Sanity checks for compartmental models of disease transmission

MATHEMATICAL MODELING FOR INFECTIOUS DISEASE PLANNING IN AFRICA

45 minutes

Learning objectives

1. Identify some key sanity checks for your models

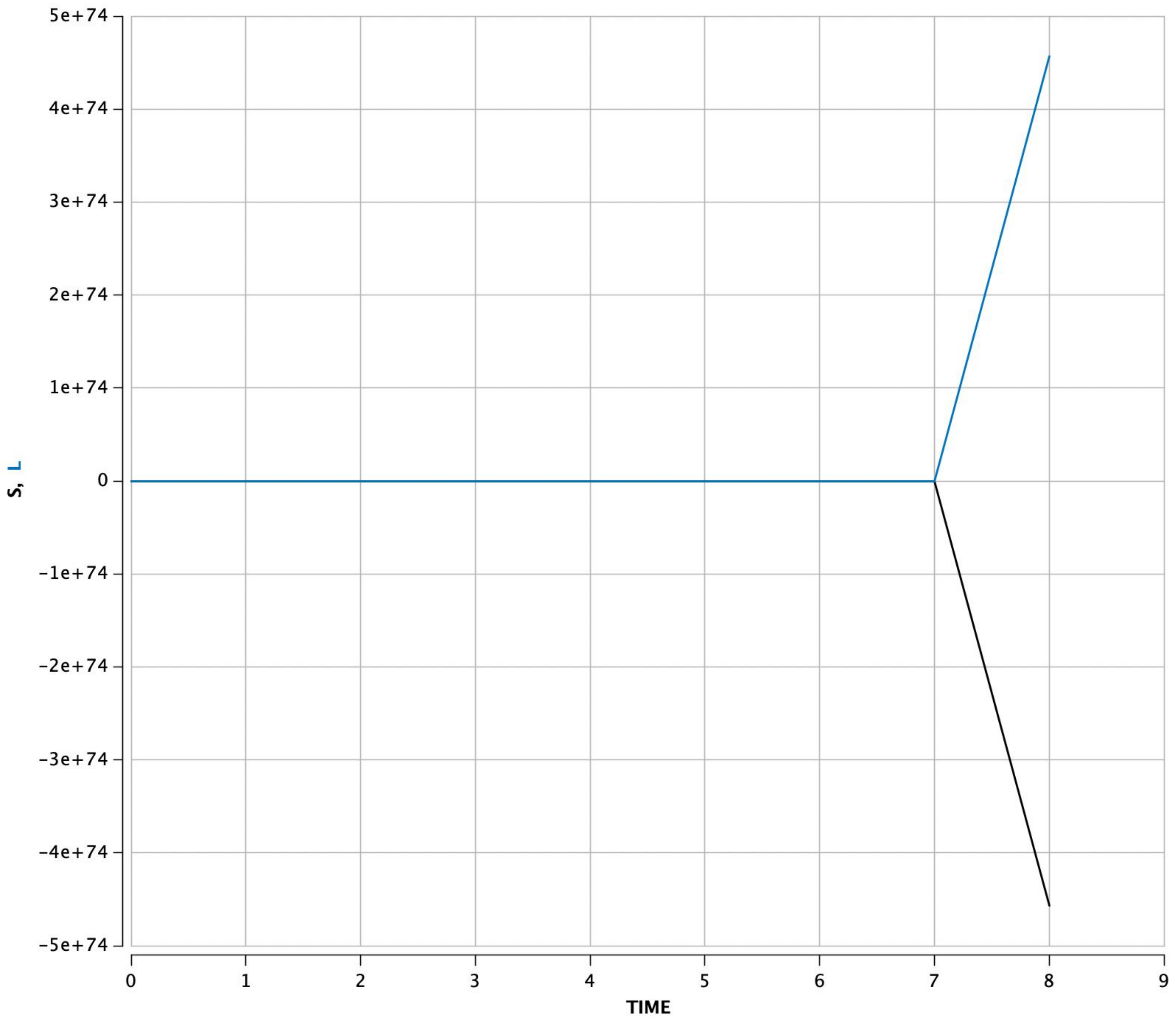
2. Understand how the checks guard against model inaccuracies

3. Apply checks to your models (activity)

Outline

1. Check 1: Positive values for state variables
2. Check 2: time step and rate parameters have equal units
3. Check 3: Model diagram reflects disease natural history and modeling assumptions
4. Check 4: Equations reflect compartmental diagram
5. Check 5: Length of analysis is realistic in relation to demographic rates
6. Summary

What is wrong with this output?



The number of susceptible individuals is negative after time = 7.

Check 1: Positive (or zero) and realistic values for state variables

$S(t), I(t), \dots, R(t) \geq 0,$
for all values of t

Realistic or unrealistic?

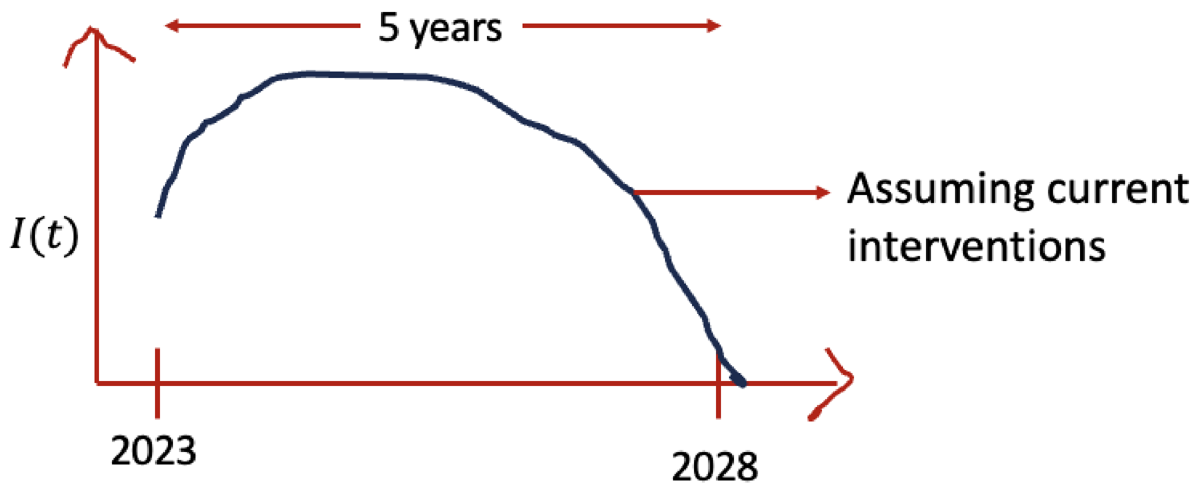
1. $I(t) \geq N$, for a model in a closed population; i.e., the number of infected individuals is more than the population size, in the absence of births

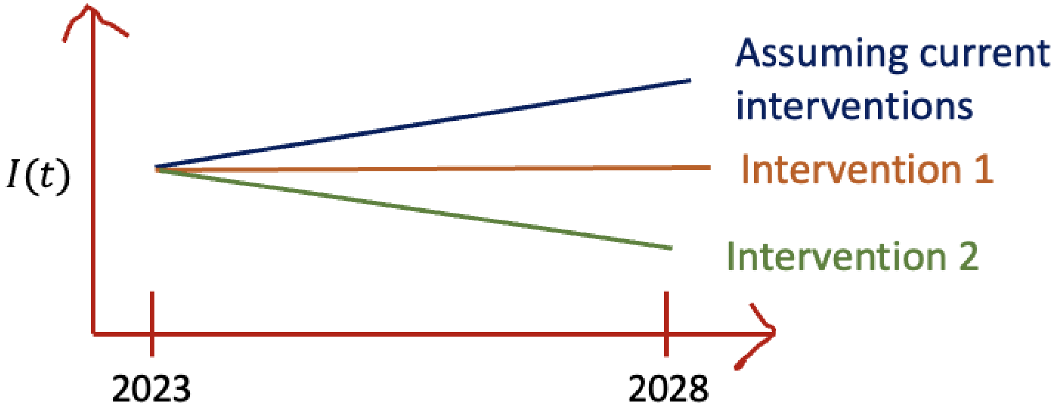
2. $S(t) = 0$ by $t = 4$ days; i.e., everyone in the population becomes infected within a short period

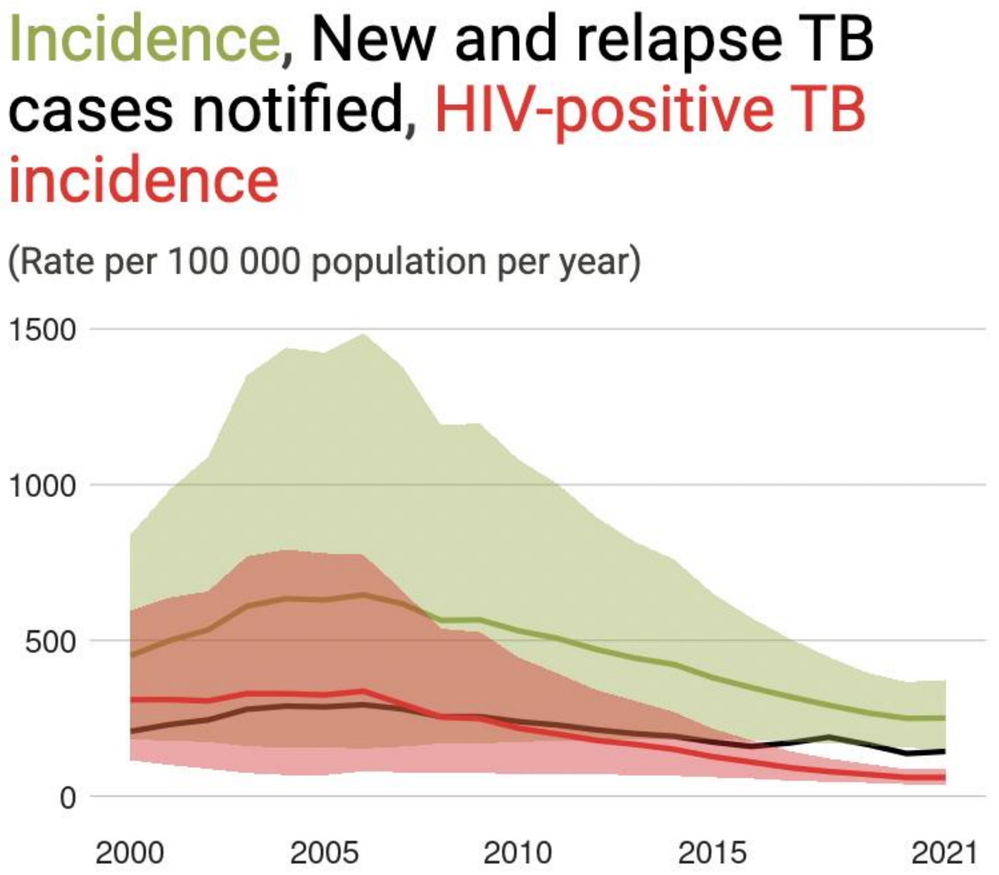
3. Note that a bell-shaped curve for the number of infections may not always be realistic. Why?

Bell-shaped curve or wrong?

Example: TB incidence







Source: Global TB Programme, World Health Organization

Possible reasons for negative or unrealistic values for state variables

1. Time step and rate parameters have unequal units
2. Equations not reflecting compartmental diagram (check that BM equations are the same as those in your worksheet)
3. Unrealistic parameter values (e.g., values sourced from the literature may be unrealistic for one's context)
4. …

Check 2: Time step and rate parameters have equal units

DT unit

Rate unit

A closer look at DT

- What is the value and unit of DT (time step) in your model?

- What influenced your choice of value for DT?
  - Speed of disease progression (COVID-19 vs TB)
  - …

A closer look at DT

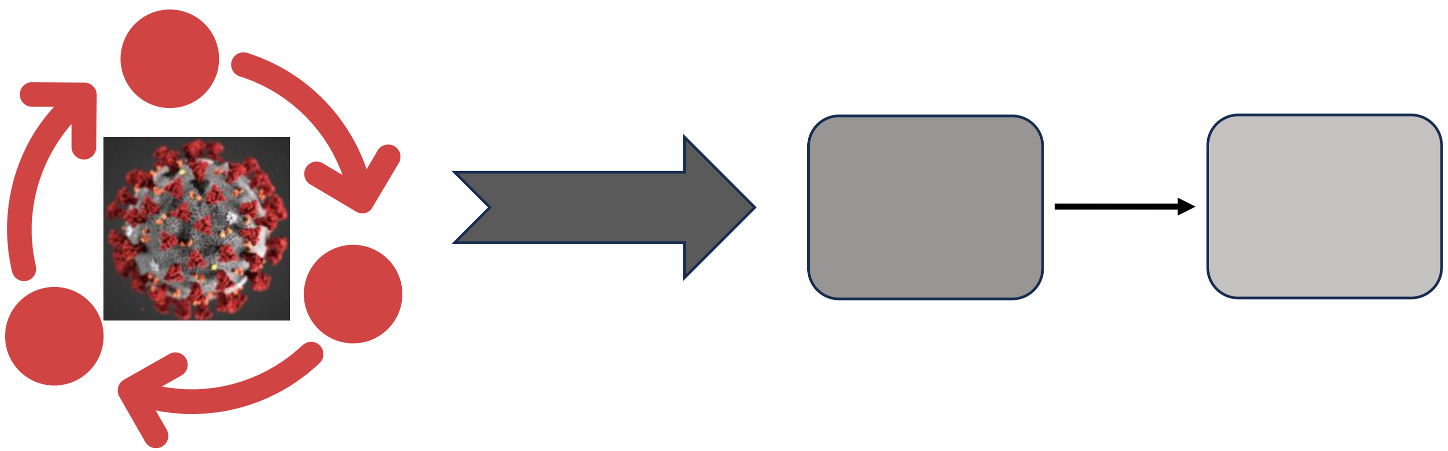
- Consider
  - DT = 1 year
  - Vaccination rate = 0.2 day^{-1}

- What is wrong with the above?

- Problem: unit of time step is inconsistent with unit of rate

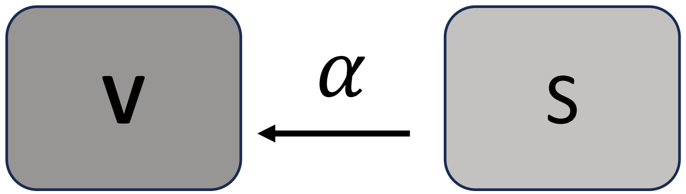
- Result: inaccurate estimates

Check 3: Compartmental diagram reflects natural history of the disease and modeling assumptions



Natural history Compartmental diagram

An example



$\alpha =$ proportion of population vaccinated

Assumption: Vaccine has imperfect efficacy.

Adjustment to account for vaccine efficacy: ?

An example

$$V \xleftarrow{\alpha * \sigma} S$$

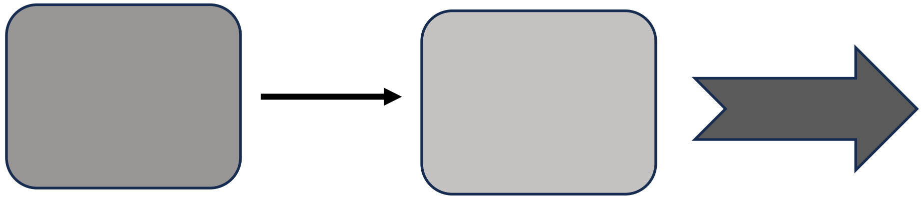
α = proportion of population vaccinated

σ = vaccine efficacy (%)

Assumption: Vaccine has imperfect efficacy.

Adjustment to account for vaccine efficacy: $\alpha * \sigma$

Check 4: Equations reflect compartmental diagram

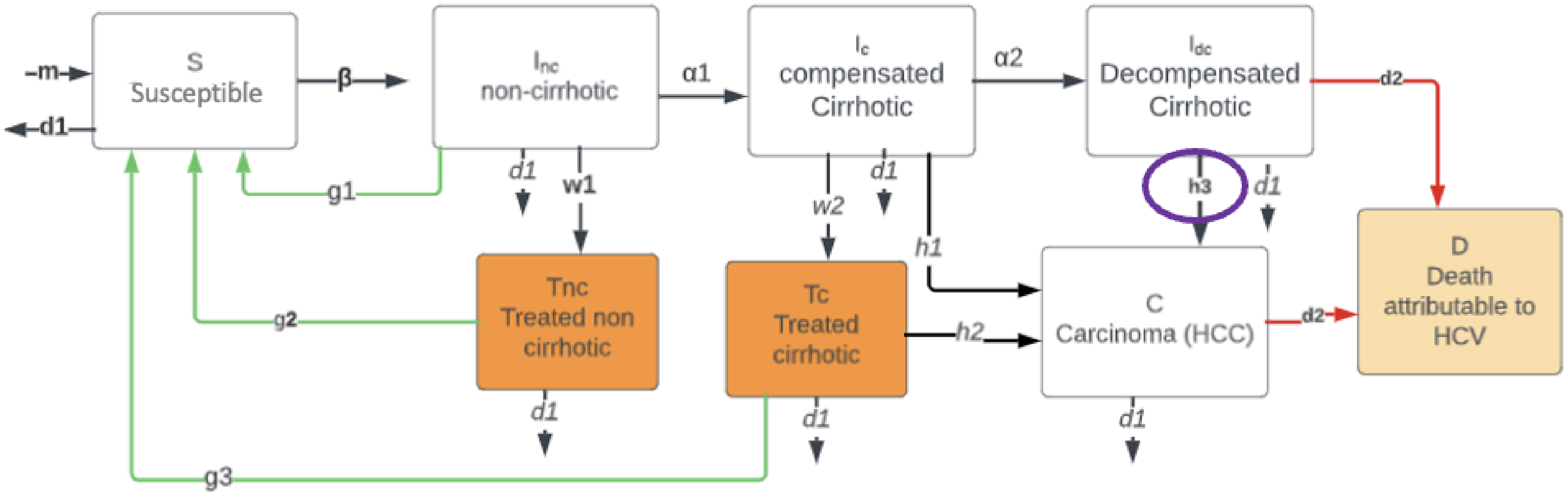


$f(X)$

Compartmental diagram

Model equations

Example



Compartmental diagram for a Hepatitis C transmission model

Credit: Hepatitis C team

Model equations:

$$\frac{dS}{dt} = -\frac{(I_{nc} + I_c + I_{dc})\beta S}{N} + (m - d1)S + g_2 T_{nc} + g_3 T_c$$

$$\frac{dI_{nc}}{dt} = \frac{(I_{nc} + I_c + I_{dc})\beta S}{N} - \alpha_1 I_{nc} - d_1 I_{nc} - w_1 I_{nc}$$

$$\frac{dI_c}{dt} = \alpha_1 I_{nc} - d_1 I_c - w_2 I_c - \alpha_2 I_c - w_2 I_c - h_1 I_c$$

$$\frac{dI_{dc}}{dt} = \alpha_2 I_c - h_3 I_{dc} - d_2 I_{dc} - d_1 I_{dc} - h_3 I_{dc}$$

$$\frac{dT_{nc}}{dt} = w_1 I_{nc} - g_2 T_{nc} - d_1 T_{nc}$$

$$\frac{dT_c}{dt} = w_2 I_c - d_1 T_c - h_2 T_c - g_3 T_c$$

$$\frac{dC}{dt} = h_1 I_c + h_2 T_c - d_1 T_c - d_2 C$$

The term $h_3 I_{dc}$ is missing here.

$$\frac{dC}{dt} = d_2 I_{dc} + d_2 C$$

Formatting note: use Math mode for greater legibility

$$\frac{dS}{dt} = -\frac{(I_{nc} + I_c + I_{dc})\beta S}{N} + (m - d1)S + g_2T_{nc} + g_3T_c$$

$$\frac{dI_{nc}}{dt} = \frac{(I_{nc} + I_c + I_{dc})\beta S}{N} - \alpha_1 I_{nc} - d_1 I_{nc} - w_1 I_{nc}$$

$$\frac{dI_c}{dt} = \alpha_1 I_{nc} - d_1 I_c - w_2 I_c - \alpha_2 I_c - w_2 I_c - h_1 I_c$$

$$\frac{dI_{dc}}{dt} = \alpha_2 I_c - h_3 I_{dc} - d_2 I_{dc} - d_1 I_{dc} - h_3 I_{dc}$$

$$\frac{dT_{nc}}{dt} = w_1 I_{nc} - g_2 T_{nc} - d_1 T_{nc}$$

$$\frac{dT_c}{dt} = w_2 I_c - d_1 T_c - h_2 T_c - g_3 T_c$$

$$\frac{dC}{dt} = h_1 I_c + h_2 T_c - d_1 T_c - d_2 C + h_3 I_{dc}$$

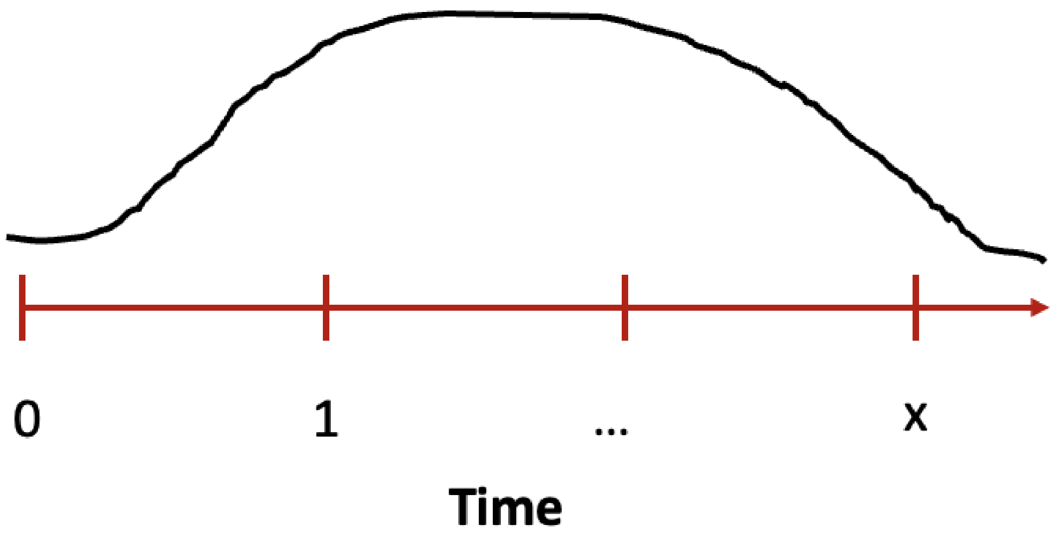
$$\frac{dC}{dt} = d_2 I_{dc} + d_2 C$$

Math mode ✓

*d/dt (S)= - (Inc+Ic+Idc)*beta*S/N +(m-d1)*S+g2*Tnc+g3*Tc*
*d/dt (Inc)= Inc*beta*S/N -alpha1*Inc -d1*Inc- w1*Inc*
*d/dt (Ic)= Ic*beta*S/N +alpha1* Inc-d1*Ic-w2*Ic-alpha2* Ic-w2*Ic-h1*Ic*
*d/dt (Idc)= Idc*beta*S/N + alpha2*Ic-h3*Idc-d2*Idc-d1*Idc -h3*Idc*
*d/dt(Tnc)=w1*Inc-g2*Tnc-d1*Tnc*
*d/dt(Tc)=w2*Ic-d1*TC-h2*Tc-g3*Tc*
*d/dt(C)=h1*Ic+h2*TC-d1*C-d2*C + h3*Idc*
*d/dt(D)=d2*Idc+d2*C*

Text mode ☹

Check 5: Length of analysis period is realistic in relation to demographic rates



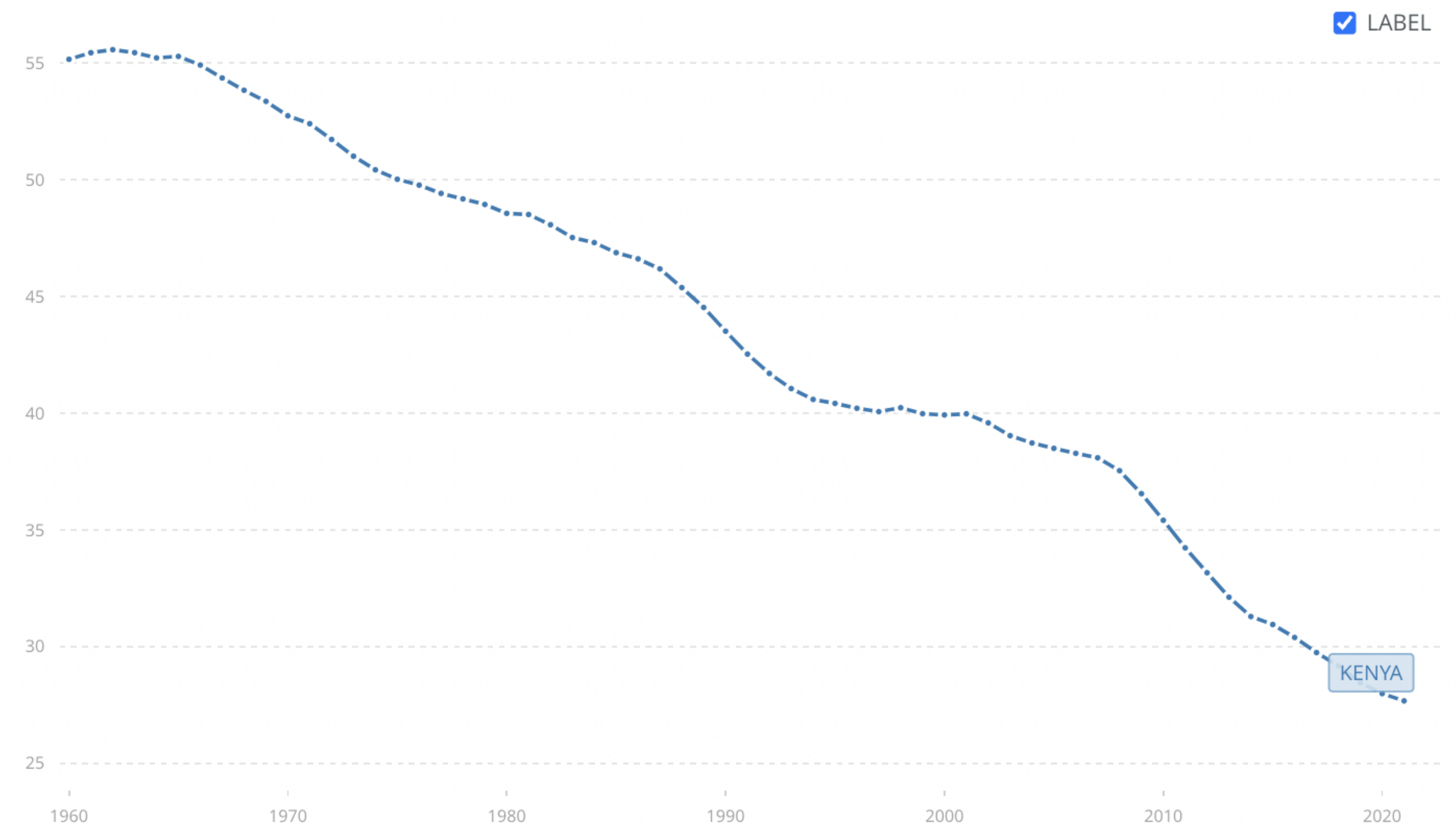
Will demographic rates remain at current levels in 60 years?

Crude birth rate in Kenya has decreased by more than 50% over the past 60 years.

Birth rate, crude (per 1,000 people) - Kenya

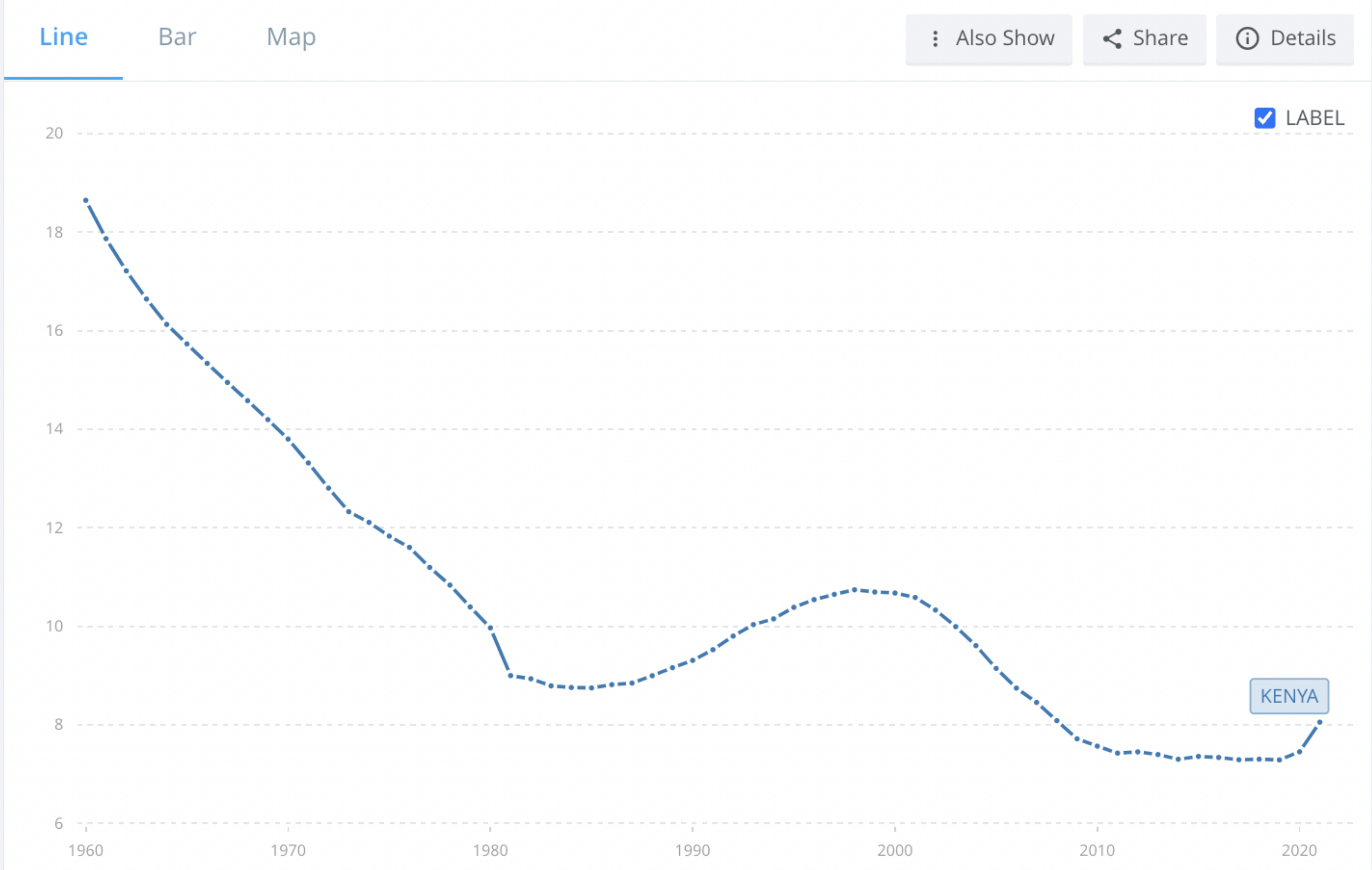
(1) United Nations Population Division. World Population Prospects: 2022 Revision. (2) Census reports and other statistical publications from national statistical offices, (3) Eurostat: Demographic Statistics, (4) United Nations Statistical Division. Population and Vital Statistics Reprot (various years), (5) U.S. Census Bureau: International Database, and (6) Secretariat of the Pacific Community: Statistics and Demography Programme.

Line Bar Map ⋮ Also Show Share Details



Death rate, crude (per 1,000 people) - Kenya

(1) United Nations Population Division. World Population Prospects: 2022 Revision. (2) Census reports and other statistical publications from national statistical offices, (3) Eurostat: Demographic Statistics, (4) United Nations Statistical Division. Population and Vital Statistics Reprot (various years), (5) U.S. Census Bureau: International Database, and (6) Secretariat of the Pacific Community: Statistics and Demography Programme.



Crude death rate in Kenya has decreased by more than 50% over the past 60 years.

Length of analysis period

Demographic rates

- Consider the following
  - Aim: Predict malaria incidence
  - Malaria model
  - Parameters include current demographic rates
  - Length of analysis period: 70 years

- What kinds of problems might arise with these incidence estimates?

Models need to account for changing demographic rates if *far* future trends are to be studied.

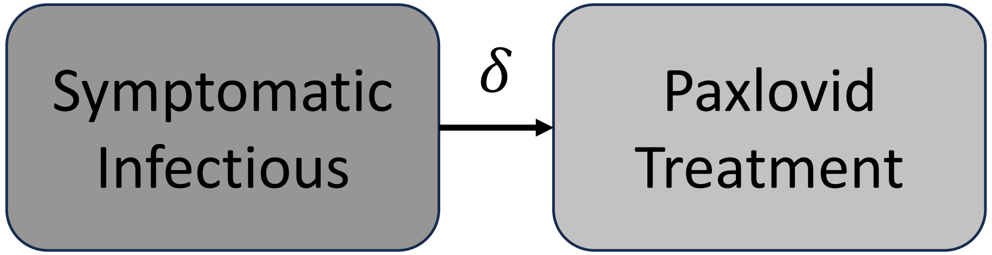
Check 6: Parameter values are realistic

Consider rates

Reminder of rate formula:

$$\text{Rate} = \frac{1}{duration\ of\ event}$$

Example: Consider the following section of a COVID-19 model diagram



What is the formula for δ?

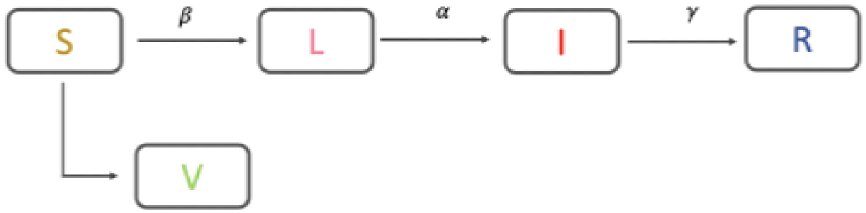
Check 6: Parameter values are realistic

- Consider vaccination rates
  - Consider a setting with up to 500 vaccine doses to be distributed in a year (program-specific information)
  - Using a rate of 3.5 doses per day translates to 1278 doses in a year, more than available doses
  - *How does one avoid this potential issue?*
  - Recommendation: Apply absolute numbers instead of rates.

Check 6: Parameter values are realistic

- For example, 500 vaccine doses administered at a constant rate throughout the year translates to $500/365 \approx 1.37$ doses per day

- One method to incorporate this into model



  - Let v = number of doses per day = 1.37
  - Assume
    - only susceptible individuals are vaccinated
    - model runs for a year

  - $\frac{dS}{dt} = \frac{-\beta SI}{N} - v,$

Check 6: Parameter values are realistic

Beware (!) of durations less than the minimum time step

- Consider a compartment, X of 100 individuals and an exit rate, e.

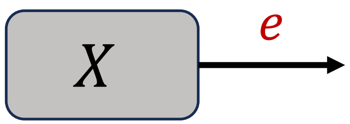
$$\boxed{X} \xrightarrow{e}$$

- Assume dt = 1 day
- Define $e =$ 1/ average length of time individuals spend in X
- Set $e = \frac{1}{1/3} = 3$ day^{-1}
- $X(1) = X(0) + \frac{dX}{dt}$. We know that $X(0)$ = 100.
- Compute $\frac{dX}{dt} = -eX = -3(100) = -300$
- Therefore, $X(1) = X(0) + \frac{dX}{dt} = 100 - 300 = -200$ ⟵ Error: Why are we observing this?

Check 6: Parameter values are realistic

Beware (!) of durations less than the minimum time step

- $X(1) = X(0) + \frac{dX}{dt} = 100 - 300 = -200$ ⟵ Why are we observing this?



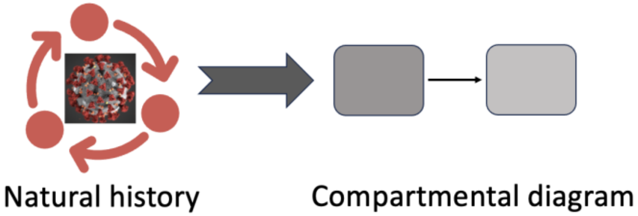
- Set $e = \frac{1}{1/3} = 3$ day^{-1}
- Reason: Duration (1/3 days) is less than the minimum time step (1 day).
- Correction: Set durations $\geq$ minimum time step.
- For duration = 2 days, e = ½ day^{-1} and $X(1) = X(0) + \frac{dX}{dt} = 100 - 100\left(\frac{1}{2}\right) = 50$

Summary of sanity checks

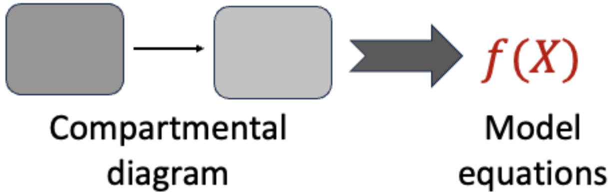
$S(t), I(t), \ldots, R(t) \geq 0,$
for all values of t

1. State variables
have positive or zero values.

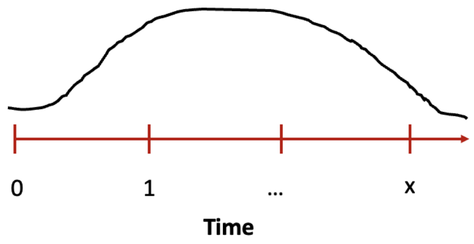
2. Time step and rate parameters have equal units.



3. Compartmental diagram reflects natural history and modeling assumptions.



4. Equations reflect compartmental diagram.



5. Length of analysis period is realistic in relation to demographic rates.

Rate = $\frac{1}{duration\ of\ event}$

6. Parameter values are realistic.