Supplementary material S3. Derivation of the results

We present the results we derived for the TIV and TV models.

S3A Area under the viral load curve

The area under the viral load curve during the course of the infection, $A_V$, is given by

$$A_V = \int_{t_{d_1}}^{t_{d_2}} V dt,$$  \hspace{1cm} (S3A.1)

where $t_{d_1}$ and $t_{d_2}$ are the times at which the viral load takes the value of the detection limit at the beginning and the end of the infection (or $t_{d_2} - t_{d_1}$ can be defined as the duration in which the patient is infectious). If the initial viral load is above the detection limit then $t_{d_1}$ is considered as the time at which virus enters the body.

TIV model

From (1) and (2) we get,

$$I = -\frac{1}{\delta_I} \frac{dT}{dt} - \frac{1}{\delta_I} \frac{dI}{dt}. \hspace{1cm} (S3A.2)$$

Substituting (S3A.2) into (3) and integrating from $t = t_{d_1}$ to $t = t_{d_2}$ we get

$$\int_{t_{d_1}}^{t_{d_2}} \frac{dV}{dt} dt = -\frac{p}{\delta_I} \int_{t_{d_1}}^{t_{d_2}} \frac{dT}{dt} dt - \frac{p}{\delta_I} \int_{t_{d_1}}^{t_{d_2}} \frac{dI}{dt} dt + c \int_{t_{d_1}}^{t_{d_2}} V dt,$$  \hspace{1cm} (S3A.3)

$$\Rightarrow A_{V(TIV)} = \frac{1}{c} \left[ -\frac{p}{\delta_I} \left( T_{t_{d_2}} - T_{t_{d_1}} + I_{t_{d_2}} - I_{t_{d_1}} \right) + V_{t_{d_2}} - V_{t_{d_1}} \right],$$  \hspace{1cm} (S3A.4)

where $T_{t_{d_1}} = T(t_{d_1})$, $T_{t_{d_2}} = T(t_{d_2})$, $I_{t_{d_1}} = I(t_{d_1})$, $I_{t_{d_2}} = I(t_{d_2})$, $V_{t_{d_1}} = V(t_{d_1})$, $V_{t_{d_2}} = V(t_{d_2})$.

Integrating (1) from $t = t_{d_1}$ to $t = t_{d_2}$ we get

$$T(t_{d_i}) = T(t_{d_1}) e^{-\beta_k(t_{d_2} - t_{d_1})}. \hspace{1cm} (S3A.5)$$

Substituting (S3A.5) into (S3A.4) we get

$$A_{V(TIV)} = \frac{1}{c} \left[ -\frac{p}{\delta_I} \left( T(t_{d_1}) e^{-\beta_k(t_{d_2} - t_{d_1})} - T_{t_{d_1}} + I_{t_{d_2}} - I_{t_{d_1}} \right) + V_{t_{d_2}} - V_{t_{d_1}} \right].$$  \hspace{1cm} (S3A.6)
Hence, the area under the viral load curve in the TIV model, $A_{V(TIV)}$, is given by the solution of equation (S3A.6). An expression for $A_{V(TIV)}$ can be obtained by using the Lambert function [1, 2], which cannot be expressed in terms of elementary functions.

Multiplying (S3A.6) by $\beta$ and rearranging we get

$$\beta A_{V(TIV)} - \frac{\beta p}{c \delta_i} T_{t_{i_1}} + \frac{\beta p}{c \delta_i} I_{t_{i_2}} - \frac{\beta p}{c \delta_i} I_{t_{i_1}} - \frac{\beta p}{c \delta_i} V_{t_{i_2}} - \frac{\beta}{c} V_{t_{i_1}} = -\frac{\beta p}{c \delta_i} T(t_0) e^{-\beta A_{V(TIV)}}. \quad (S3A.7)$$

Let

$$x_1 = \beta A_{V(TIV)} - \frac{\beta p}{c \delta_i} T_{t_{i_1}} + \frac{\beta p}{c \delta_i} I_{t_{i_2}} - \frac{\beta p}{c \delta_i} I_{t_{i_1}} - \frac{\beta p}{c \delta_i} V_{t_{i_2}} - \frac{\beta}{c} V_{t_{i_1}}. \quad (S3A.8)$$

From (S3A.7) and (S3A.8) we obtain

$$x_1 e^{x_1} = -\frac{\beta p}{c \delta_i} T(t_0) e^{\frac{\beta p}{c \delta_i} T_{t_{i_1}}} + \frac{\beta p}{c \delta_i} I_{t_{i_2}} - \frac{\beta p}{c \delta_i} I_{t_{i_1}} - \frac{\beta p}{c \delta_i} V_{t_{i_2}} - \frac{\beta}{c} V_{t_{i_1}}. \quad (S3A.9)$$

Let

$$z_1 = -\frac{\beta p}{c \delta_i} T(t_0) e^{\frac{\beta p}{c \delta_i} T_{t_{i_1}}} + \frac{\beta p}{c \delta_i} I_{t_{i_2}} - \frac{\beta p}{c \delta_i} I_{t_{i_1}} - \frac{\beta p}{c \delta_i} V_{t_{i_2}} - \frac{\beta}{c} V_{t_{i_1}}. \quad (S3A.10)$$

$z_1 \in \mathbb{R}$ and $-\frac{1}{e} < z_1 \leq 0$.

$x_1 = w(z_1)$ is the upper branch of the Lambert W function, i.e. $w(z_1)e^{w(z_1)} = z_1$.

Hence, from (S3A.8)

$$A_{V(TIV)} = \frac{1}{\beta} \left( w(z_1) + \frac{\beta p}{c \delta_i} T_{t_{i_1}} + \frac{\beta p}{c \delta_i} I_{t_{i_2}} - \frac{\beta p}{c \delta_i} I_{t_{i_1}} + \frac{\beta p}{c \delta_i} V_{t_{i_2}} - \frac{\beta}{c} V_{t_{i_1}} \right). \quad (S3A.11)$$

To approximate (S3A.11) we can assume that $T_{t_{i_1}} \approx T_0$, $I_{t_{i_1}} \approx I_0$, $I_{t_{i_2}} \approx 0$, $V_{t_{i_1}} = V_{t_{i_2}}$, and $T_0 >> I_0$:

$$A_{V(TIV)App1} = \frac{1}{\beta} \left( w(z_1) + \frac{\beta p}{c \delta_i} T_0 \right), \text{ with } z_1 \approx -\frac{\beta p}{c \delta_i} T_0 e^{\frac{\beta p T_0}{c \delta_i}}. \quad (S3A.12)$$

In terms of the basic reproduction ratio, $R_0 = \beta p T_0 / c \delta_i$, $A_{V(TIV)App1}$ is given by

$$A_{V(TIV)App1} = \frac{1}{\beta} \left( w(z_1) + R_0 \right), \text{ with } z_1 \approx -R_0 e^{-R_0}. \quad (S3A.13)$$

The Taylor series of the upper branch of the W function is given by
\[ w(z_i) = z_i - z_i^2 + \frac{3}{2} z_i^3 - \frac{8}{3} z_i^4 + \ldots. \]  

(S3A.14)

Since \(-\frac{1}{e} < z_i \leq 0\), although \(1/\beta\) is typically a very big number, the area under the viral load curve can be approximated very well by taking up to the second order terms of the Taylor expansion of \(w(z_i)\). This results in the following approximation of \(A_{(TV)}\):

\[ A_{(TV)^{\text{app}}} = \frac{R_0}{\beta} \left( 1 - e^{-R_0} - R_0 e^{-2R_0} \right). \]  

(S3A.15)

Note that in the case where all the target cells die due to the infection, that is \(T_{d_2} = 0\), then from (S3A.4) we obtain

\[ A_{(TV), T_{d_2} = 0} = \frac{1}{c} \left[ V_0 + \frac{P}{\delta} (T_0 + I_0) \right]. \]  

(S3A.16)

**TV model**

As in [2], from equation (5)

\[ \frac{dT}{dt} = -\beta VT \Rightarrow VT = -\frac{1}{\beta} \frac{dT}{dt}. \]  

(S3A.17)

Substituting (S3A.17) into (6) and integrating from \(t = t_{d_1}\) to \(t = t_{d_2}\) we get

\[ \int_{t_1}^{t_{d_2}} \frac{dV}{dt} = \int_{t_1}^{t_{d_2}} \frac{dT}{dt} - \gamma \int_{t_1}^{t_{d_2}} V dt \]  

(S3A.18)

\[ \Rightarrow A_{(TV)} = \frac{1}{\gamma} \left[ -r (T(t_{d_1}) - T(t_{d_2})) + V(t_{d_1}) - V(t_{d_2}) \right]. \]  

(S3A.19)

As before, from (5) we get

\[ T(t_{d_2}) = T(t_{d_1}) e^{-\beta A_{(TV)}}. \]  

(S3A.20)

It should be noted that due to the very similar structure of the TV model to that of the SIR model in infectious disease epidemiology, the area under the viral load curve is 'equivalent' to the final epidemic size in the SIR model, which can be obtained by solving a similar expression as (S3A.20) [3, 4].

Substituting (S3A.20) into (S3A.19) we get

\[ A_{(TV)} = \frac{1}{\gamma} \left[ -r T(t_{d_1}) (e^{-\beta A_{(TV)}} - 1) + V(t_{d_1}) - V(t_{d_2}) \right]. \]  

(S3A.21)
Hence, the area under the viral load curve in the TV model, \( A_{v(TV)} \), is given by the solution of equation (S3A.21). As in the case of the TIV model, since this cannot be solved using elementary functions, to get an expression of \( A_{v(TV)} \) we use the Lambert function [1, 2].

Multiplying equation (S3A.21) by \( \beta \) and rearranging we get

\[
\beta A_{v(TV)} - \frac{r \beta}{\gamma} T(t_a) + \frac{\beta}{\gamma} V(t_a) - \frac{\beta}{\gamma} V(t_a) = -\frac{r \beta}{\gamma} T(t_a)e^{-\frac{r \beta}{\gamma} T(t_a)}. 
\]  

(S3A 22)

Let

\[
x_2 = \beta A_{v(TV)} - \frac{r \beta}{\gamma} T(t_a) + \frac{\beta}{\gamma} V(t_a) - \frac{\beta}{\gamma} V(t_a). 
\]  

(S3A.23)

Then, from (S3A 22) and (S3A.23) we obtain

\[
x_2 e^{x_2} = -\frac{r \beta}{\gamma} T(t_a)e^{-\frac{r \beta}{\gamma} T(t_a) + \frac{\beta}{\gamma} V(t_a) - \frac{\beta}{\gamma} V(t_a)}. 
\]  

(S3A 24)

Let

\[
z_2 = -\frac{r \beta}{\gamma} T(t_a)e^{-\frac{r \beta}{\gamma} T(t_a) + \frac{\beta}{\gamma} V(t_a) - \frac{\beta}{\gamma} V(t_a)}. 
\]  

(S3A.25)

\( z_2 \in \mathbb{R} \) and \(-\frac{1}{e} < z_2 \leq 0 \).

\( x_2 = w(z_2) \) is the Lambert W function, i.e. \( w(z_2)e^{w(z_2)} = z_2 \).

Hence, from (S3A.23),

\[
A_{v(TV)} = \frac{1}{\beta} \left( w(z_2) + \frac{r \beta}{\gamma} T(t_a) + \frac{\beta}{\gamma} V(t_a) - \frac{\beta}{\gamma} V(t_a) \right). 
\]  

(S3A 26)

As in the case of the TIV model, to approximate \( A_{v(TV)} \) in (S3A.26) we can assume that \( T_{v_a} \approx T_0 \) and \( V_{v_a} = V_{T_0} \) to obtain:

\[
A_{v(TV) \text{Appl}} = \frac{1}{\beta} \left( w(z_2) + \frac{r \beta}{\gamma} T_0 \right), \text{ with } z_2 \approx -\frac{r \beta}{\gamma} T_0 e^{-\frac{r \beta}{\gamma} T_0}. 
\]  

(S3A 27)

In terms of the basic reproduction ratio, \( R_0 = \frac{r \beta}{\gamma} T_0 \),

\[
A_{v(TV) \text{Appl}} = \frac{1}{\beta} \left( w(z_2) + R_0 \right), \text{ where } z_2 = -R_0 e^{-R_0}, 
\]  

(S3A 28)

which is the same as (S3A.13).
S3B Fraction of dead cells at the end of the infection

The fraction of cells that die during the duration in which the virus is above the detection limit, $D$, is

$$D = 1 - \frac{T_{t_d}}{T_0},$$

(S3B.1)

where $T_{t_d}$ is the number of susceptible cells at time $t_{d_2}$.

TIV model

Solving (S3A.4) for $T_{t_d}$ and using (S3A.11) we obtain that the total number of susceptible cells at time $t_{d_2}$ in the TIV model, $T_{t_d(V)}$, is given by

$$T_{t_d(V)} = -\frac{c\delta_l}{\beta p} w(z_1),$$

(S3B.2)

where $w$ is the Lambert function with $z_1$ given by (S3A.10).

Hence, the fraction of cells that die during the infection in the TIV model, $D_{t_d(V)}$, is

$$D_{t_d(V)} = 1 + \frac{c\delta_l}{\beta p T_0} w(z_1) = 1 + \frac{1}{R_0} w(z_1).$$

(S3B.3)

Assuming that at $t_{d_1}$, $T_{t_d} = T_0$, $I_{t_d} \approx I_0$ and $V_{t_d} \approx V_0$, that $t_{d_2}$ is the time at which all infected cells are killed and the virus is cleared, and so $I_{t_d} = 0$ and $V_{t_d} = 0$, and using the second order Taylor’s expansion of the W function given by (S3A.14), then the fraction of dead cells at the end of the infection can be approximated by

$$D_{(TIV)App1} = 1 - e^{-\frac{c\delta_l}{\beta p T_0} w(z_1)} - R_0 e^{-\frac{c\delta_l}{\beta p T_0} w(z_1)}.$$

(S3B.4)

Given that $\frac{I_0}{T_0} + \frac{\delta V_0}{p T_0} << 1$ then $D_{t_d(V)}$ can be approximated by

$$D_{(TIV)App2} = 1 - e^{-R_0} - R_0 e^{-R_0} = \frac{\beta A_{(TIV)App2}}{R_0}.$$

(S3B.5)

TV model

As before, rearranging equation (S3A.19) and using (S3A.26) we obtain that the number of susceptible cells at the point $t = t_{d_2}$ at which virus reaches the detection limit in the decay phase in the TV model is given by
\[
T_{\nu t}(TV) = -\frac{\gamma}{r \beta} w(z_2),
\]
\hspace{1cm} \text{(S3B.6)}

where \( w \) is the Lambert function with \( z_2 \) given by (S3A.25). Thus, the fraction of cells that die during the infection in the TV model, \( D_{\nu t} \), is

\[
D_{\nu t} = 1 + \frac{\gamma}{r \beta T_0} w(z_2) = 1 + \frac{1}{R_0} w(z_2),
\]
\hspace{1cm} \text{(S3B.7)}

which is of the same form as (S3B.3). Assuming that \( T_{\nu t} = T_0 \), \( V_{\nu t} = V_0 \), \( V_{\nu 2} = 0 \) and approaching \( w(z_2) \) by the second order Taylor’s expansion of the W function given by (S3A.14), and given that \( \frac{V_0}{rT_0} \ll 1 \), then the fraction of dead cells at the end of the infection can also be approximated by (S3B.5).

**S3C Peak viral load**

Let the maximum of the viral load be achieved at \( t = t_{\text{peak}} \).

**TIV model**

At \( t = t_{\text{peak}} \), \( \frac{dV}{dt} = 0 \). From (3) we then get

\[
I(t_{\text{peak}}) = \frac{c}{p} V(t_{\text{peak}}).
\]
\hspace{1cm} \text{(S3C.1)}

Substituting (S3A.2) into (3), integrating from \( t = 0 \) to \( t = t_{\text{peak}} \) and using (S3C.1) and (4) we obtain

\[
V(t_{\text{peak}}) = \frac{\delta_t}{c + \delta_t} \left[ V_0 - \frac{p}{\delta_t} (T(t_{\text{peak}}) - T_0) + \frac{c}{\beta} (\ln T(t_{\text{peak}}) - \ln T_0) + \frac{p}{\delta_t} I_0 \right].
\]
\hspace{1cm} \text{(S3C.2)}

Assume that \( T(t_{\text{peak}}) = aT_0 \). Substituting into (S3C.2) we obtain

\[
V(t_{\text{peak}}) = \frac{\delta_t}{c + \delta_t} \left[ V_0 + \frac{p}{\delta_t} T_0 (1-a) + \frac{c}{\beta} \ln a + \frac{p}{\delta_t} I_0 \right].
\]
\hspace{1cm} \text{(S3C.3)}

In the examples we have considered in the main text, the average value of \( a \) is approximately equal to 0.13.
TV model

In the TV model, from equation (6) at \( t = t_{\text{peak}} \)

\[
T(t_{\text{peak}}) = \frac{\gamma}{r \beta}.
\]  

(S3C.4)

From equation (5) we get

\[
\int_{t_0}^{t_{\text{peak}}} \frac{dT}{T} = -\int_{0}^{t_{\text{peak}}} \beta V(t) dt \Rightarrow \int_{0}^{t_{\text{peak}}} V(t) dt = -\frac{1}{\beta} \left( \ln T(t_{\text{peak}}) - \ln T_0 \right)
\]  

(S3C.5)

\[
\Rightarrow \int_{0}^{t_{\text{peak}}} V(t) dt = \frac{1}{\beta} \ln \frac{r T_0}{\gamma}.
\]  

(S3C.6)

Integrating equation (6) from \( t = 0 \) to \( t = t_{\text{peak}} \) and using (5) and (S3C.6) we get

\[
\int_{t_0}^{t_{\text{peak}}} dV = -r \int_{t_0}^{t_{\text{peak}}} dT - \frac{\gamma}{\beta} \ln \frac{r T_0}{\gamma}
\]  

(S3C.7)

\[
\Rightarrow V(t_{\text{peak}})_{(TV)} = V_0 + r T_0 - \frac{\gamma}{\beta} \left( \ln \frac{r T_0}{\gamma} + 1 \right) = V_0 + r T_0 - \frac{\gamma}{\beta} (\ln R_0 + 1).
\]  

(S3C.8)

S3D Time to peak viral load

TIV model

As shown in previous work [5, 6], assuming that at the initial phase of the infection the number of target cells remains constant, i.e. \( T(t) = T_0 \), then the initial viral growth rate \( r_0 \) can be approximated by the dominant root of the characteristic equation of the Jacobian matrix of the resulting linear system. Hence, the viral load at the initial phase of the infection, \( V_{\text{init}}(t) \), can be approximated by

\[
V_{\text{init}}(t) = A \tilde{u} e^{r_0 t},
\]  

(S3D.1)

where \( \tilde{u} \) is the eigenvector corresponding to \( r_0 \) and \( A \) is a constant (see [5, 6]). Clearly this is a good approximation as long as \( T \approx T_0 \). If we assume that the viral load continues to increase linearly until the peak, then using (S3D.1), we can approximate peak viral load by

\[
V(t_{\text{peak}}) = c \tilde{u} e^{r_0 t_{\text{peak}}}.
\]  

(S3D.2)

Solving (S3D.2) for \( t_{\text{peak}} \) we derive an approximation of the time to peak viral load in the TIV model:

\[
t_{\text{peak}}(TV) = \frac{\ln V(t_{\text{peak}}) - \ln c \tilde{u}}{r_0}.
\]  

(S3D.3)
Clearly this will always be an underestimation as the viral growth decelerates when approaching peak viral load.

**TV model**

Integrating equation (6) from \( t = 0 \) to \( t = t_{V_{\text{peak}}} \) and rearranging we get

\[
t_{V_{\text{peak}}} = \frac{1}{\gamma} \left( \frac{\gamma}{r} \int_0^{t_{V_{\text{peak}}}} T dt + \ln \left( \frac{V_0}{V(t_{V_{\text{peak}}})} \right) \right),
\]

where \( V(t_{V_{\text{peak}}}) \) is the maximum viral load in the TV model given by (S3C.8).

Dividing equation (6) by equation (5) we obtain

\[
\frac{dV}{dT} = -r + \frac{\gamma}{\beta} T.
\]

Integrating (S3D.5) and using (7) we obtain

\[
V(t)_{(TV)} = -rT(t) + \frac{\gamma}{\beta} \ln T(t) + V_0 + rT_0 - \frac{\gamma}{\beta} \ln T_0.
\]

Integrating (S3D.6) from \( t = 0 \) to \( t = t_{V_{\text{peak}}} \) and using (S3C.6) we get

\[
\int_0^{t_{V_{\text{peak}}}} T dt = \frac{1}{r \beta} \ln \left( \frac{\gamma}{r \beta} \right) + \frac{\gamma}{r \beta} \int_0^{t_{V_{\text{peak}}}} \ln T(t) dt + \frac{1}{r} \left( V_0 + rT_0 - \frac{\gamma}{\beta} \ln T_0 \right) t_{V_{\text{peak}}}. \tag{S3D.7}
\]

For \( t \in [0, t_{V_{\text{peak}}}] \) we approximate \( \ln T(t) \) by \( \ln T_0 \), and thus \( \int_0^{t_{V_{\text{peak}}}} \ln T(t) dt \approx t_{V_{\text{peak}}} \ln T_0 \). Substituting into equation (S3D.7), and then (S3D.7) into (S3D.4), after some algebra we get

\[
t_{V_{\text{peak}}(TV)} \approx \frac{1}{\gamma - \beta (V_0 + rT_0)} \ln \left( \frac{\gamma V_0}{r \beta T_0 V(t_{V_{\text{peak}}})_{(TV)}} \right), \tag{S3D.8}
\]

where \( V(t_{V_{\text{peak}}})_{(TV)} \) is given by (S3C.8).

It should be noted that in equation (S3D.7), as \( \int_0^{t_{V_{\text{peak}}}} \ln T(t) dt \) is multiplied by \( \gamma / r \beta \) which is large, the approximation \( \int_0^{t_{V_{\text{peak}}}} \ln T(t) dt = t_{V_{\text{peak}}} \ln T_0 \) introduces a non-negligible degree of inaccuracy.
S3E Duration of infection

TV model

We define the duration of the infection as the time the virus in the body is above the detection limit (this was set to be equal to 0.7 TCID$_{50}$/ml, which is 0.05 TCID$_{50}$/ml below the smallest measurement value in the two datasets considered). From equation (S3D.6), at time $t_{d2}$, which is the time at which the viral load reaches the detection limit during the decay phase, the viral load is given by

$$V(t_{d2})_{TV} = -rT(t_{d2}) + \frac{\gamma}{\beta} \ln T(t_{d2}) + V_{t_{d1}} + rT_{t_{d1}} - \frac{\gamma}{\beta} \ln T_{t_{d1}},$$  \hfill (S3E.1)

where $V_0$ and $T_0$ in (S3D.6) have been substituted by $V_{t_{d1}}$ and $T_{t_{d1}}$, respectively.

Dividing both sides of equation (5) by $-\beta VT$, substituting (S3E.1) into this and integrating from $t = t_{d1}$ to $t = t_{d2}$, we derive the infection duration $t_d = t_{d2} - t_{d1}$:

$$t_d = -\frac{1}{\beta} \int_{t_{d1}}^{t_{d2}} \frac{dT}{-rT + \frac{\gamma}{\beta} \ln T + V_{t_{d1}} + rT_{t_{d1}} - \frac{\gamma}{\beta} \ln T_{t_{d1}}},$$  \hfill (S3E.2)

where $T(t_{d2})$ is given by (S3B.6).

To get an approximation of the infection duration we follow the following process. Dividing (6) by $V$ and integrating from $t = t_{d1}$ to $t = t_{d2}$, we get

$$\int_{t_{d1}}^{t_{d2}} Tdt = \frac{1}{r\beta} \left( \ln V(t_{d1}) - \ln V(t_{d2}) + \gamma \left(t_{d2} - t_{d1}\right) \right)$$  \hfill (S3E.3)

$$\Rightarrow t_d = \frac{r\beta}{\gamma} \int_{t_{d1}}^{t_{d2}} Tdt + \frac{1}{\gamma} \left( \ln V(t_{d1}) - \ln V(t_{d2}) \right).$$  \hfill (S3E.4)

Assume that

$$\int_{t_{d1}}^{t_{d2}} Tdt = \int_{t_{d1}}^{t_{peak}} T(t)dt + \left(t_{d2} - t_{peak}\right)T_{t_{peak}}(TV).$$  \hfill (S3E.5)

Integrating (S3D.6) from $t = t_{d1}$ to $t = t_{peak}$ and using (S3C.6) we get

$$\int_{t_{d1}}^{t_{peak}} T(t)dt = -\frac{1}{r\beta} \ln \frac{r\beta T_{t_{d1}}}{\gamma} + \frac{\gamma}{r\beta} \int_{t_{d1}}^{t_{peak}} \ln T(t)dt + \frac{1}{r} \left( V_{t_{d1}} + rT_{t_{d1}} - \frac{\gamma}{\beta} \ln T_{t_{d1}} \right)(t_{peak} - t_{d1}).$$  \hfill (S3E.6)

Assume that

$$\int_{t_{d1}}^{t_{peak}} \ln T(t)dt = \left(t_{peak} - t_{d1}\right)\ln T_{t_{d1}}.$$  \hfill (S3E.7)
Substituting (S3E.7) into (S3E.6) we get

$$\int_{t_{d_1}}^{t_{d_2}} T(t)dt = -\frac{1}{r\beta} \ln \frac{r\beta T_{t_{d_1}}}{\gamma} + \frac{1}{r}(V_{t_{d_1}} + rT_{t_{d_1}})(t_{v\text{peak}} - t_{d_1}).$$  \hspace{1cm} (S3E.8)

Substituting (S3E.8) into (S3E.5) we get

$$\int_{t_{d_1}}^{t_{d_2}} T(t)dt = -\frac{1}{r\beta} \ln \frac{r\beta T_{t_{d_1}}}{\gamma} + \frac{1}{r}(V_{t_{d_1}} + rT_{t_{d_1}})(t_{v\text{peak}} - t_{d_1}) + (t_{d_2} - t_{v\text{peak}})T_{t_{d_2}(TV)}. \hspace{1cm} (S3E.9)$$

Substituting (S3E.9) into (S3E.4) we get

$$t_{d} = \frac{1}{\gamma} \left( \ln \frac{\gamma}{r\beta} - \ln T(t_{d_1}) \right) + \frac{B}{\gamma} \left( V_{t_{d_1}} + rT_{t_{d_1}} \right)(t_{v\text{peak}} - t_{d_1})$$

$$+ \frac{rB}{\gamma} (t_{d_2} - t_{v\text{peak}})T_{t_{d_2}(TV)} + \frac{1}{\gamma} \left( \ln V(t_{d_1}) - \ln V(t_{d_2}) \right). \hspace{1cm} (S3E.10)$$

Assuming that $t_{d_1} = 0$ we get

$$t_{d\text{App}} = \frac{1}{\gamma - r\beta T_{t_{d_2}(TV)}} \left[ \ln \frac{\gamma}{r\beta T_0} + r\beta t_{v\text{peak}(TV)} \left( \frac{V_0}{r} + T_0 - T_{t_{d_2}(TV)} \right) - \ln \frac{V_{t_{d_2}}}{V_0} \right]. \hspace{1cm} (S3E.11)$$

where $T_{t_{d_2}(TV)}$ is given explicitly by (S3B.6), $t_{v\text{peak}(TV)}$ by (S3D.8) and $V_{t_{d_2}}$ by (S3E.1) (with $t_{d_1} = 0$).

**S3F Generation time**

Under the assumption that infectiousness is proportional to viral shedding and the population is homogeneous, the average generation time (at the population level) during the time the virus is detectable is given by

$$T_g = \int_{t_{d_1}}^{t_{d_2}} tV(t)dt \hspace{1cm} (S3F.1)$$

where $A_v$ is the area under the viral load curve; $T_g$ is the mean of the infectiousness distribution [7-9].

**TIV model**

Assume that $t_{d_1} = 0$. 
Substituting (S3A.2) into (3), multiplying by $t$ and integrating from $t = 0$ to $t = t_d$ we get

$$\int_0^{t_d} tV(t)\,dt = -\frac{p}{c\delta_1} \int_0^{t_d} tdT - \frac{p}{c\delta_1} \int_0^{t_d} tdI - \frac{1}{c} \int_0^{t_d} tdV.$$

(S3F.2)

Using integration by parts we get

$$\int_0^{t_d} tdT = t_d T_{i_2(IV)} - \int_0^{t_d} T(t)\,dt.$$

(S3F.3)

$$\int_0^{t_d} tdI = -\int_0^{t_d} I(t)\,dt = \frac{1}{\delta_1} \left( T_{i_2(IV)} - T_0 - I_0 \right).$$

(S3F.4)

$$\int_0^{t_d} tdV = -\int_0^{t_d} V(t)\,dt = -A_{V(IV)}.$$

(S3F.5)

$T_{i_2(IV)}$ is given by (S3B.2).

Substituting (S3F.3)-(S3F.5) into (S3F.2) and using (S3A.4) we get

$$\int_0^{t_d} tV(t)\,dt = \frac{p}{c\delta_1} \int_0^{t_d} T(t)\,dt - \frac{p}{c\delta_1} t_d T_0 - \frac{1}{c} \left( t_d + \frac{1}{\delta_1} \right) V_0 - \frac{p}{c\delta_1} t_d I_0 + \left( t_d + \frac{1}{\delta_1} + \frac{1}{c} \right) A_{V(IV)}. $$

(S3F.6)

The area under the curve of target cells is given by

$$\int_0^{t_d} T(t)\,dt = \int_0^{t^*} T(t)\,dt + \left( t_d - t^* \right) T_{i_2(IV)},$$

(S3F.7)

where $t^*$ is the time required for the target cells to reach the state $T_{i_2}$ ($t^* < t_d$). We assume that the target cells remain almost constant before their rapid decline to $T_{i_2}$, that is $\int_0^{t^*} T(t)\,dt = T_{i_2}^*.$

Although this approximation introduces a degree of inaccuracy, this is small due to the division of this term by $A_{V(IV)}$. Substituting into (S3F.6) and using (S3F.1) we derive

$$T_g = \frac{-\frac{1}{c} \left( \frac{1}{\delta_1} + t^* \right) V_0 - \frac{p}{c\delta_1} t^* I_0}{A_{V(IV)}} + t^* + \frac{1}{\delta_1} + \frac{1}{c},$$

(S3F.8)

A good approximation of $t^*$ is $t_{\text{peak}(IV)}$ given by (S3D.3).

Increasing the infection rate, the viral production rate, the initial number of target cells or the initial viral load yields lower $T_g$ values. In this case, the generation time approaches $1/\delta + 1/c$, which is the average life span of an infected cell and the average life span of a free virion (see also [10]).
TV model

Multiplying (6) by $t$, using (5) and integrating from $t = t_{d_1}$ to $t = t_{d_2}$ we get

$$\int_{t_{d_1}}^{t_{d_2}} tV dt = -\frac{r}{\gamma} \int_{t_{d_1}}^{t_{d_2}} t dT - \frac{1}{\gamma} \int_{t_{d_1}}^{t_{d_2}} t dV. \quad (S3F.9)$$

Using integration by parts we get

$$\int_{t_{d_1}}^{t_{d_2}} t \frac{dV}{dt} dt = t_{d_2} V(t_{d_2}) - t_{d_1} V(t_{d_1}) - A_{V(TV)}. \quad (S3F.10)$$

$$\int_{t_{d_1}}^{t_{d_2}} t dT = t_{d_2} T(t_{d_2}) - t_{d_1} T(t_{d_1}) - \int_{t_{d_1}}^{t_{d_2}} T dt. \quad (S3F.11)$$

Substituting (S3F.10) and (S3F.11) into (S3F.9) and then into (6) we get

$$T_{g(TV)} = \frac{-\frac{r}{\gamma} \left( t_{d_2} T(t_{d_2}) - t_{d_1} T(t_{d_1}) - \int_{t_{d_1}}^{t_{d_2}} T dt \right) - \frac{1}{\gamma} \left( t_{d_2} V(t_{d_2}) - t_{d_1} V(t_{d_1}) - A_{V(TV)} \right)}{A_{V(TV)}}. \quad (S3F.12)$$

Substituting (S3E.3) into (S3F.12) we get

$$T_{g(TV)} = \frac{-\frac{r}{\gamma} t_{d_1} T(t_{d_1}) + \frac{r}{\gamma} t_{d_2} T(t_{d_2}) + \frac{1}{\beta \gamma} \ln \frac{V(t_{d_2})}{V(t_{d_1})} - \frac{1}{\gamma} t_{d_2} V(t_{d_2}) + \frac{1}{\gamma} t_{d_1} V(t_{d_1}) + \frac{1}{\beta} t_{d_1} - \frac{1}{\beta} t_{d_2}}{A_{V(TV)}} + \frac{1}{\gamma}. \quad (S3F.13)$$

Assuming that $t_{d_1} \approx 0$ and using (S3A.20) and (S3E.1) we get

$$T_{g(TV)App} = \frac{t_{dApp} \left( \frac{1}{\beta} - \frac{1}{\gamma} V_0 - \frac{r}{\gamma} T_0 + A_{V(TV)} \right) + \frac{1}{\beta \gamma} \ln \frac{V_0 - \gamma A_{V(TV)} + \gamma T_0 \left(1-e^{-\beta T_0} \right)}{V_0} + \frac{1}{\gamma}}{A_{V(TV)}} + \frac{1}{\gamma}, \quad (S3F.14)$$

where $t_{dApp}$ is the duration of the infection given by (S3E.11).

References