

# Mathematical modelling for malaria elimination

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# Elimination versus control

- Control strategies target clinical disease
- Elimination strategies must target transmission
  - sub-clinical infection makes a significant contribution to transmission especially in high intensity settings
- The sparing use of new anti-malarial drugs has been recommended to minimize the selective pressure on the parasite

## BUT

- Optimal elimination strategies may include use of anti-malarial drugs at high coverage
- Thus strategies designed to extend the lifespan of chemotherapies conflict with those required to successfully and rapidly eliminate the disease



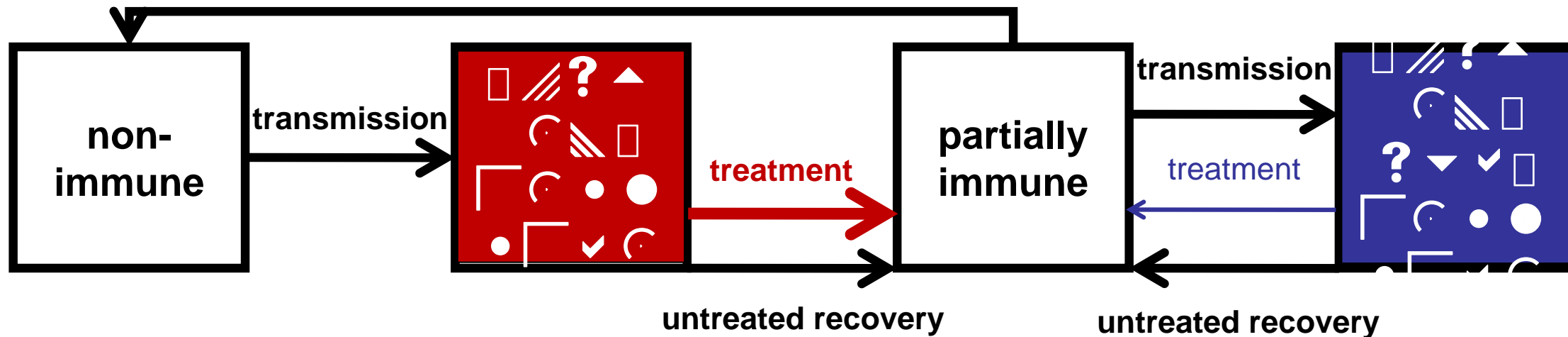
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# A simple model structure

loss of immunity in the absence of challenge



- For a range of transmission intensities the model can:
  - reproduce age profiles of clinical infection in a range of transmission intensities
  - reproduce measured relationship between clinical and sub-clinical infections

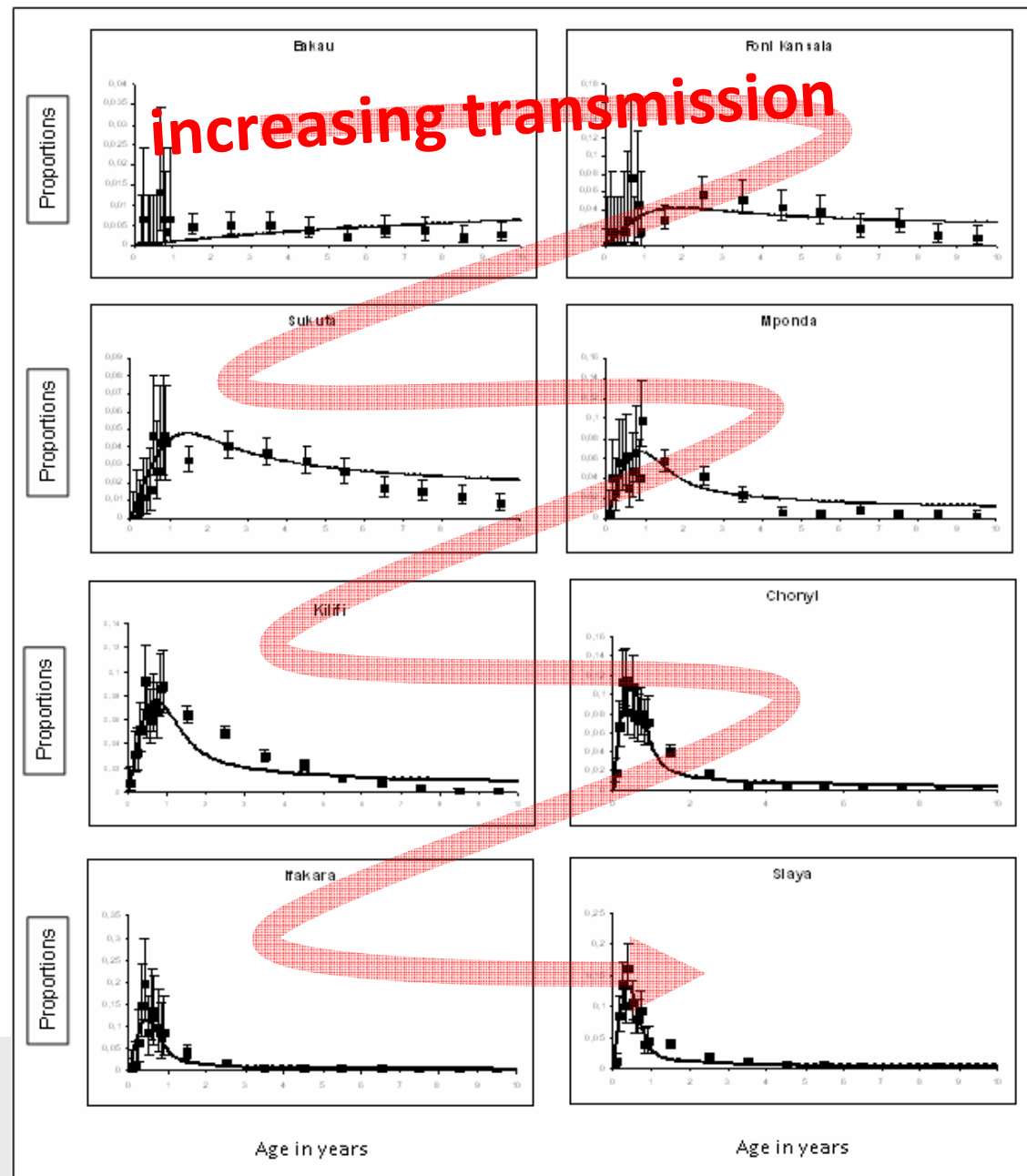


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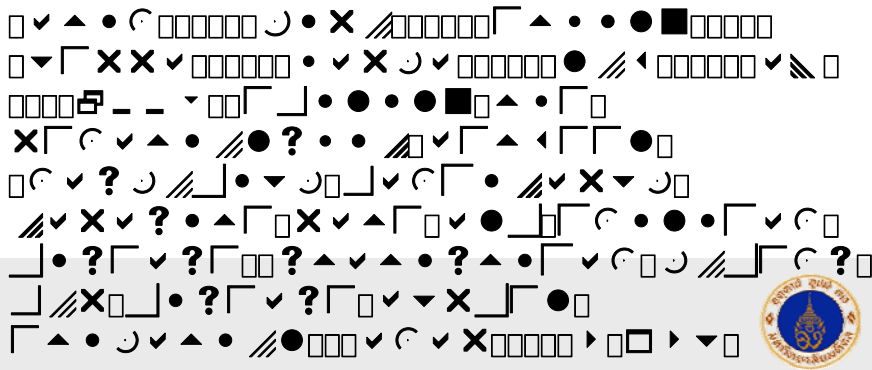
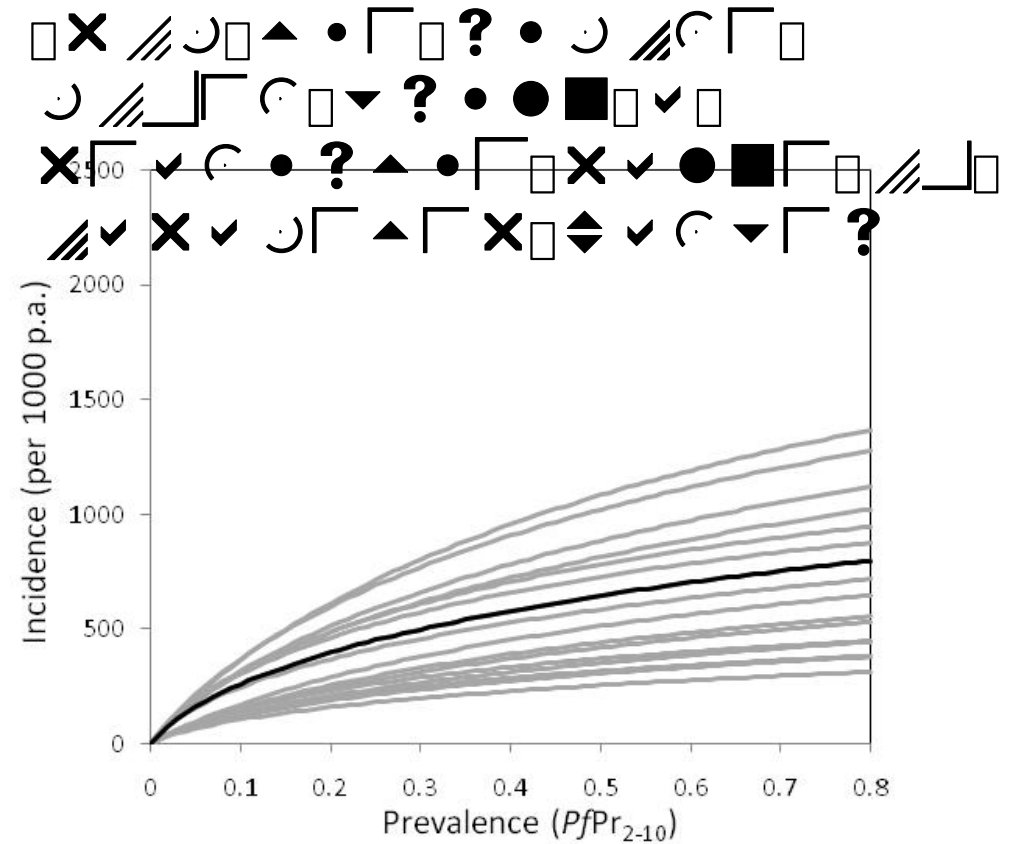
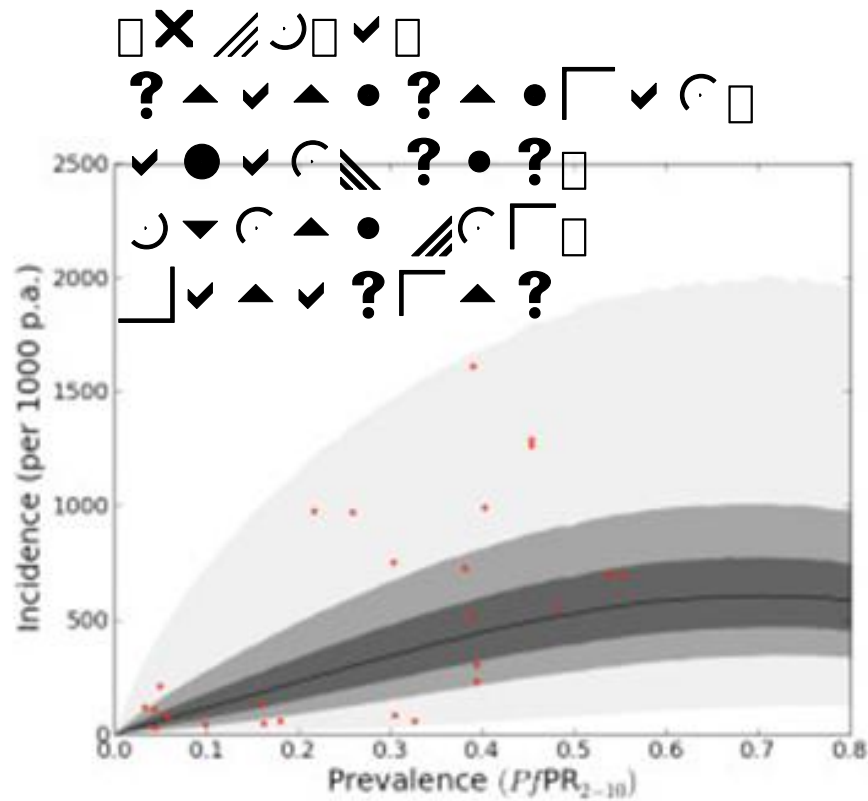


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# Reproducing clinical infection age profiles



# Reproducing relationship between parasite prevalence and clinical infection



# Elimination model

$$S' = (1 - c_b) \frac{N}{L} - \left( \pi\lambda + \frac{1}{L} \right) S + \frac{1}{d_{imm}} R - x(t)S + yS_v$$

$$I_1' = \pi\lambda S - \left( \frac{\eta p_1 + m}{d_{treat}} + \frac{1}{L} + \frac{1}{d_{treat}} \right) I_1 - x(t)I_1 + yI_{1v} - m(t)I_1$$

$$I_2' = \pi\lambda R - \left( \frac{\eta p_2 + m}{d_{treat}} + \frac{1}{L} + \frac{1}{d_{treat}} \right) I_2 - x(t)I_2 + yI_{2v} - m(t)I_2$$

$$R' = \left( \frac{\eta p_1 + m}{d_{treat}} + \frac{1}{L} + \frac{1}{d_{treat}} \right) I_1 + \left( \frac{\eta p_2 + m}{d_{treat}} + \frac{1}{L} + \frac{1}{d_{treat}} \right) I_2 - \left[ \pi\lambda + \frac{1}{d_{imm}} + \frac{1}{L} \right] R - x(t)R + yR_v$$

$$S_v' = c_b \frac{N}{L} - \left( \rho\pi\lambda + \frac{1}{L} \right) S_v + \frac{1}{d_{imm}} R - x(t)S_v + yS_v$$

$$I_{1v}' = \rho\pi\lambda S_v - \left( \frac{\eta p_1 + m}{d_{treat}} + \frac{1}{L} + \frac{1}{d_{treat}} \right) I_{1v} - x(t)I_{1v} + yI_{1v}$$

$$I_{2v}' = \rho\pi\lambda R - \left( \frac{\eta p_2 + m}{d_{treat}} + \frac{1}{L} + \frac{1}{d_{treat}} \right) I_{2v} - x(t)I_{2v} + yI_{2v}$$

$$R_v' = \left( \frac{\eta p_1 + m}{d_{treat}} + \frac{1}{L} + \frac{1}{d_{treat}} \right) I_{1v} + \left( \frac{\eta p_2 + m}{d_{treat}} + \frac{1}{L} + \frac{1}{d_{treat}} \right) I_{2v} - \left[ \rho\pi\lambda + \frac{1}{d_{imm}} + \frac{1}{L} \right] R_v - x(t)R_v + yR_v$$

$$\lambda = \frac{R_0 \left( \frac{1}{L} + \frac{1}{d_{treat}} \right)}{C + P}$$

$$C = p_1 (I_1 + I_{1v}) + p_2 (I_2 + I_{2v})$$

$$P = \eta p_1 (I_1 + I_{1v}) + \eta p_2 (I_2 + I_{2v})$$

$$x(t) = \begin{cases} 0 & \text{for } \text{mod}(t, 1) < \frac{9}{12} \\ -4 \ln \left( \frac{100 - c}{100} \right) & \text{for } \text{mod}(t, 1) \geq \frac{9}{12} \end{cases}$$

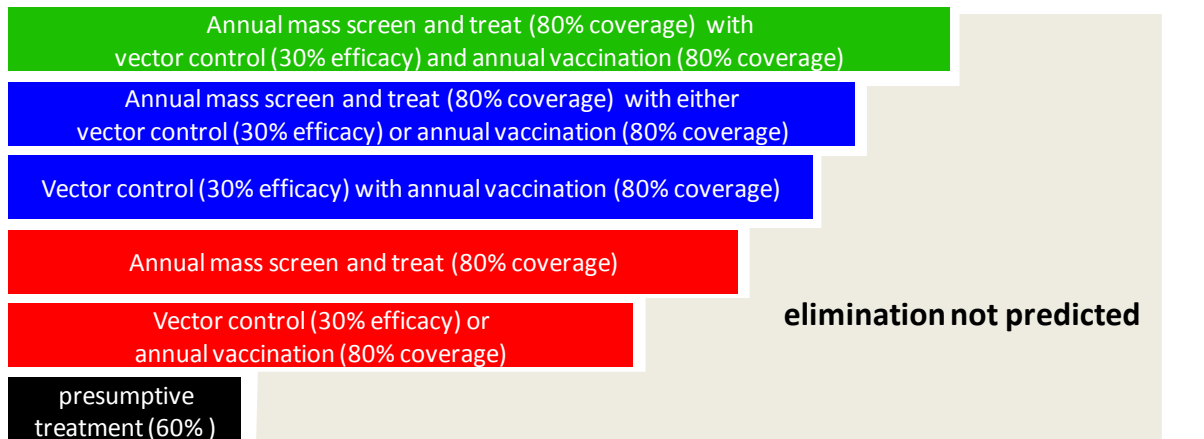
$$m(t) = \begin{cases} 0 & \text{for } \text{mod}(t, 1) < \frac{9}{12} \\ \exp \left( -4 \ln \left( \frac{100 - c}{100} \right) \left( t - \frac{9}{12} \right) \right) & \text{for } \text{mod}(t, 1) \geq \frac{9}{12} \end{cases}$$

- **Vaccination using the RTS,S vaccine**
- **Annual mass screen and treat (MSAT) policy reaching a coverage of 80% of the infected population within three months of each year assuming that the drug will effectively clear blood stage parasites in an average of two weeks' time**
- **Artemisinin combination therapy resulting in a reduction in the force of infection by 30%**
- **Immunity acquisition and loss**
- **Spread of resistance**
- **ITNs and other vector control methods**
- **assuming a vaccine induced reduction in the force of infection by 50% a duration of immunity of between 1 and 10 years**
- **Given annually to all age groups, reaching a coverage of 80% within a three-month period. The method of administration could be similar to or in conjunction with a MSAT programme**

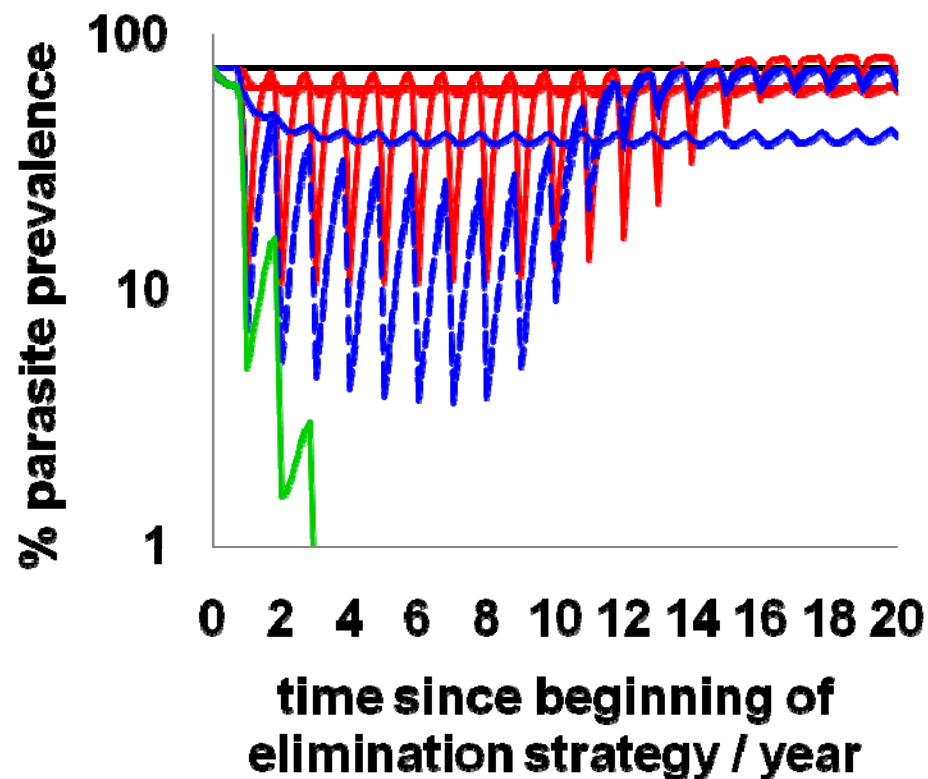
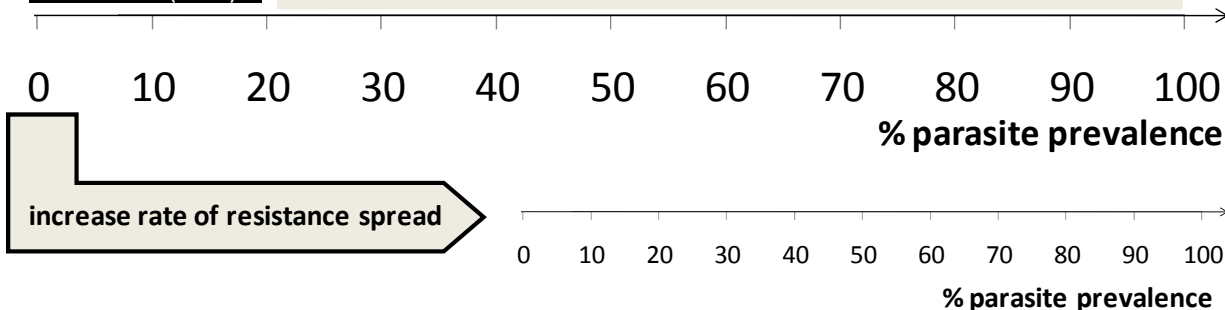


# Combining strategies

elimination predicted with given strategy



elimination not predicted



- Combining strategies that seem ineffective independently can result in elimination
- especially if resistance is not spreading

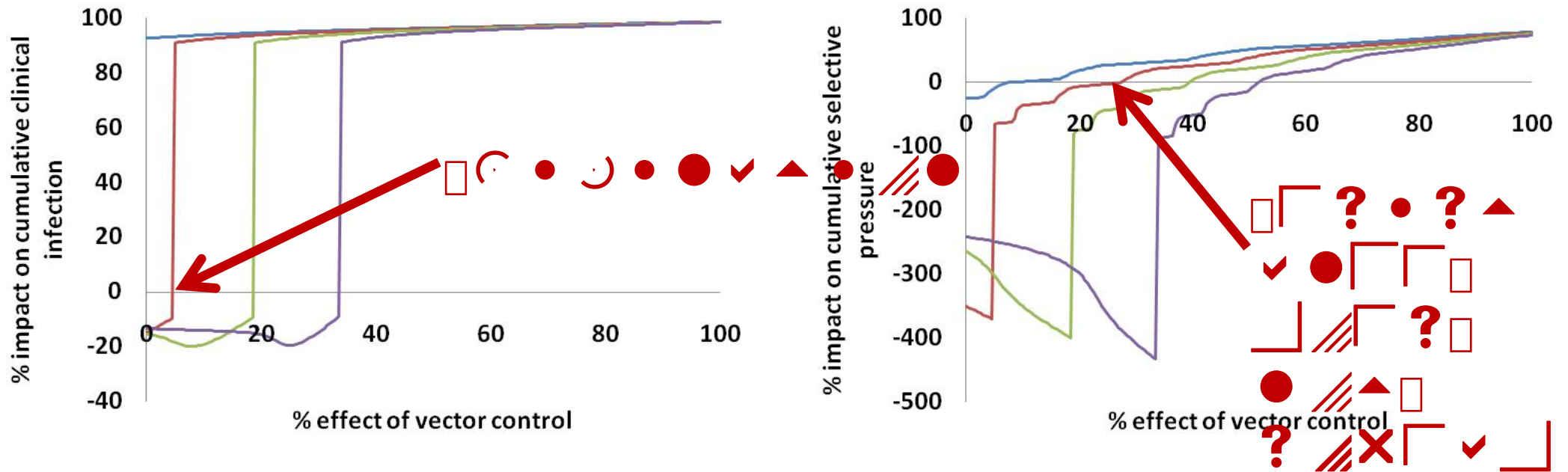


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# Protecting ACTs

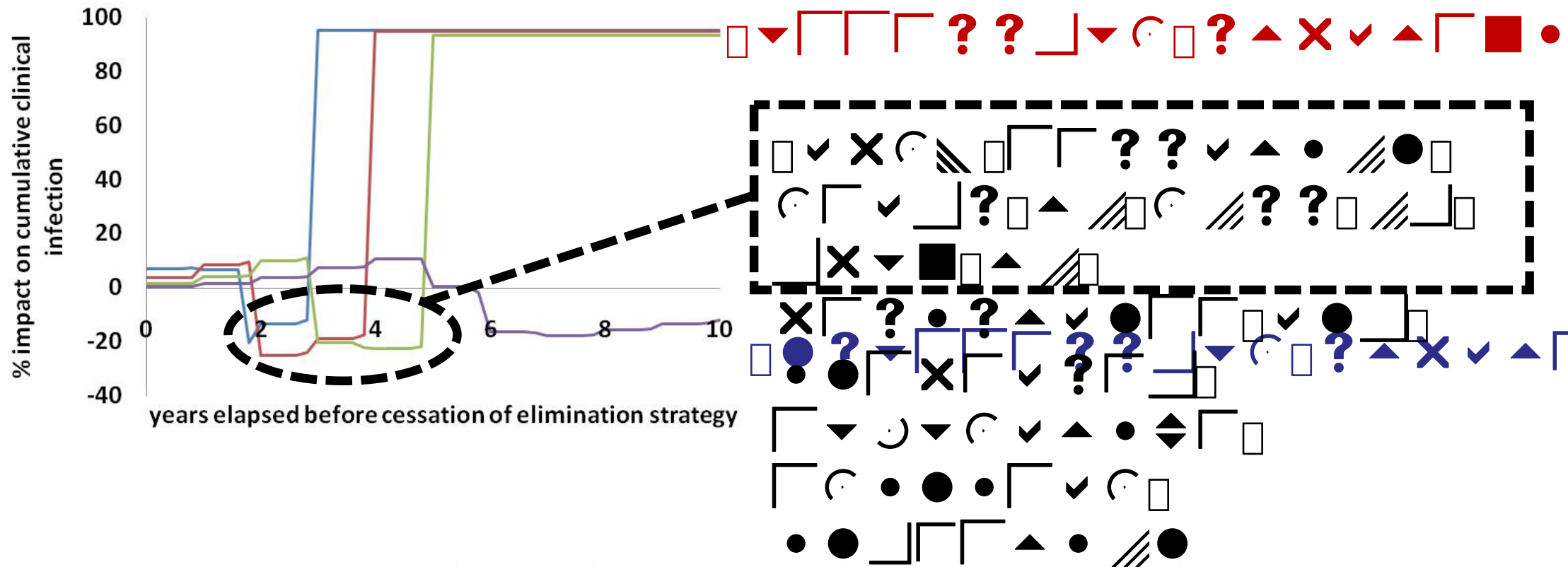


- **Combining strategies at suitable levels can eliminate while protecting against the spread of resistance**



# Early cessation of strategy

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- Early cessation of a potentially successful strategy can have a negative impact on clinical infection if resistance is already spreading



# Future challenges for modelling elimination

- **Simple deterministic models are not up to the job of modelling the final stages of elimination and long term dynamics**
- **Detailed stochastic models are required**
- **These models exist but require**
  - **large, precise and diverse data that are**
    - **geographically explicit**
- **Do we have those data?**



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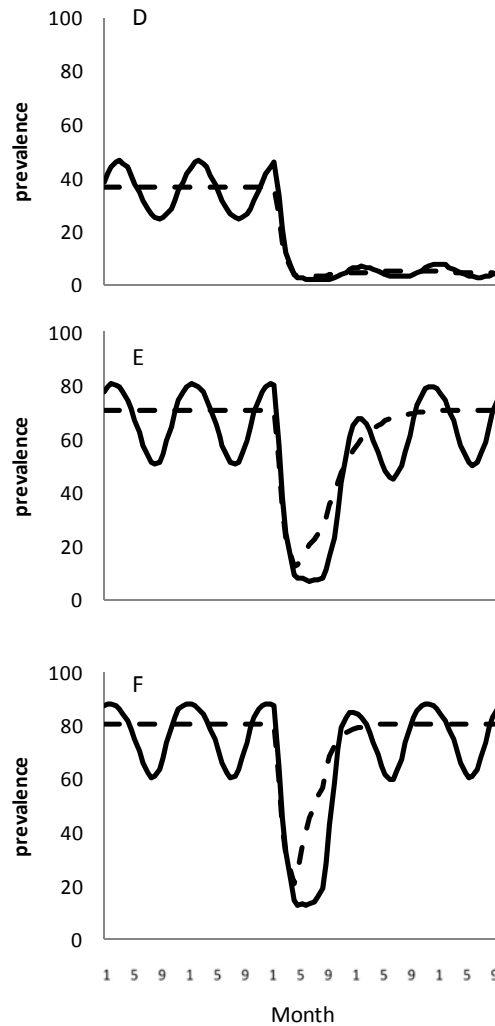
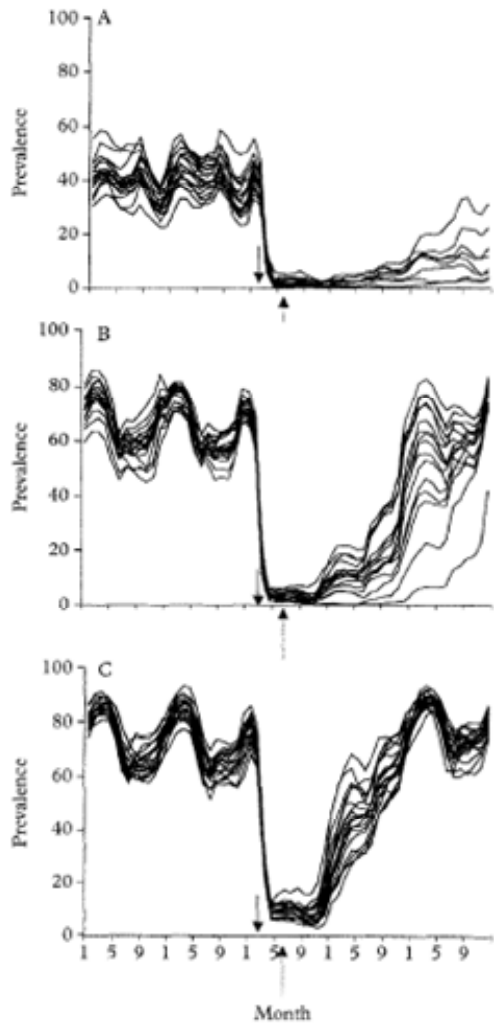
# Any questions?

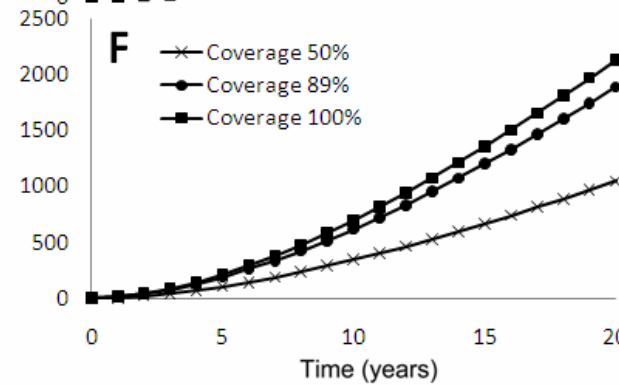
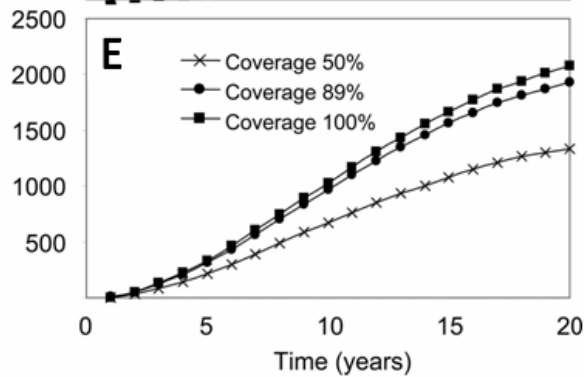
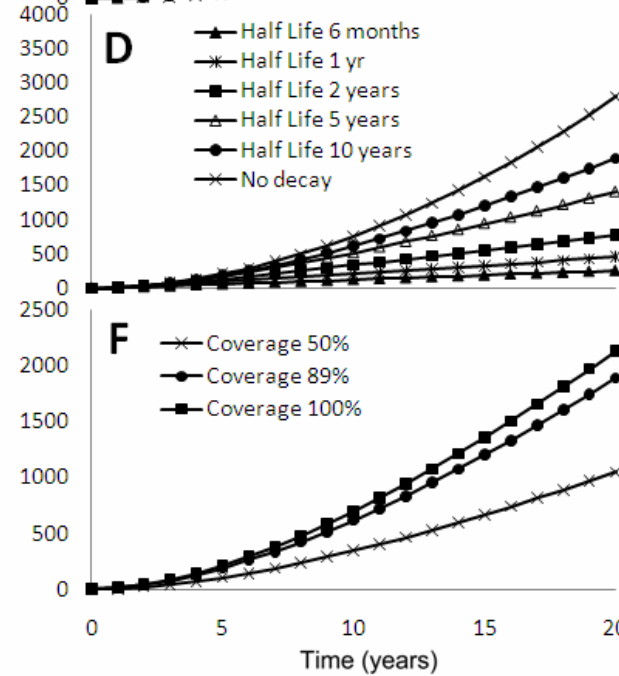
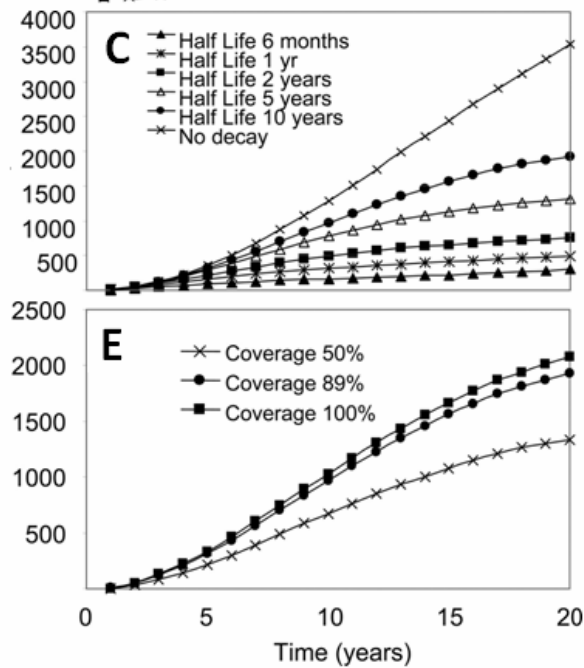
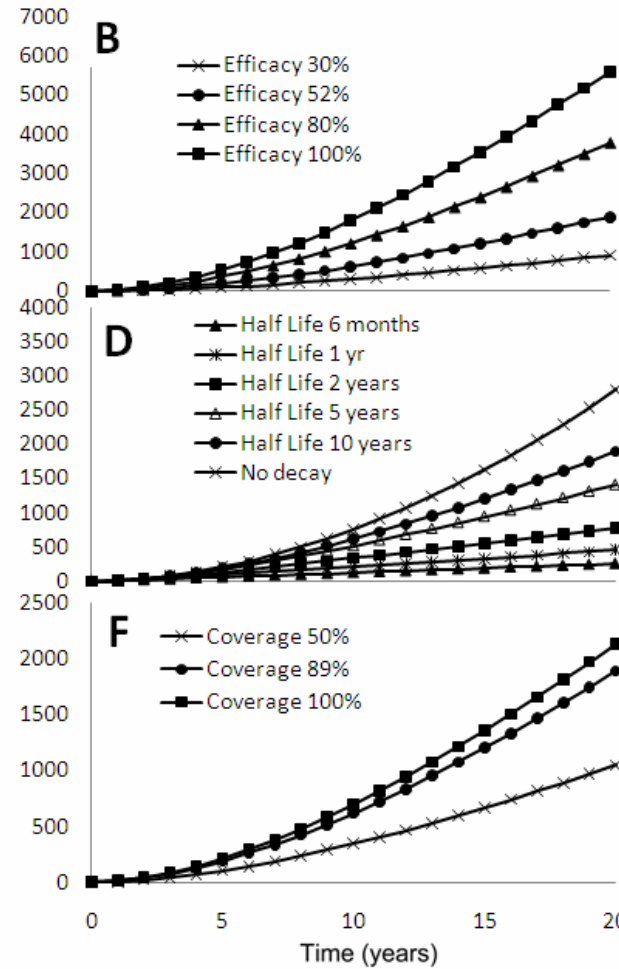
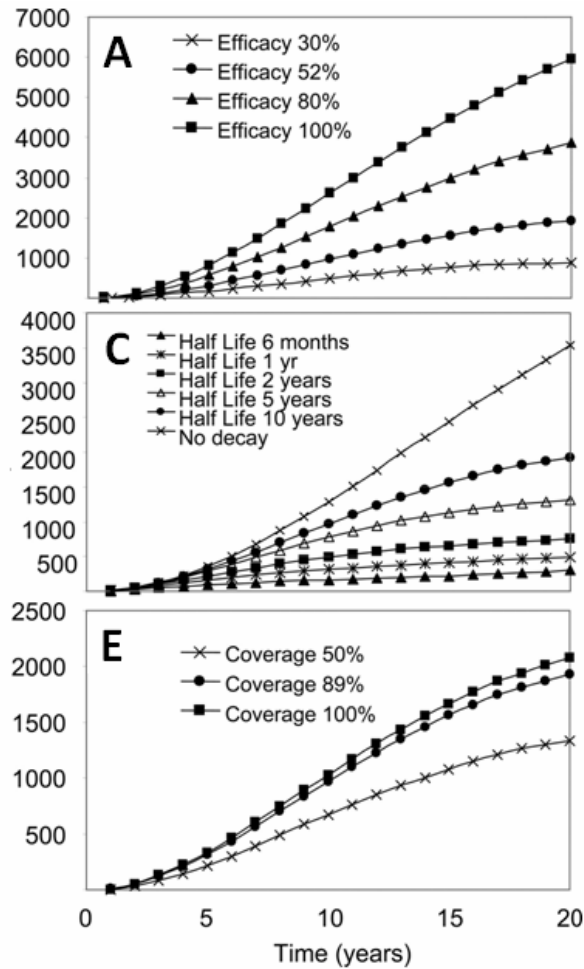


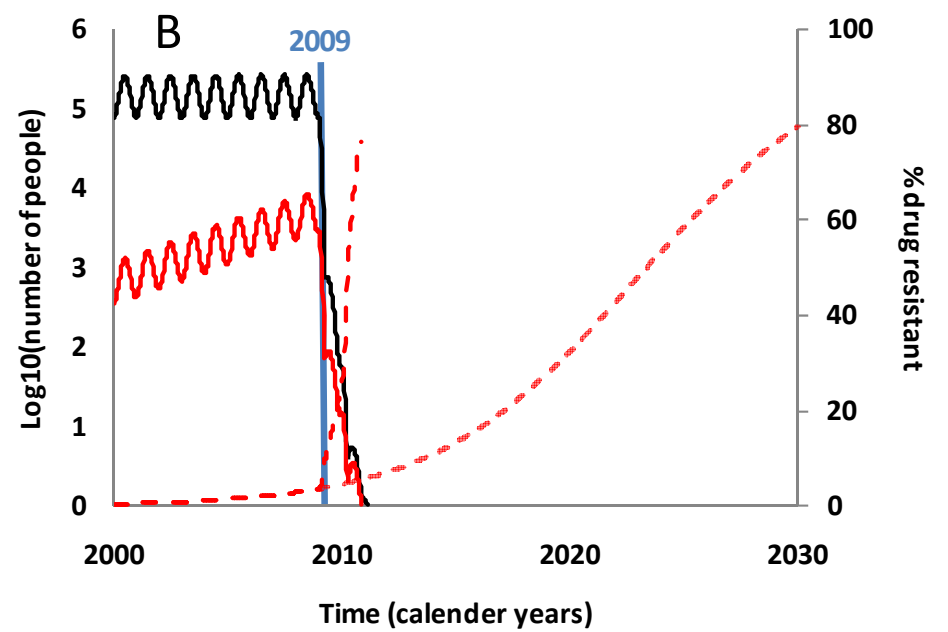
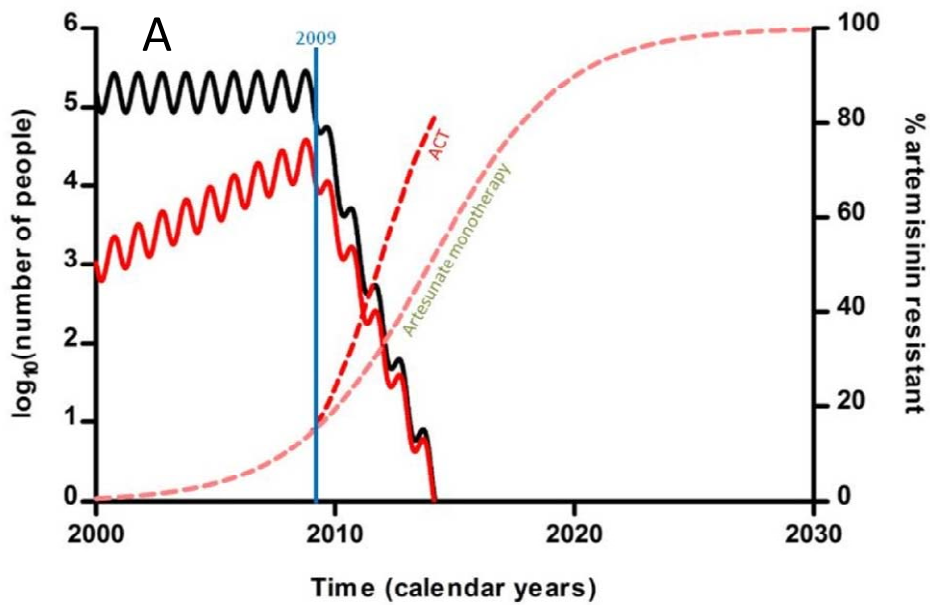
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