Mathematical modelling for malaria elimination

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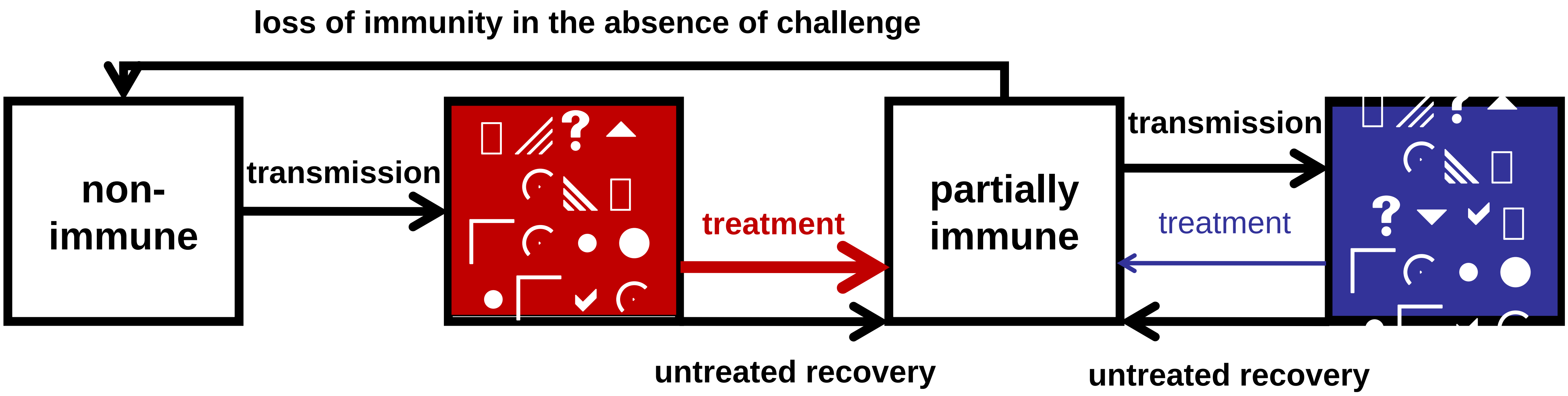
Elimination versus control

- **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

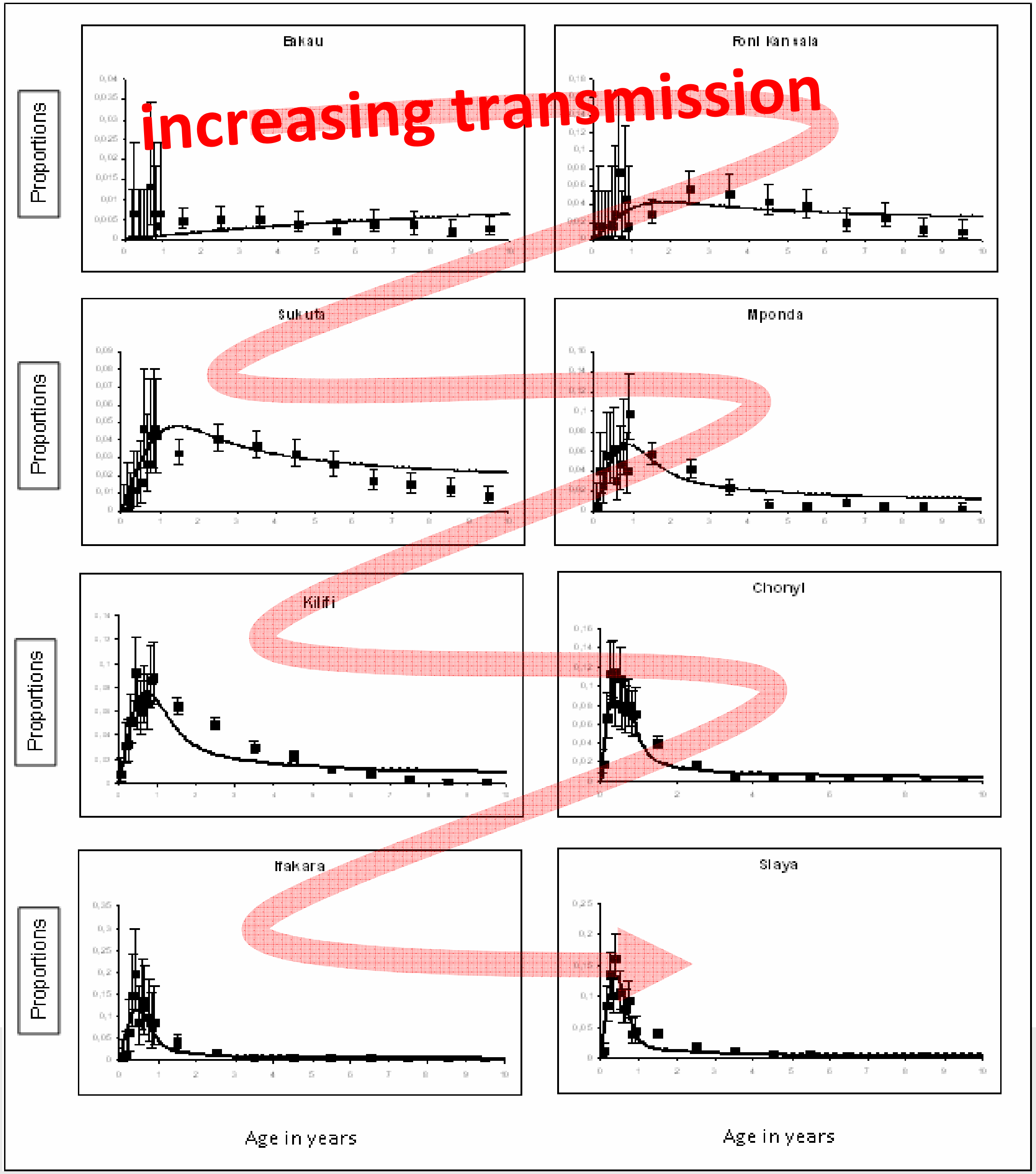
- **Optimal elimination strategies may include use of anti-malarial drugs at high coverage**
- **Thus strategies designed to extend the lifespan of chemotherapies conflict with those required to successfully and rapidly eliminate the disease**

A simple model structure

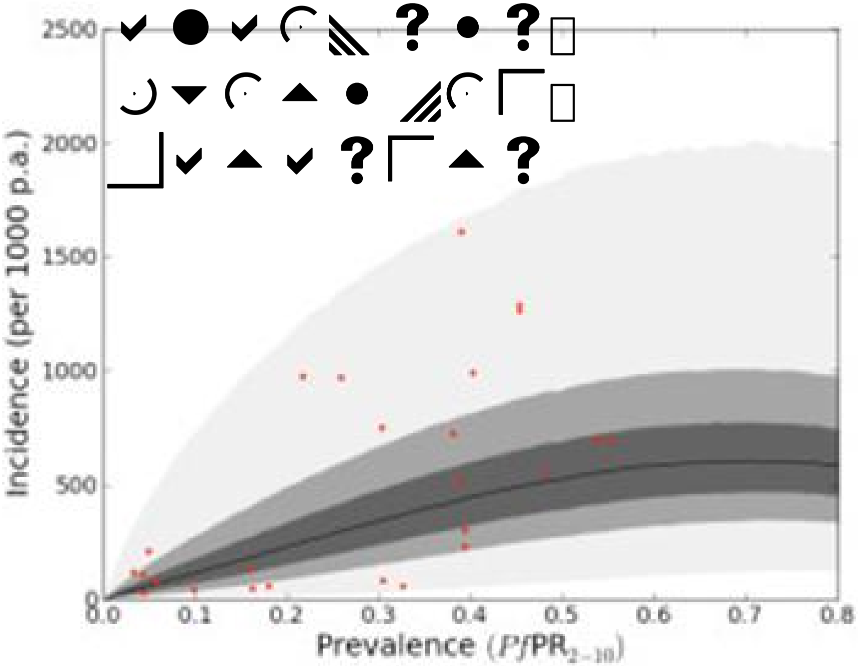


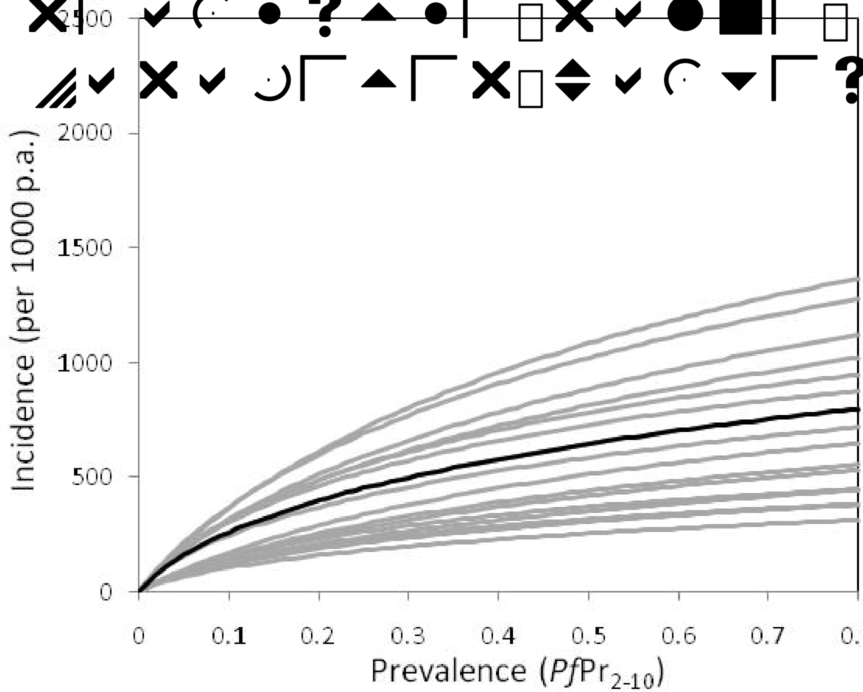
- **For a range of transmission intensities the model can:**
  - **reproduce age profiles of clinical infection in a range of transmission intensities**
  - **reproduce measured relationship between clinical and sub-clinical infections**

Reproducing clinical infection age profiles



Reproducing relationship between parasite prevalence and clinical infection



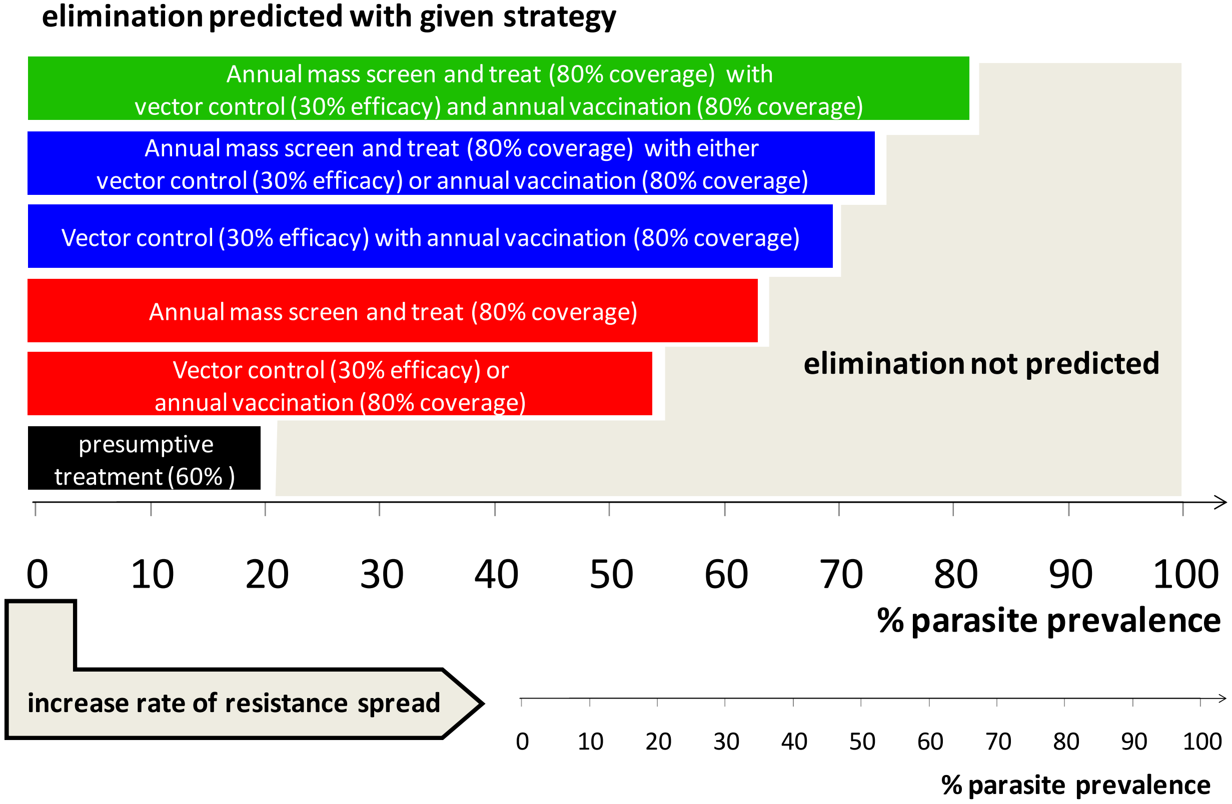


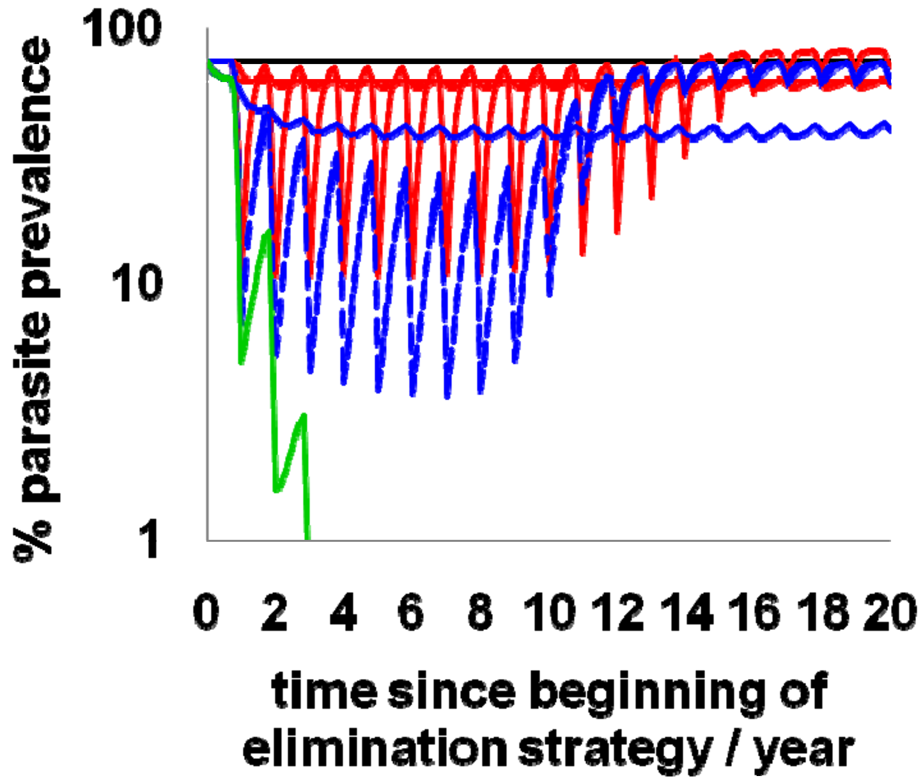
Elimination model

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

- An extension of the transmission model
- Immunity
  - acquisition and loss
- Spread of resistance
- ITNs and other vector control methods
  - resulting in a reduction in the force of infection by 30%
- Artemisinin combination therapy
  - 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
- Vaccination using the RTS,S vaccine
  - 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

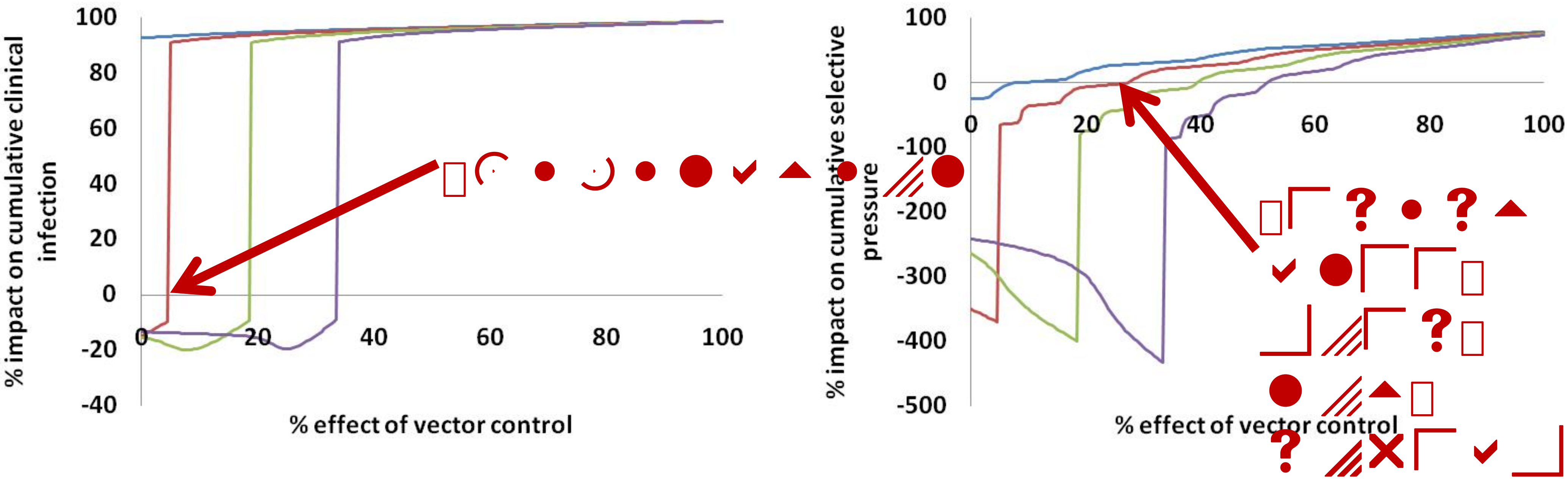
Combining strategies





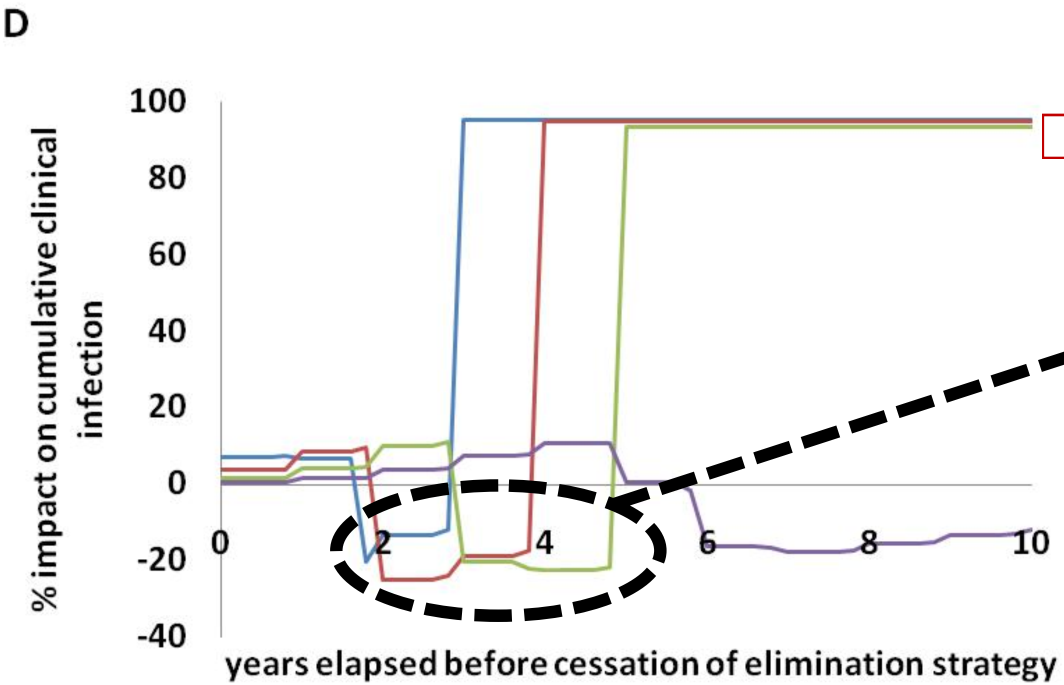
- **Combining strategies that seem ineffective independently can result in elimination**
- **especially if resistance is not spreading**

Protecting ACTs



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

Early cessation of strategy



- **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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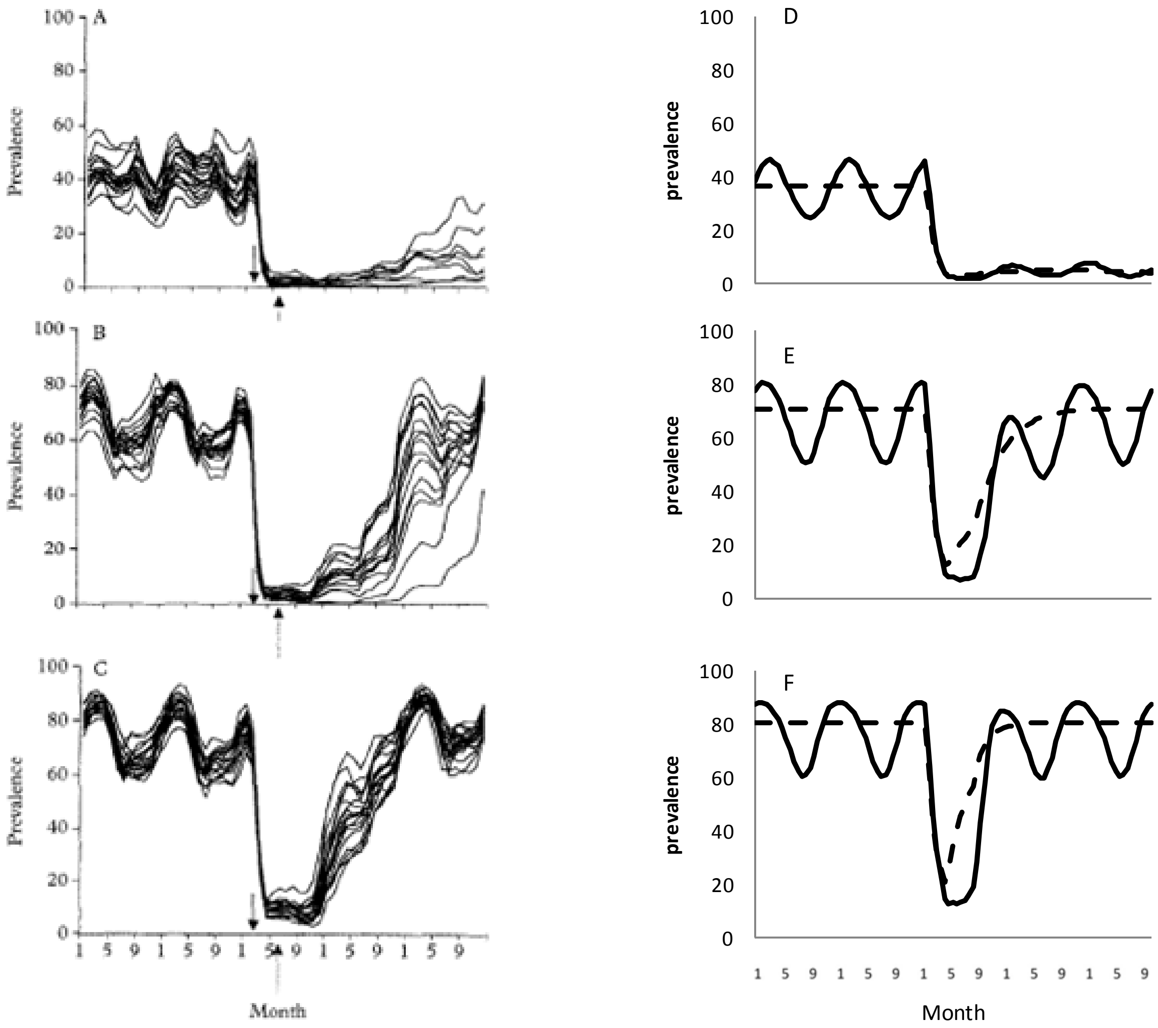
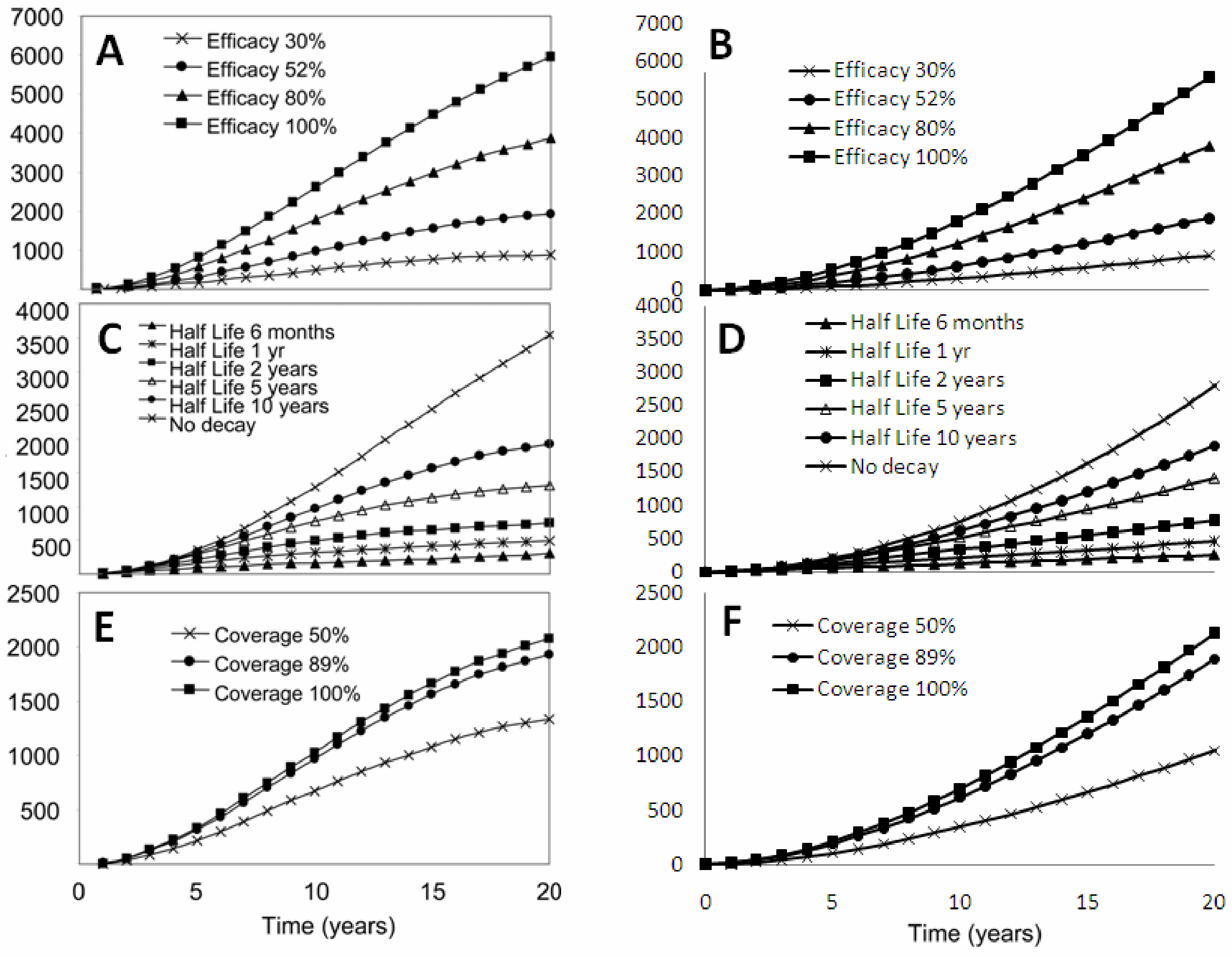
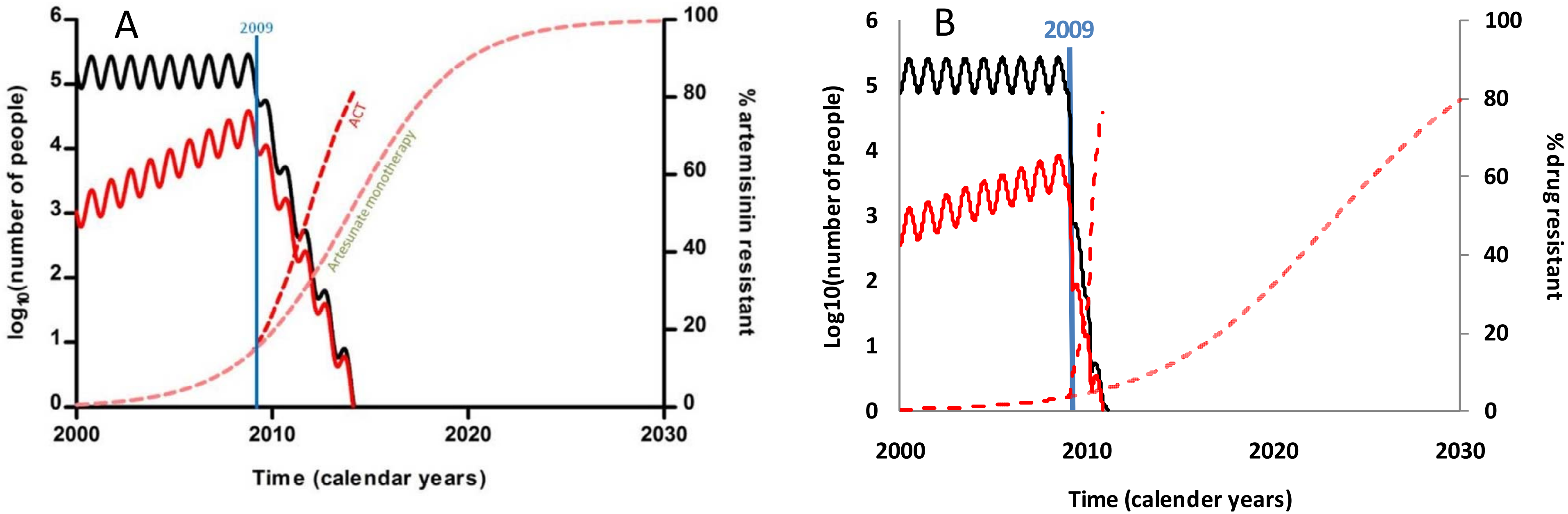
Any questions?


A
B
C
D
E
F
Prevalence
prevalence
100
80
60
40
20
0
1 5 9 1 5 9 1 5 9 1 5 9 1 5 9
Month



A
Efficacy 30%
Efficacy 52%
Efficacy 80%
Efficacy 100%
B
Efficacy 30%
Efficacy 52%
Efficacy 80%
Efficacy 100%
C
Half Life 6 months
Half Life 1 yr
Half Life 2 years
Half Life 5 years
Half Life 10 years
No decay
D
Half Life 6 months
Half Life 1 yr
Half Life 2 years
Half Life 5 years
Half Life 10 years
No decay
E
Coverage 50%
Coverage 89%
Coverage 100%
F
Coverage 50%
Coverage 89%
Coverage 100%
Time (years)
Time (years)



A
2009
ACT
Artesunate monotherapy
log10(number of people)
% artemisinin resistant
Time (calendar years)
2000
2010
2020
2030
0
1
2
3
4
5
6
0
20
40
60
80
100
B
2009
Log10(number of people)
% drug resistant
Time (calender years)