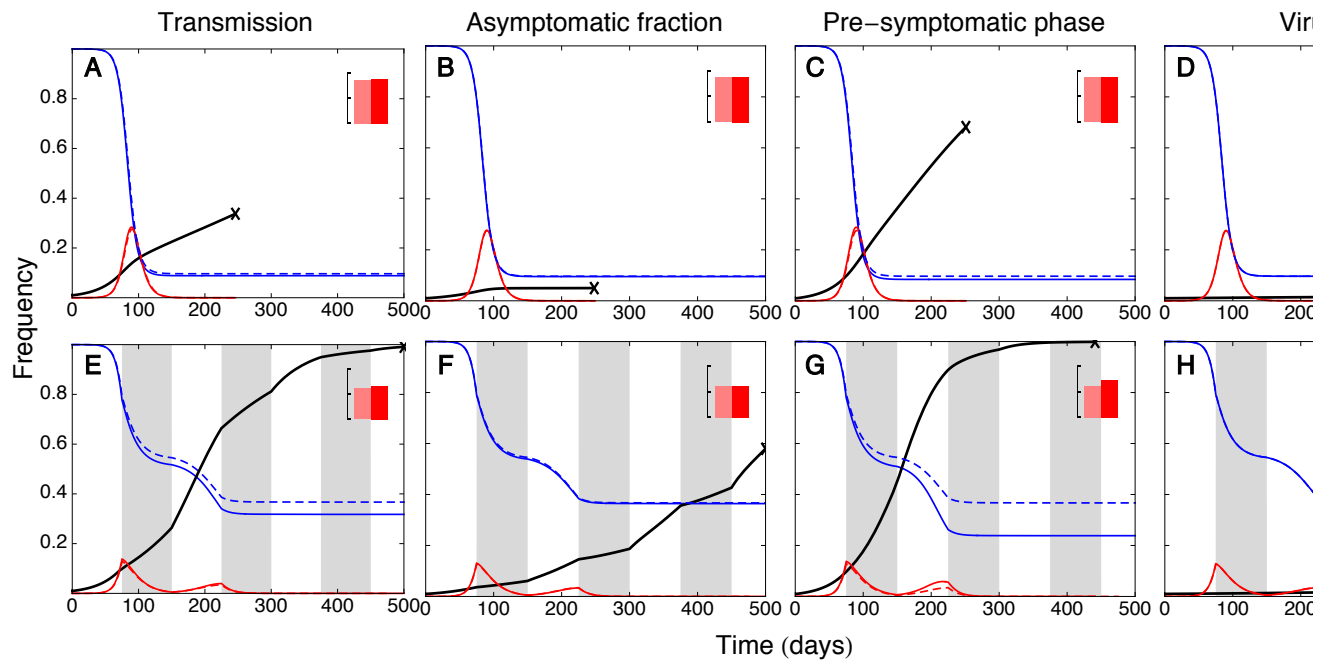
477

{0.0267739}



## ■ Altogether

```
Show[
GraphicsGrid[{{FigTOP1, FigTOP2, FigTOP3, FigTOP4}, {FigBOT1, FigBOT2, FigBOT3, FigBOT4}},
FrameLabel -> label, Spacings -> {-10, 10}],
Graphics[Text[Style["A", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {45, -33}]],
Graphics[Text[Style["B", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {379, -33}]],
Graphics[Text[Style["C", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {729, -33}]],
Graphics[Text[Style["D", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {1080, -33}]],
Graphics[Text[Style["E", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {45, -315}]],
Graphics[Text[Style["F", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {379, -315}]],
Graphics[Text[Style["G", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {729, -315}]],
Graphics[Text[Style["H", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {1080, -315}]],
Graphics[Text[Style["Transmission", 16, FontFamily -> "Helvetica"], {180, 10}]],
Graphics[Text[Style["Asymptomatic fraction", 16, FontFamily -> "Helvetica"], {520, 10}]],
Graphics[Text[Style["Pre-symptomatic phase", 16, FontFamily -> "Helvetica"], {870, 10}]],
Graphics[Text[Style["Virulence", 16, FontFamily -> "Helvetica"], {1220, 10}]],
Graphics[Text[Style["Time (days)", 16, FontFamily -> "Helvetica"], {700, -580}]],
Graphics[Rotate[Text[Style["Frequency", 16, FontFamily -> "Helvetica"], {-20, -270}], Pi / 2]]
]
```



## ■ Figure 3alt - Main change is more transmission in all infectious stages ( $\beta_A = \beta_I = \beta_P$ )

$\beta$  adjusted to keep  $R_0$  and doubling time of the disease within range observed, and mutant effect on  $\kappa P$  increased to visualize.

Also, in panels b and f, the mutant is started at a higher frequency (10%), to help see its decline.

## ■ Code

Common settings

```
Clear["Global`*"]
```

```
Off[General::spell1]
```

```
Off[General::spell]
```

```
Off[NDSolve::nlnum]
```

```
tfinal = 500;
```

```
tfig = 500;
```

```
label = {"Time (days)", "Frequency"};
```

```
label = None;
```

```
parvec = { $\beta$ ,  $\beta_m$ ,  $\alpha$ ,  $\alpha_m$ ,  $\kappa y_P$ ,  $\kappa y_{Pm}$ ,  $f$ ,  $f_m$ ,  $\kappa y_E$ ,  $\kappa y_I$ ,  $\kappa y_A$ ,  $c_1$ ,  $c_2$ ,  $c_3$ , mut};
```

```
Clear[finalfreq, NSolution]
```

```
finalfreq[vec_] :=
```

```
finalfreq[vec] = Block[{ $\beta$  = vec[[1]],  $\beta_m$  = vec[[2]],  $\alpha$  = vec[[3]],  $\alpha_m$  = vec[[4]],  $\kappa y_P$  = vec[[5]],  
 $\kappa y_{Pm}$  = vec[[6]],  $f$  = vec[[7]],  $f_m$  = vec[[8]],  $\kappa y_E$  = vec[[9]],  $\kappa y_I$  = vec[[10]],
```

```

κyA = vec[[11]], c1 = vec[[12]], c2 = vec[[13]], c3 = vec[[14]], mut = vec[[15]]},

(*REMAINING PARAMETERS*)
βyA = β; βyP = β; βyI = β;
κyAm = κyA; κyIm = κyI;
βyAm = βm; βyPm = βm; βyIm = βm;

(* E: Exposed (non-infectious) cases *)
(* A: asymptomatic cases *)
(* P: pre-symptomatic cases *)
(* S: symptomatic cases *)
(* f: proportion of fsymptomatic hosts *)
(* c: amount of distancing applied *)

(*INOCULATION*)
start = 10-5;

t = .;
c = .;

c[t_] := Evaluate[If[t < t1min, 0,
  If[t < t1max, c1, If[t < t2min, 0, If[t < t2max, c2, If[t < t3min, 0, If[t < t3max, c3, 0]]]]]];
h[t] = (1 - c[t]) (βyA yA[t] + βyP yP[t] + βyI yI[t]);
hm[t] = (1 - c[t]) (βyAm yAm[t] + βyPm yPm[t] + βyIm yIm[t]);

sys = {S'[t] == - (h[t] + hm[t]) S[t],
  yE'[t] == h[t] S[t] - κyE yE[t],
  yA'[t] == f κyE yE[t] - κyA yA[t],
  yP'[t] == (1 - f) κyE yE[t] - κyP yP[t],
  yI'[t] == κyP yP[t] - (κyI + α) yI[t],
  yR'[t] == κyA yA[t] + κyI yI[t],
  yD'[t] == α yI[t]}; (*yD serves as a counter of the cumulative number of deaths*)

sysm = {
  yEm'[t] == hm[t] S[t] - κyE yEm[t],
  yAm'[t] == fm κyE yEm[t] - κyAm yAm[t],
  yPm'[t] == (1 - fm) κyE yEm[t] - κyPm yPm[t],
  yIm'[t] == κyPm yPm[t] - (κyIm + αm) yIm[t],
  yRm'[t] == κyAm yAm[t] + κyIm yIm[t],
  yDm'[t] == αm yIm[t]}; (*yDm serves as a counter of the cumulative number of deaths*)

(*FIRST BOUT OF CONTROL*)
t1min = 75;
t1max = 150;
(*SECOND BOUT OF CONTROL*)
t2min = 225;
t2max = 300;
(*THIRD BOUT OF CONTROL*)
t3min = 375;
t3max = 450;

init = {S[0] == 1, yE[0] == start (1 - mut), yA[0] == 0, yP[0] == 0, yI[0] == 0, yR[0] == 0, yD[0] == 0};
initm = {yEm[0] == start (mut), yAm[0] == 0, yPm[0] == 0, yIm[0] == 0, yRm[0] == 0, yDm[0] == 0};

var = {S, yE, yA, yP, yI, yR, yD};
varm = {yEm, yAm, yPm, yIm, yRm, yDm};

NDSolution[vec] =
  NDSolve[
    Flatten[{sys, sysm, init, initm}], Flatten[{var, varm}], {t, 0, tfinal}, AccuracyGoal -> 100];

(*R0*)
Print["R0 of the wild type = ",  $\frac{\beta yA f}{\kappa yA} + \frac{(1 - f) (\beta yP (\alpha + \kappa yI) + \beta yI \kappa yP)}{(\alpha + \kappa yI) \kappa yP}$ ];

(*Rm*)
Print["R0 of the mutant type = ",  $\frac{\beta yAm f}{\kappa yAm} + \frac{(1 - f) (\beta yPm (\alpha m + \kappa yIm) + \beta yIm \kappa yPm)}{(\alpha m + \kappa yIm) \kappa yPm}$ ];

(*CASE MORTALITY*)
Print["Case mortality = ",  $(1 - f) \frac{\alpha}{\kappa yI + \alpha}$ ];
Print["Case mortality (mutant) = ",  $(1 - fm) \frac{\alpha m}{\kappa yI + \alpha m}$ ];

(*CUMULATIVE MORTALITY*)
Print["Cumulative mortality (total) = ", yD[tfinal] + yDm[tfinal] /. Flatten[NDSolution[vec]]];

```

```
Print["Cumulative mortality (mutant) = ", yDm[tfinal] /. Flatten[NSolution[vec]]];
```

```
]
```

### ■ Figure 3a: Evolution of transmission $\beta$ , no control measures

```
pars = { $\beta \rightarrow 0.42$ ,  $\beta_m \rightarrow 1.2 \times 0.42$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha \rightarrow 0.005$ ,  $\alpha_m \rightarrow 0.005$ , (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P \rightarrow 1$ ,  $\kappa y_{Pm} \rightarrow 1$ , (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f  $\rightarrow 0.2$ ,  $f_m \rightarrow 0.2$ , (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E \rightarrow 0.25$ , (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I \rightarrow 0.2$ , (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A \rightarrow 0.11$ , (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1  $\rightarrow 0$ , c2  $\rightarrow 0$ , c3  $\rightarrow 0$ 
};
```

The doubling time of the disease when rare, as calculated from the eigenvalue ("poly") of the stability matrix:

```
Sort[Solve[
  ( $\kappa E (-S \alpha \beta \kappa A + f S \alpha \beta P \kappa A - S \beta P \kappa A \kappa I + f S \beta P \kappa A \kappa I - f S \alpha \beta A \kappa P + \alpha \kappa A \kappa P - S \beta I \kappa A \kappa P + f S \beta I \kappa A \kappa P - f S \beta A \kappa I \kappa P + \kappa A \kappa I \kappa P) +$ 
    ( $-f S \alpha \beta A \kappa E - S \alpha \beta P \kappa E + f S \alpha \beta P \kappa E + \alpha \kappa A \kappa E - S \beta P \kappa A \kappa E + f S \beta P \kappa A \kappa E - f S \beta A \kappa E \kappa I - S \beta P \kappa E \kappa I + f S \beta P \kappa E \kappa I +$ 
       $\kappa A \kappa E \kappa I + \alpha \kappa A \kappa P + \alpha \kappa E \kappa P - f S \beta A \kappa E \kappa P - S \beta I \kappa E \kappa P + f S \beta I \kappa E \kappa P + \kappa A \kappa E \kappa P + \kappa A \kappa I \kappa P + \kappa E \kappa I \kappa P) \lambda +$ 
    ( $\alpha \kappa A + \alpha \kappa E - f S \beta A \kappa E - S \beta P \kappa E + f S \beta P \kappa E + \kappa A \kappa E + \kappa A \kappa I + \kappa E \kappa I + \alpha \kappa P + \kappa A \kappa P + \kappa E \kappa P + \kappa I \kappa P) \lambda^2 +$ 
    ( $\alpha + \kappa A + \kappa E + \kappa I + \kappa P) \lambda^3 + \lambda^4) /. S \rightarrow 1 /. \beta A \rightarrow \beta / 10 /. \beta P \rightarrow \beta /.
    \beta I \rightarrow \beta / 3 /. \kappa A \rightarrow \kappa y_A /. \kappa E \rightarrow \kappa y_E /. \kappa P \rightarrow \kappa y_P /. \kappa I \rightarrow \kappa y_I /. pars) == 0,  $\lambda$ ]]

Solve[
  (Exp[
     $\lambda$ 
    t] ==
    2) /.
  Last[
    %],
  t]
{{ $\lambda \rightarrow -1.06334$ }, { $\lambda \rightarrow -0.380156$ }, { $\lambda \rightarrow -0.116562$ }, { $\lambda \rightarrow -0.00494074$ }}
{{t  $\rightarrow -140.292$ }}

parset = parvec /. pars /. mut  $\rightarrow 0$ ;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange  $\rightarrow$  {{0, tfig}, {10-7, 1}},
  PlotStyle  $\rightarrow$  {{Thickness[0.005], Red, Dashed}}, AspectRatio  $\rightarrow$  0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange  $\rightarrow$  {{0, tfig}, {0, 1}}, PlotStyle  $\rightarrow$  {Thickness[0.005], Dashed, Blue}, AspectRatio  $\rightarrow$  0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];
R0 of the wild type = 2.73866
R0 of the mutant type = 3.28639
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0179391
Cumulative mortality (mutant) = 0.$ 
```



```

parset = parvec /. pars /. mut -> 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}}, PlotStyle -> {{Thickness[0.005], Red}}, AspectRatio -> 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t -> tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}, PlotRange -> {{0, tfig}, {0, 1}},
  PlotStyle -> {{Thickness[0.008], Black}}, AspectRatio -> 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Blue}, AspectRatio -> 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling -> Axis, FillingStyle -> LightGray,
  PlotStyle -> None, Frame -> True, PlotRange -> {{0, tfig}, {0, 1}}, AspectRatio -> 0.75, Frame -> True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

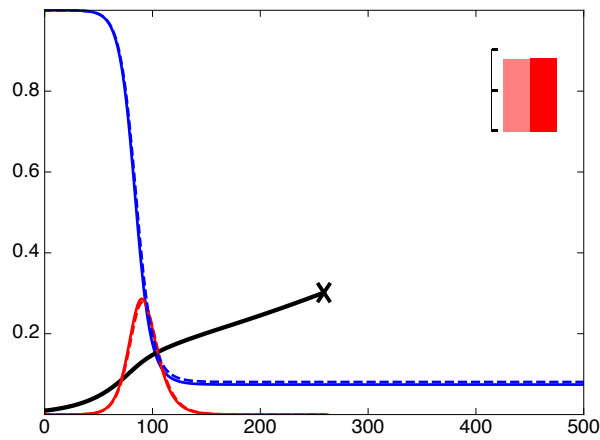
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% ("], ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP1 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame -> True,
  TicksStyle -> Directive[Black, FontFamily -> "Helvetica", 11],
  LabelStyle -> Directive[12, FontFamily -> "Helvetica", Black],
  FrameTicks -> {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle -> {{Directive[FontSize -> 12], Directive[FontOpacity -> 0, FontSize -> 0]},
    {Directive[FontSize -> 12], Directive[FontOpacity -> 0, FontSize -> 0]}}
]

R0 of the wild type = 2.73866
R0 of the mutant type = 3.28639
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0180649
Cumulative mortality (mutant) = 0.00233935
259
{0.301727}

```



■ Figure 3b: Evolution of asymptomatic fraction  $f$ , no control measures

```

pars = { $\beta$  -> 0.42,  $\beta_m$  -> 0.42, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1$  -> 0,  $c_2$  -> 0,  $c_3$  -> 0
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.73866
R0 of the mutant type = 2.73866
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0179391
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut -> 0.1; (*Started at high frequency to help show decline*)
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange -> {{0, tfig}, {10-7, 1}}, PlotStyle -> {{Thickness[0.005], Red}}, AspectRatio -> 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t -> tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange -> {{0, tfig}, {0, 1}},
  PlotStyle -> {{Thickness[0.008], Black}}, AspectRatio -> 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Blue}, AspectRatio -> 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling -> Axis, FillingStyle -> LightGray,
  PlotStyle -> None, Frame -> True, PlotRange -> {{0, tfig}, {0, 1}}, AspectRatio -> 0.75, Frame -> True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% ("], ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

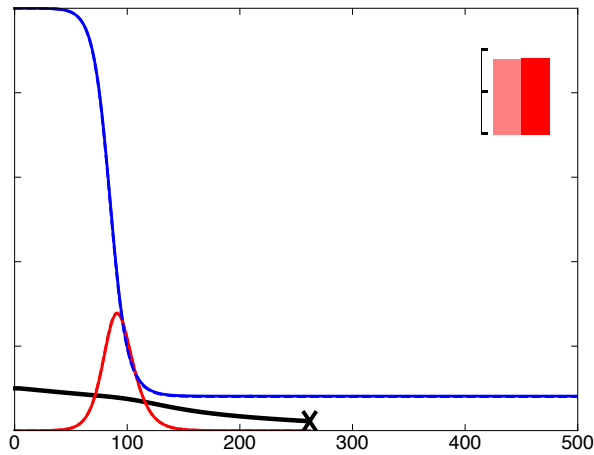
DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP2 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame -> True,
  TicksStyle -> Directive[Black, FontFamily -> "Helvetica", 11],
  LabelStyle -> Directive[12, FontFamily -> "Helvetica", Black],
  FrameTicks -> {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle -> {{Directive[FontOpacity -> 0, FontSize -> 0], Directive[FontOpacity -> 0, FontSize -> 0]},
    {Directive[FontSize -> 12], Directive[FontOpacity -> 0, FontSize -> 0]}}
]

R0 of the wild type = 2.73866
R0 of the mutant type = 2.73866
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0180961
Cumulative mortality (mutant) = 0.00159256

262
{0.0222533}

```



■ Figure 3c: Evolution of pre-symptomatic phase  $\kappa$ , no control measures

```

pars = {β → 0.42, βm → 0.42, (*TRANSMISSION OF THE MUTANT*)
  α → 0.005, αm → 0.005, (*VIRULENCE OF THE MUTANT*)
  κyP → 1, κyPm → 1/3, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

  f → 0.2, fm → 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
  κyE → 0.25, (* 1/TIME IN EXPOSED CLASS *)
  κyI → 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
  κyA → 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

  (*Strength of control measures*)
  c1 → 0, c2 → 0, c3 → 0
};

parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange → {{0, tfig}, {10-7, 1}},
  PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.73866
R0 of the mutant type = 3.41066
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0179391
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

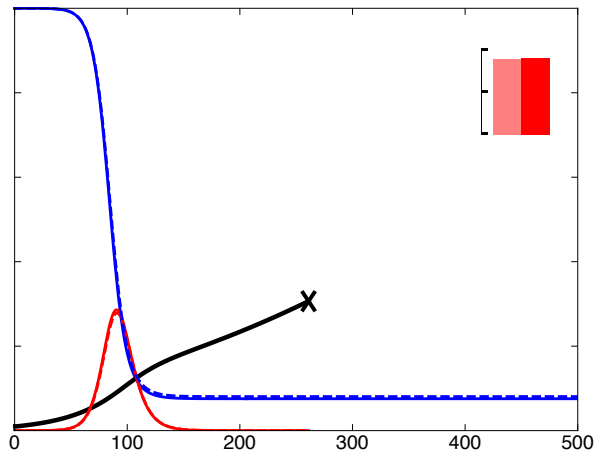
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP3 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.73866
R0 of the mutant type = 3.41066
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0180397
Cumulative mortality (mutant) = 0.00150901
261
{0.306414}

```



■ Figure 3d: Evolution of virulence  $\alpha$ , no control measures

```

pars = { $\beta \rightarrow 0.42$ ,  $\beta_m \rightarrow 0.42$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha \rightarrow 0.005$ ,  $\alpha_m \rightarrow 0.0$ , (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P \rightarrow 1$ ,  $\kappa y_{Pm} \rightarrow 1$ , (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f  $\rightarrow 0.2$ ,  $f_m \rightarrow 0.2$ , (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E \rightarrow 0.25$ , (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I \rightarrow 0.2$ , (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A \rightarrow 0.11$ , (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1 \rightarrow 0$ ,  $c_2 \rightarrow 0$ ,  $c_3 \rightarrow 0$ 
};

parset = parvec /. pars /. mut  $\rightarrow 0$ ;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange  $\rightarrow$  {{0, tfig}, {10-7, 1}},
  PlotStyle  $\rightarrow$  {{Thickness[0.005], Red, Dashed}}, AspectRatio  $\rightarrow$  0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange  $\rightarrow$  {{0, tfig}, {0, 1}}, PlotStyle  $\rightarrow$  {Thickness[0.005], Dashed, Blue}, AspectRatio  $\rightarrow$  0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.73866
R0 of the mutant type = 2.77964
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0179391
Cumulative mortality (mutant) = 0.

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

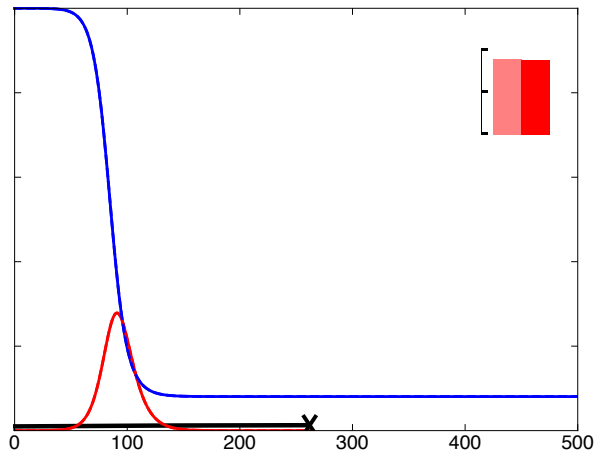
line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigTOP4 = Show[fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
  ]
R0 of the wild type = 2.73866
R0 of the mutant type = 2.77964
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0177372
Cumulative mortality (mutant) = 0.
262
{0.0128192}

```



■ Figure 3e: Evolution of transmission  $\beta$ , control measures

```

pars = { $\beta \rightarrow 0.42$ ,  $\beta_m \rightarrow 0.42 \times 1.2$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha \rightarrow 0.005$ ,  $\alpha_m \rightarrow 0.005$ , (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P \rightarrow 1$ ,  $\kappa y_{Pm} \rightarrow 1$ , (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f  $\rightarrow 0.2$ ,  $f_m \rightarrow 0.2$ , (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E \rightarrow 0.25$ , (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I \rightarrow 0.2$ , (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A \rightarrow 0.11$ , (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1 \rightarrow 0.6$ ,  $c_2 \rightarrow 0.6$ ,  $c_3 \rightarrow 0.6$ 
};

parset = parvec /. pars /. mut  $\rightarrow 0$ ;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange  $\rightarrow$  {{0, tfig}, {10-7, 1}},
  PlotStyle  $\rightarrow$  {{Thickness[0.005], Red, Dashed}}, AspectRatio  $\rightarrow$  0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange  $\rightarrow$  {{0, tfig}, {0, 1}}, PlotStyle  $\rightarrow$  {Thickness[0.005], Dashed, Blue}, AspectRatio  $\rightarrow$  0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.73866
R0 of the mutant type = 3.28639
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0135654
Cumulative mortality (mutant) = 0.

```



```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

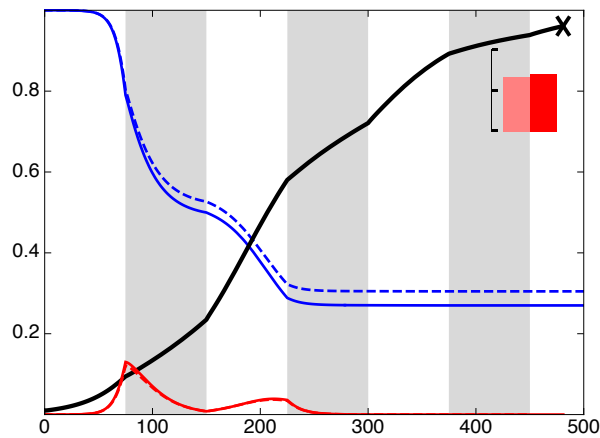
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT1 = Show[fcontrol, fS, fSDashed, FIGfreq, fnoevol, fevol, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

R0 of the wild type = 2.73866
R0 of the mutant type = 3.28639
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0142448
Cumulative mortality (mutant) = 0.00335457
481
{0.960941}

```



■ **Figure 3f: Evolution of asymptomatic fraction  $f$ , control measures**

```

pars = { $\beta$  -> 0.42,  $\beta_m$  -> 0.42, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.005, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.1, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
c1 -> 0.6, c2 -> 0.6, c3 -> 0.6
};

parset = parvec /. pars /. mut -> 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
  {t, 0, tNOevolNC}, PlotRange -> {{0, tfig}, {10-7, 1}},
  PlotStyle -> {{Thickness[0.005], Red, Dashed}}, AspectRatio -> 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange -> {{0, tfig}, {0, 1}}, PlotStyle -> {Thickness[0.005], Dashed, Blue}, AspectRatio -> 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.73866
R0 of the mutant type = 2.73866
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0135654
Cumulative mortality (mutant) = 0.
448

```

```

Cumulative mortality (mutant) = 0.
Cumulative mortality (total) = 0.0135654
Case mortality (mutant) = 0.0219512
Case mortality = 0.0195122
R0 of the mutant type = 2.73866
R0 of the wild type = 2.73866
R0 of the wild type = 2.58866
R0 of the mutant type = 2.58866
Case mortality = 0.0195122
Case mortality (mutant) = 0.0219512
Cumulative mortality (total) = 0.0123517
Cumulative mortality (mutant) = 0.

475

parset = parvec /. pars /. mut → 0.1; (*Started at high frequency to help show decline*)
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% ("], ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

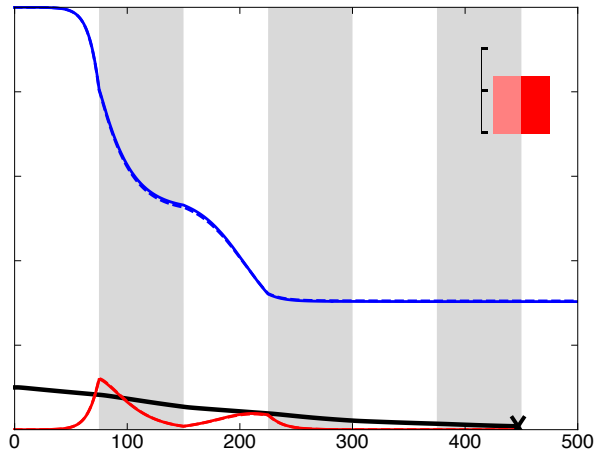
FigBOT2 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

```

$R_0$  of the wild type = 2.73866  
 $R_0$  of the mutant type = 2.73866  
 Case mortality = 0.0195122  
 Case mortality (mutant) = 0.0219512  
 Cumulative mortality (total) = 0.0137095  
 Cumulative mortality (mutant) = 0.00102427

447

{0.0079099}



Cumulative mortality (mutant) = 0.0000998203

Cumulative mortality (total) = 0.0135796

Case mortality (mutant) = 0.0219512

Case mortality = 0.0195122

 $R_0$  of the mutant type = 2.73866 $R_0$  of the wild type = 2.73866 $R_0$  of the wild type = 2.58866 $R_0$  of the mutant type = 2.58866

Case mortality = 0.0195122

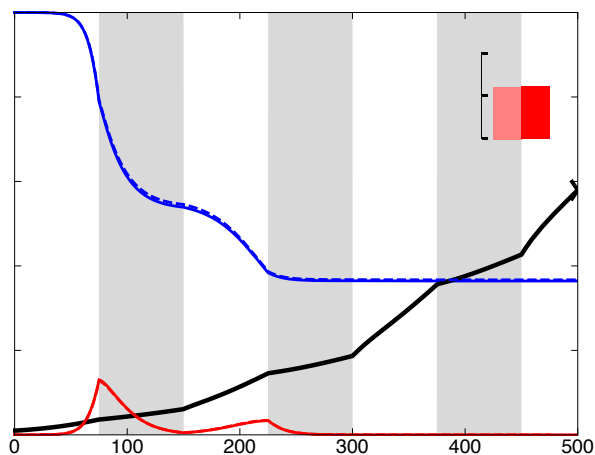
Case mortality (mutant) = 0.0219512

Cumulative mortality (total) = 0.0125058

Cumulative mortality (mutant) = 0.000907129

500

{0.579283}



■ **Figure 3g: Evolution of pre-symptomatic phase  $\kappa$ , control measures**

```

pars = { $\beta \rightarrow 0.42$ ,  $\beta_m \rightarrow 0.42$ , (*TRANSMISSION OF THE MUTANT*)
 $\alpha \rightarrow 0.005$ ,  $\alpha_m \rightarrow 0.005$ , (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P \rightarrow 1$ ,  $\kappa y_{Pm} \rightarrow 1/3$ , (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f  $\rightarrow 0.2$ ,  $f_m \rightarrow 0.2$ , (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E \rightarrow 0.25$ , (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I \rightarrow 0.2$ , (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A \rightarrow 0.11$ , (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1 \rightarrow 0.6$ ,  $c_2 \rightarrow 0.6$ ,  $c_3 \rightarrow 0.6$ 
};

parset = parvec /. pars /. mut  $\rightarrow 0$ ;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]],
  {t, 0, tNOevolNC}, PlotRange  $\rightarrow$  {{0, tfig}, {10-7, 1}},
  PlotStyle  $\rightarrow$  {{Thickness[0.005], Red, Dashed}}, AspectRatio  $\rightarrow$  0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange  $\rightarrow$  {{0, tfig}, {0, 1}}, PlotStyle  $\rightarrow$  {Thickness[0.005], Dashed, Blue}, AspectRatio  $\rightarrow$  0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.73866
R0 of the mutant type = 3.41066
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0135654
Cumulative mortality (mutant) = 0.
448
Cumulative mortality (mutant) = 0.
Cumulative mortality (total) = 0.0123517
Case mortality (mutant) = 0.0195122
Case mortality = 0.0195122
R0 of the mutant type = 3.43666
R0 of the wild type = 2.58866
R0 of the wild type = 2.58866
R0 of the mutant type = 2.80066
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0123517
Cumulative mortality (mutant) = 0.
475

```

```

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}], PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}], PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

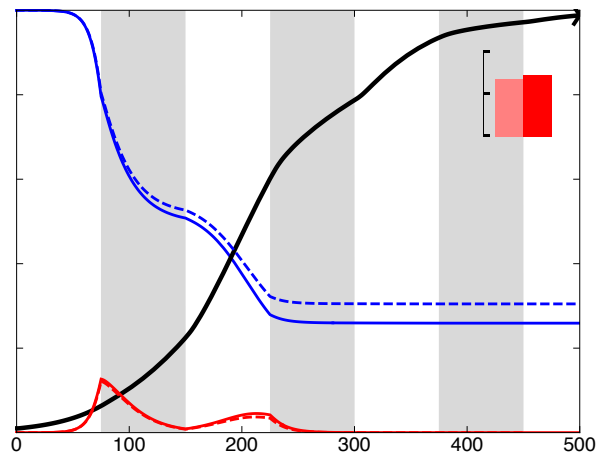
mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]}];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT3 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

R0 of the wild type = 2.73866
R0 of the mutant type = 3.41066
Case mortality = 0.0195122
Case mortality (mutant) = 0.0195122
Cumulative mortality (total) = 0.0144555
Cumulative mortality (mutant) = 0.00303203
500
{0.98803}

```



Cumulative mortality (mutant) = 0.00549454

Cumulative mortality (total) = 0.014861

Case mortality (mutant) = 0.0195122

Case mortality = 0.0195122

R0 of the mutant type = 3.43666

R0 of the wild type = 2.58866

R0 of the wild type = 2.58866

R0 of the mutant type = 2.80066

Case mortality = 0.0195122

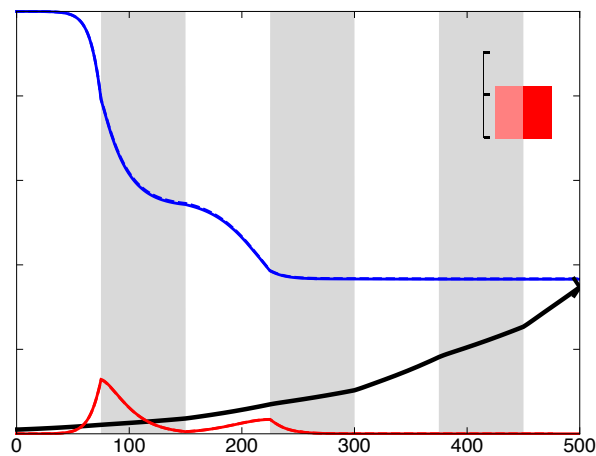
Case mortality (mutant) = 0.0195122

Cumulative mortality (total) = 0.0123701

Cumulative mortality (mutant) = 0.000411584

500

{0.347002}



■ Figure 3h: Evolution of virulence  $\alpha$ , control measures

```
pars = { $\beta$  -> 0.42,  $\beta_m$  -> 0.42, (*TRANSMISSION OF THE MUTANT*)
 $\alpha$  -> 0.005,  $\alpha_m$  -> 0.00, (*VIRULENCE OF THE MUTANT*)
 $\kappa y_P$  -> 1,  $\kappa y_{Pm}$  -> 1, (* 1/TIME IN PRESYMPTOMATIC CLASS FOR THE MUTANT *)

f -> 0.2,  $f_m$  -> 0.2, (* PROPORTION OF ASYMPTOMATIC CASES *)
 $\kappa y_E$  -> 0.25, (* 1/TIME IN EXPOSED CLASS *)
 $\kappa y_I$  -> 0.2, (* 1/TIME IN SYMPTOMATIC CLASS *)
 $\kappa y_A$  -> 0.11, (* 1/TIME IN ASYMPTOMATIC CLASS *)

(*Strength of control measures*)
 $c_1$  -> 0.6,  $c_2$  -> 0.6,  $c_3$  -> 0.6
};
```

```

parset = parvec /. pars /. mut → 0;
finalfreq[parset]

tNOevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]

fnoevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
  {t, 0, tNOevolNC}, PlotRange → {{0, tfig}, {10-7, 1}},
  PlotStyle → {{Thickness[0.005], Red, Dashed}}, AspectRatio → 0.75];

fSDashed = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Dashed, Blue}, AspectRatio → 0.75];

mortalitynoevol = yD[tNOevolNC] + yDm[tNOevolNC] /. Flatten[NSolution[parset]];

R0 of the wild type = 2.73866
R0 of the mutant type = 2.77964
Case mortality = 0.0195122
Case mortality (mutant) = 0.
Cumulative mortality (total) = 0.0135654
Cumulative mortality (mutant) = 0.
448

parset = parvec /. pars /. mut → 0.01;
finalfreq[parset]

tevolNC = LengthWhile[
  Flatten[Table[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]],
    {t, 1, tfig, 1}]], # > 10-7 &]
fevol = Plot[Evaluate[{{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /. NSolution[parset]]], {t,
  0, tevolNC}, PlotRange → {{0, tfig}, {10-7, 1}}, PlotStyle → {{Thickness[0.005], Red}}, AspectRatio → 0.75];

freqERADIC =
  Evaluate[
$$\frac{(yEm[t] + yAm[t] + yPm[t] + yIm[t])}{(yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])}$$
 /. NSolution[parset]] /. t → tevolNC

FIGfreq = Plot[
  Evaluate[{{(yEm[t] + yAm[t] + yPm[t] + yIm[t]) / (yE[t] + yA[t] + yP[t] + yI[t] + yEm[t] + yAm[t] + yPm[t] + yIm[t])} /.
    NSolution[parset]]], {t, 0, tevolNC}, PlotRange → {{0, tfig}, {0, 1}},
  PlotStyle → {{Thickness[0.008], Black}}, AspectRatio → 0.75];

fS = Plot[Evaluate[S[t] /. NSolution[parset]], {t, 0, tfig},
  PlotRange → {{0, tfig}, {0, 1}}, PlotStyle → {Thickness[0.005], Blue}, AspectRatio → 0.75];

fcontrol = Plot[2 * c[t] /. pars, {t, 0, tfig}, Filling → Axis, FillingStyle → LightGray,
  PlotStyle → None, Frame → True, PlotRange → {{0, tfig}, {0, 1}}, AspectRatio → 0.75, Frame → True];

line1 = Graphics[{Thickness[0.007], Black,
  Line[{Flatten[{tevolNC - 5, freqERADIC - 0.02}], Flatten[{tevolNC + 5, freqERADIC + 0.02}]}]}];
line2 = Graphics[{Thickness[0.007], Black, Line[{Flatten[{tevolNC - 5, freqERADIC + 0.02}],
  Flatten[{tevolNC + 5, freqERADIC - 0.02}]}]}];

mortalityevol = yD[tevolNC] + yDm[tevolNC] /. Flatten[NSolution[parset]];
(*mortality=Graphics[{Text[Style[StringJoin[ToString[N[Round[100 mortalitynoevol, 10-1]]], "% (" , ToString[
  N[Round[100 (mortalityevol), 10-1]]], "%) "], 12, FontFamily->"Helvetica"], {(t3min+t3max)/2, 0.3}]]];*)

DeathRates = Graphics[{Pink, Rectangle[{t3max - tfig / 20, 0.7}, {t3max, 0.7 + 10 * mortalitynoevol}],
  Red, Rectangle[{t3max, 0.7}, {t3max + tfig / 20, 0.7 + 10 * mortalityevol}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.2 / 20, 0.705}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.8}, {t3max - tfig 1.2 / 20, 0.805}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.9}, {t3max - tfig 1.2 / 20, 0.905}],
  Black, Rectangle[{t3max - tfig 1.4 / 20, 0.7}, {t3max - tfig 1.42 / 20, 0.905}]}];

FigBOT4 = Show[fcontrol, fS, FIGfreq, fnoevol, fevol, fSDashed, line1, line2, DeathRates, Frame → True,
  TicksStyle → Directive[Black, FontFamily → "Helvetica", 11],
  LabelStyle → Directive[12, FontFamily → "Helvetica", Black],
  FrameTicks → {{N[{0.2, 0.4, 0.6, 0.8}], N[{0.2, 0.4, 0.6, 0.8}]},
    {{0, 100, 200, 300, 400, 500}, {0, 100, 200, 300, 400, 500}}},
  FrameTicksStyle → {{Directive[FontOpacity → 0, FontSize → 0], Directive[FontOpacity → 0, FontSize → 0]},
    {Directive[FontSize → 12], Directive[FontOpacity → 0, FontSize → 0]}}
]

```



$R_0$  of the wild type = 2.73866

$R_0$  of the mutant type = 2.77964

Case mortality = 0.0195122

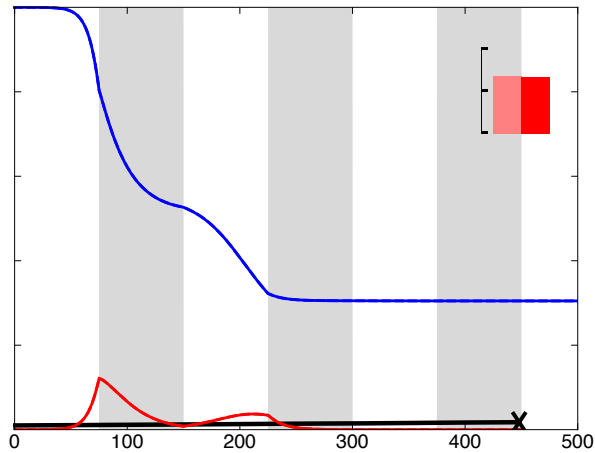
Case mortality (mutant) = 0.

Cumulative mortality (total) = 0.0134027

Cumulative mortality (mutant) = 0.

448

{0.0176213}



#### ■ Altogether

Similar results except that selection now favors increases in the asymptomatic fraction (because they are now the main source of new infections).

```
Show[
GraphicsGrid[{{FigTOP1, FigTOP2, FigTOP3, FigTOP4}, {FigBOT1, FigBOT2, FigBOT3, FigBOT4}},
FrameLabel -> label, Spacings -> {-10, 10}],
Graphics[Text[Style["A", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {45, -33}]],
Graphics[Text[Style["B", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {379, -33}]],
Graphics[Text[Style["C", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {729, -33}]],
Graphics[Text[Style["D", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {1080, -33}]],
Graphics[Text[Style["E", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {45, -315}]],
Graphics[Text[Style["F", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {379, -315}]],
Graphics[Text[Style["G", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {729, -315}]],
Graphics[Text[Style["H", 16, FontFamily -> "Helvetica", FontWeight -> Bold], {1080, -315}]],
Graphics[Text[Style["Transmission", 16, FontFamily -> "Helvetica"], {180, 10}]],
Graphics[Text[Style["Asymptomatic fraction", 16, FontFamily -> "Helvetica"], {520, 10}]],
Graphics[Text[Style["Pre-symptomatic phase", 16, FontFamily -> "Helvetica"], {870, 10}]],
Graphics[Text[Style["Virulence", 16, FontFamily -> "Helvetica"], {1220, 10}]],
Graphics[Text[Style["Time (days)", 16, FontFamily -> "Helvetica"], {700, -580}]],
Graphics[Rotate[Text[Style["Frequency", 16, FontFamily -> "Helvetica"], {-20, -270}], Pi / 2]]
]
```

