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Power calculation for Cluster Randomised Trials (CRT) with truncated outcomes

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MRC Centre for Global Infectious Disease Analysis

21st November 2018

Introduction

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What is the probability that a research finding reflects a true effect?

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(Button et al., 2013)

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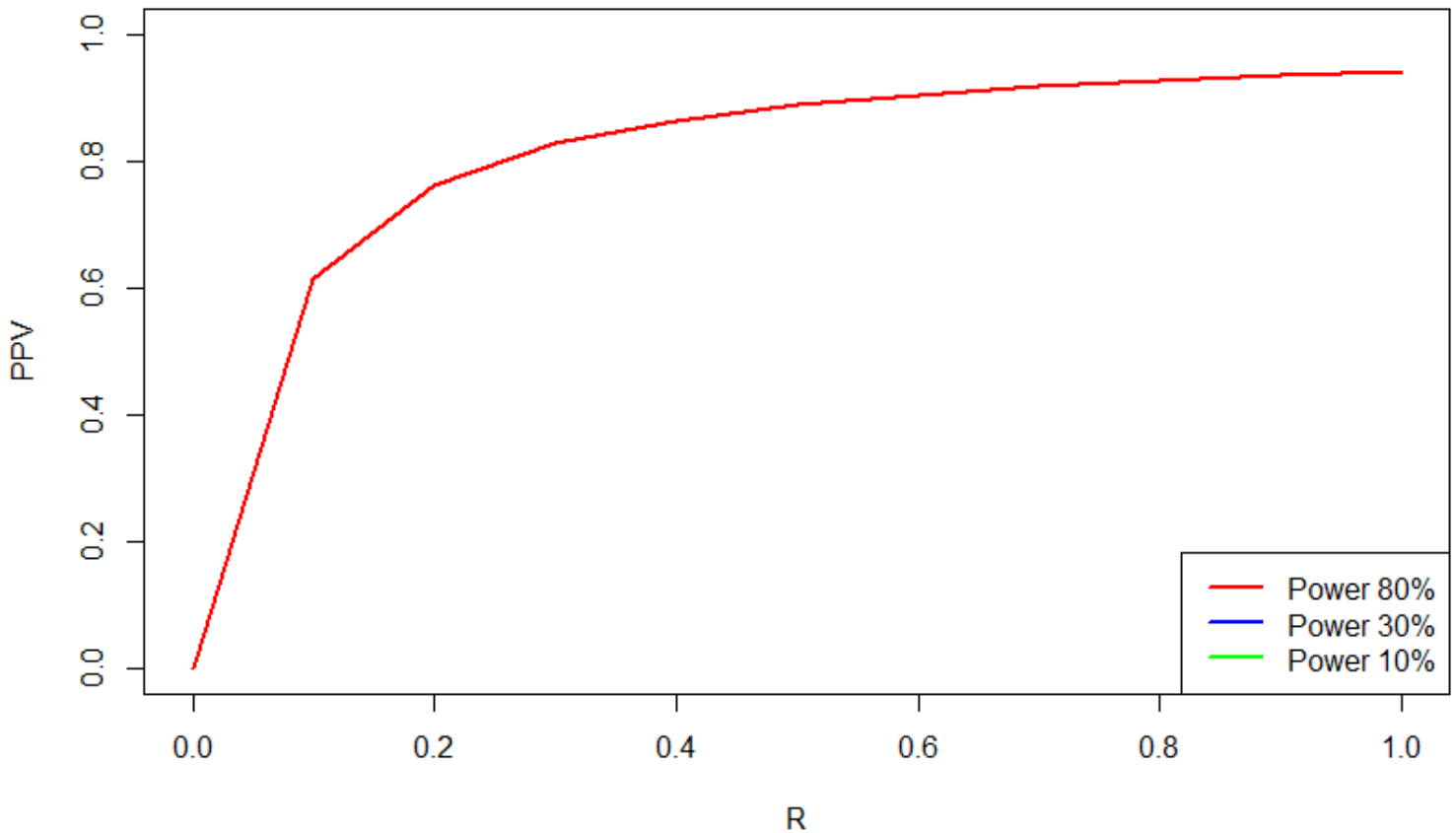

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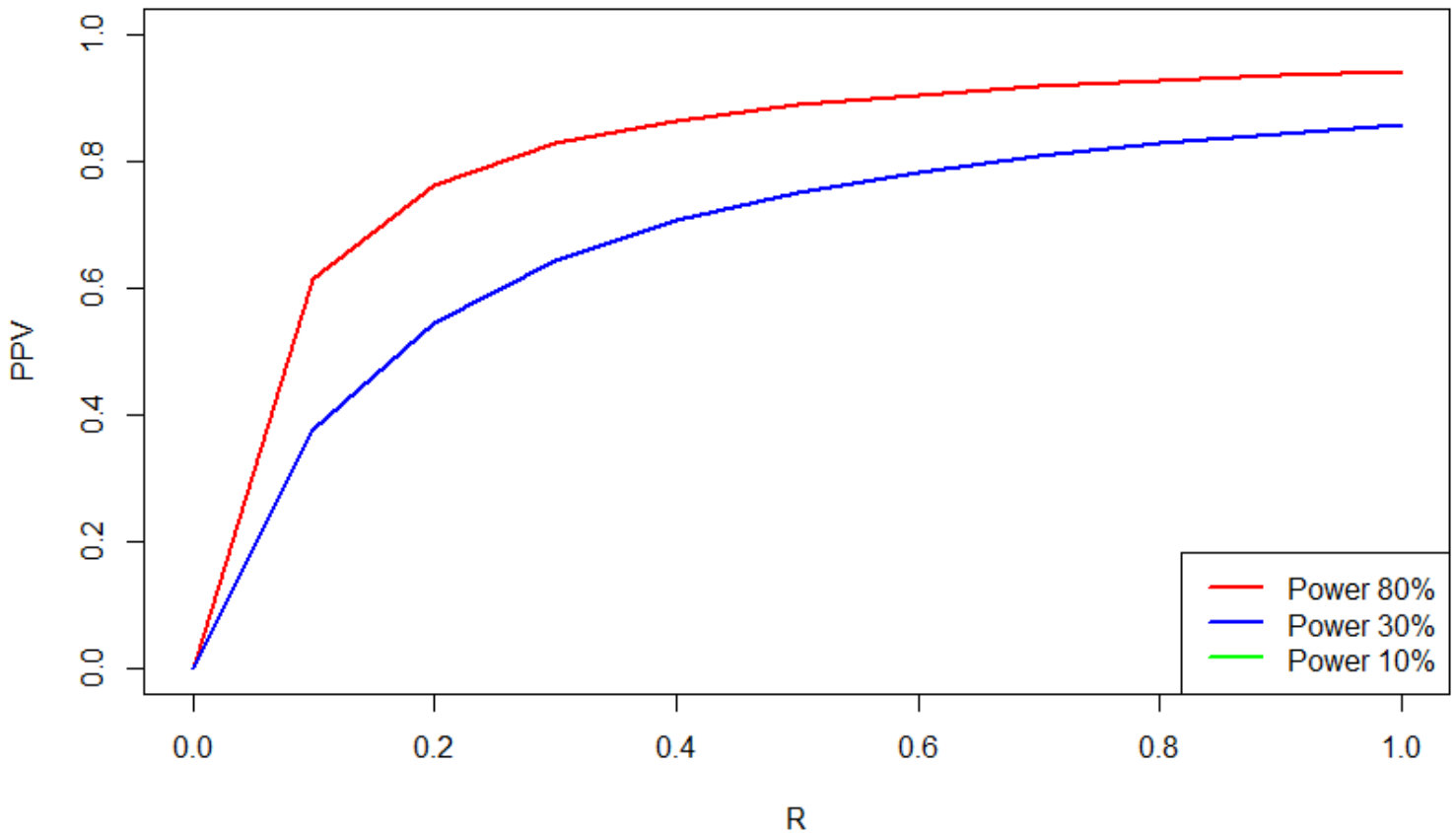

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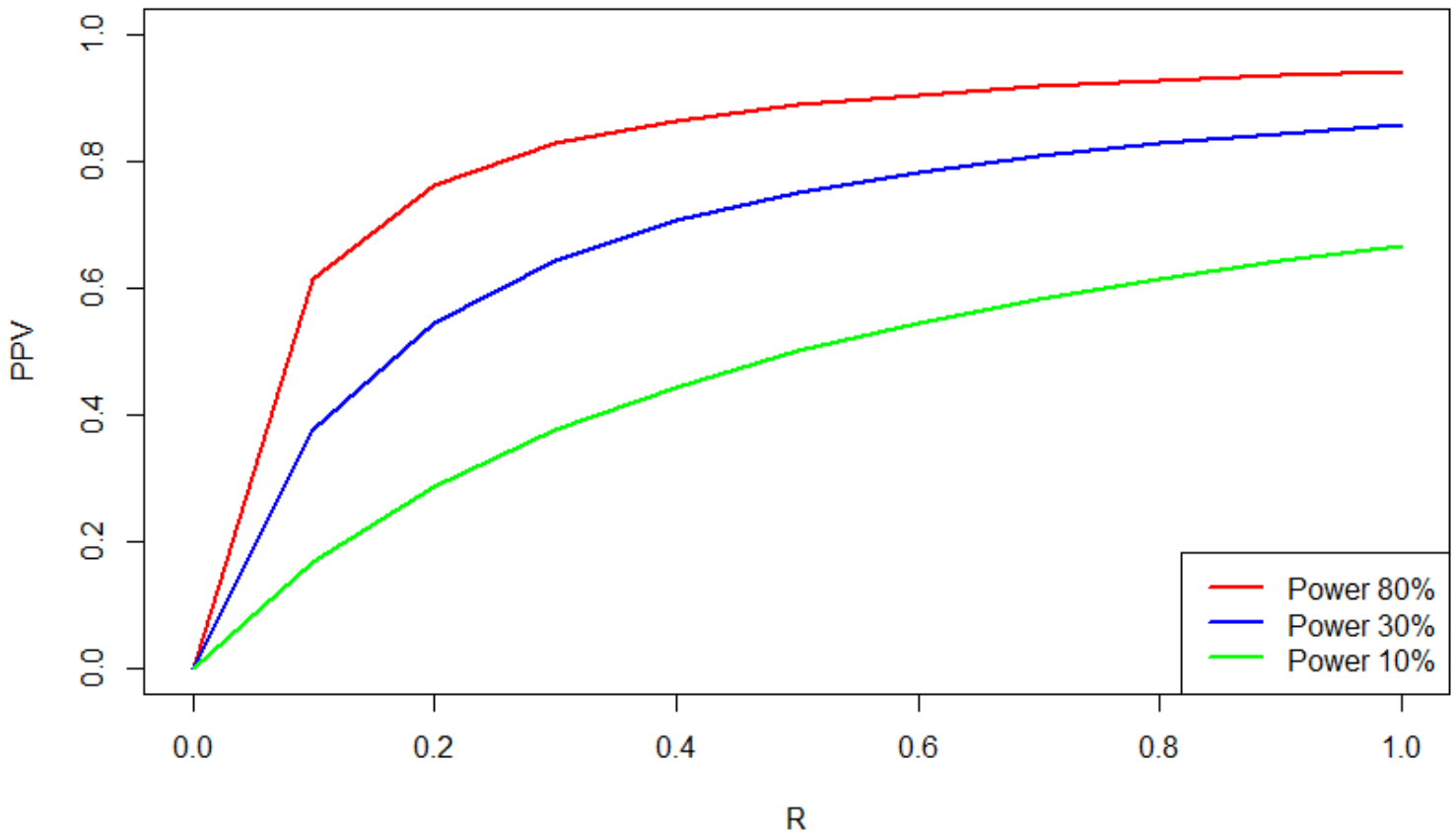

Power

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- Minimum Detectable Effect Size (Δ)
- Variability (T=$\sigma_b^2 + \sigma_w^2$)
- Type I error (α)
- Type II error (β)

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1. All quantities pre-specified
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   $\rightarrow$ Sample size required for desired Power=$1 - \beta$

Statistical toolbox

Formulae

Statistical toolbox

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Formulae

1. Outcome (Normal, Binary, Count, Survival, . . .)
2. Design complexities (CRT, Stepped Wedge, Cross-over trials . . .)

(Amatya, Bhaumik, and Gibbons, 2013; Hayes and Bennett, 1999; Heo and Leon, 2008; Roy et al., 2007; Rutterford, Copas, and Eldridge, 2015)

Software

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Software

1. Stand-alone programs (*G*Power, PS, PASS, nQuery*)
2. R software (*pwr, TrialSize, PowerUpR*^{c}*,powerSurvEpi*)
3. SAS (*proc power*)
4. SPSS (*Sample Power*)
5. Stata (*power*)
6. Microsoft Excel (*PowerUpR*^{c})
7. Specialist simulation software (*IcebergSim, FACT,Clinical trial simulation*)

See (Hickey et al., 2018) for a detailed list

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  → Lack of support for higher levels of variability
  → **Truncated outcomes not standard consideration**

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What's the big deal anyway?

1. **Standard PDF/ PMF assume events may occur across entire range of values**
2. **Gap between theory and practice warrants redress?**

Case study: malaria vector control trial

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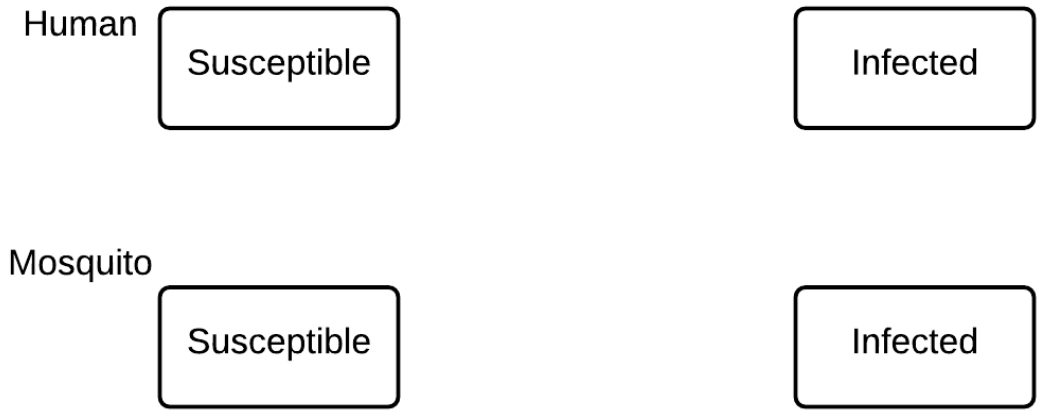

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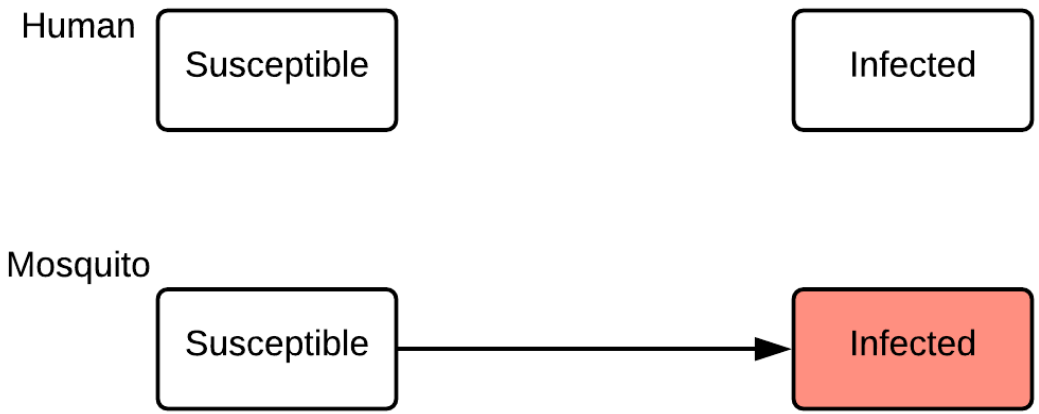

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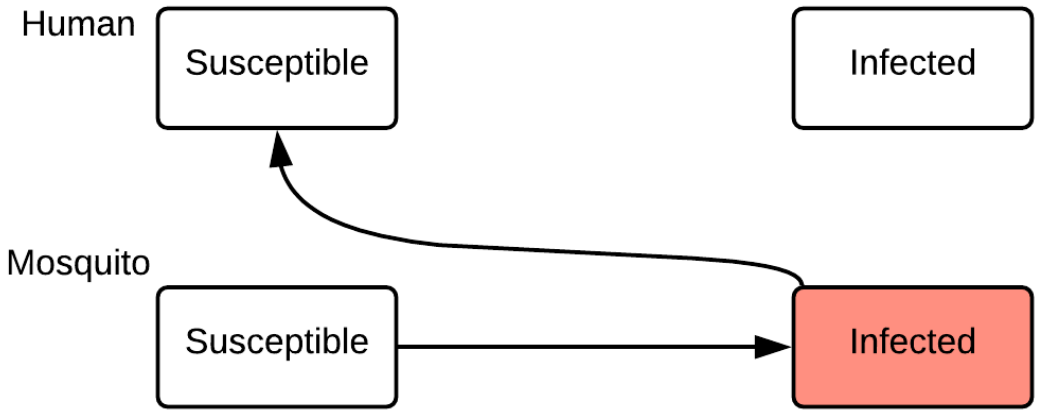

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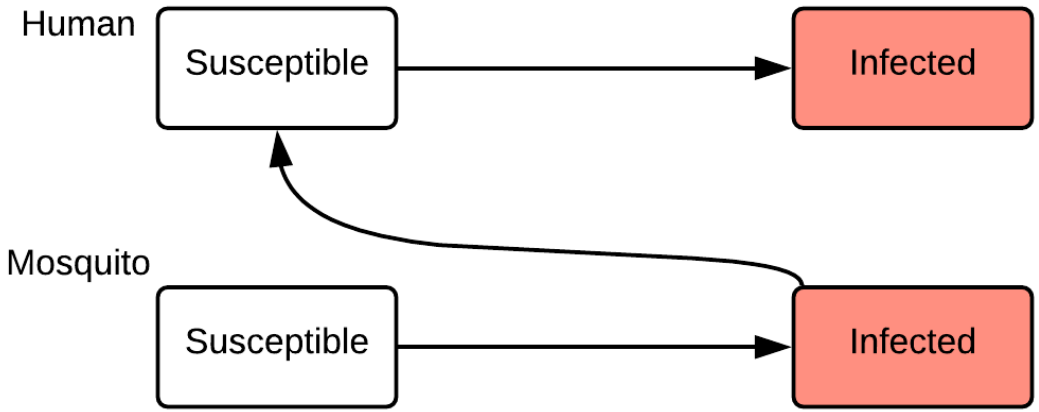

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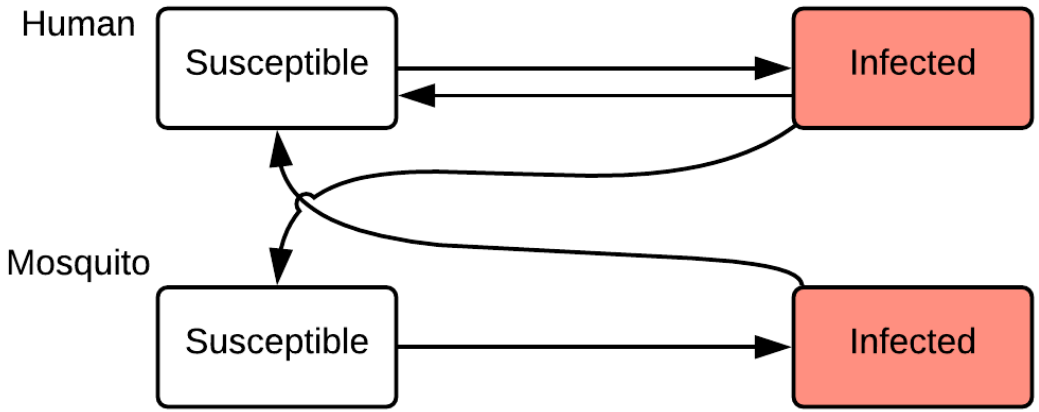

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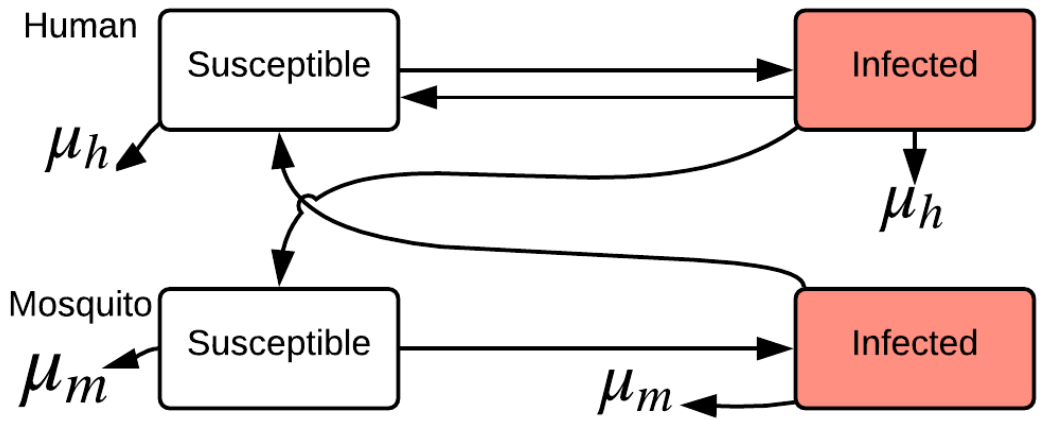

Conceptual model for malaria transmission

Case study: malaria vector control trial

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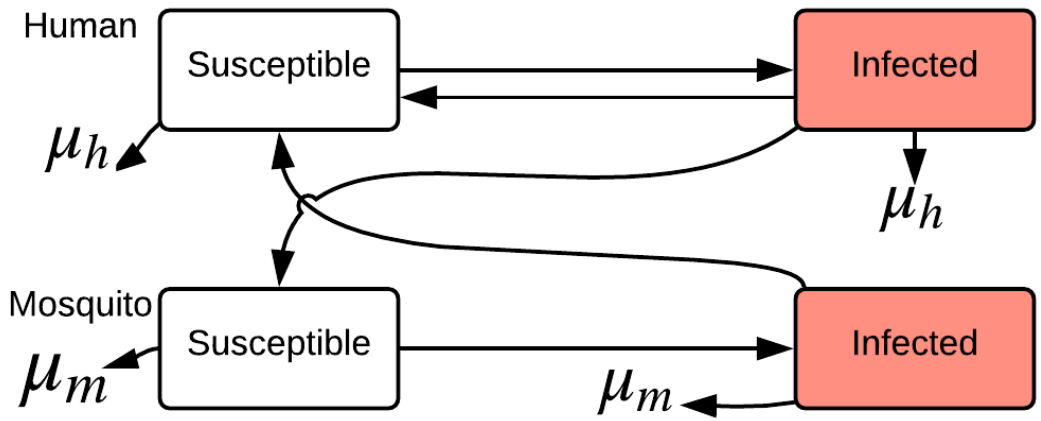

Conceptual model for malaria transmission

1. Target $I_m \nRightarrow S_h$ and $I_h \nRightarrow S_m$

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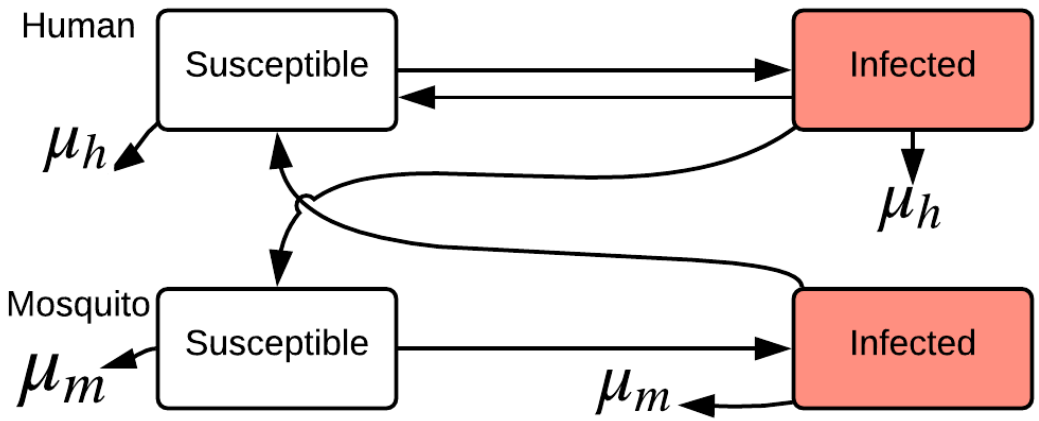

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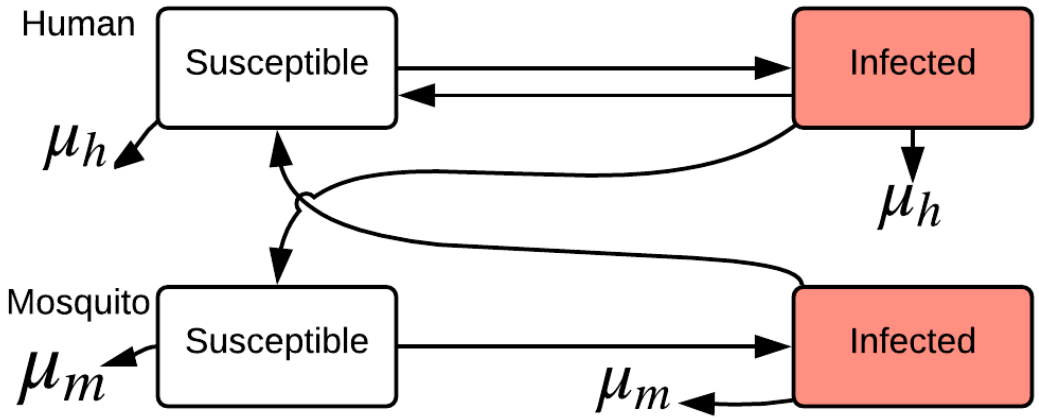

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1. Target $I_m \not\Rightarrow S_h$ and $I_h \not\Rightarrow S_m$
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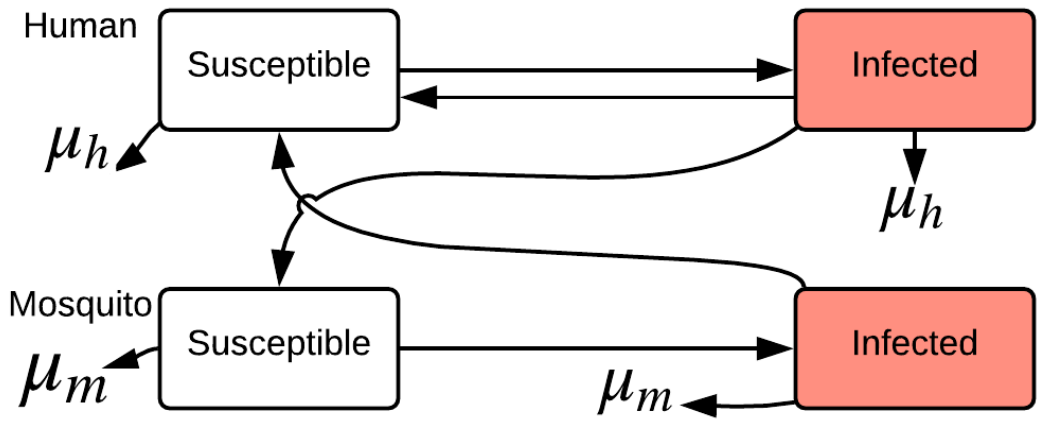

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2. Attractive Toxic Sugar Baits $\rightarrow \mu_m + \mu_{atsb}$
3. Reduce the population of mosquito available to transmit malaria
4. Several entomological trials in Africa suggest promising mosquito feeding and death rate

Case study: malaria vector control trial

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How novel is this?

Case study: malaria vector control trial

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1. The first malaria ATSB based entomological trial with primary epidemiological end points

Key features of the Cluster Randomised Trial

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- Standard of care in the two arms $\rightarrow$ Insecticide Treated Nets (ITNs)

Effect of truncation?

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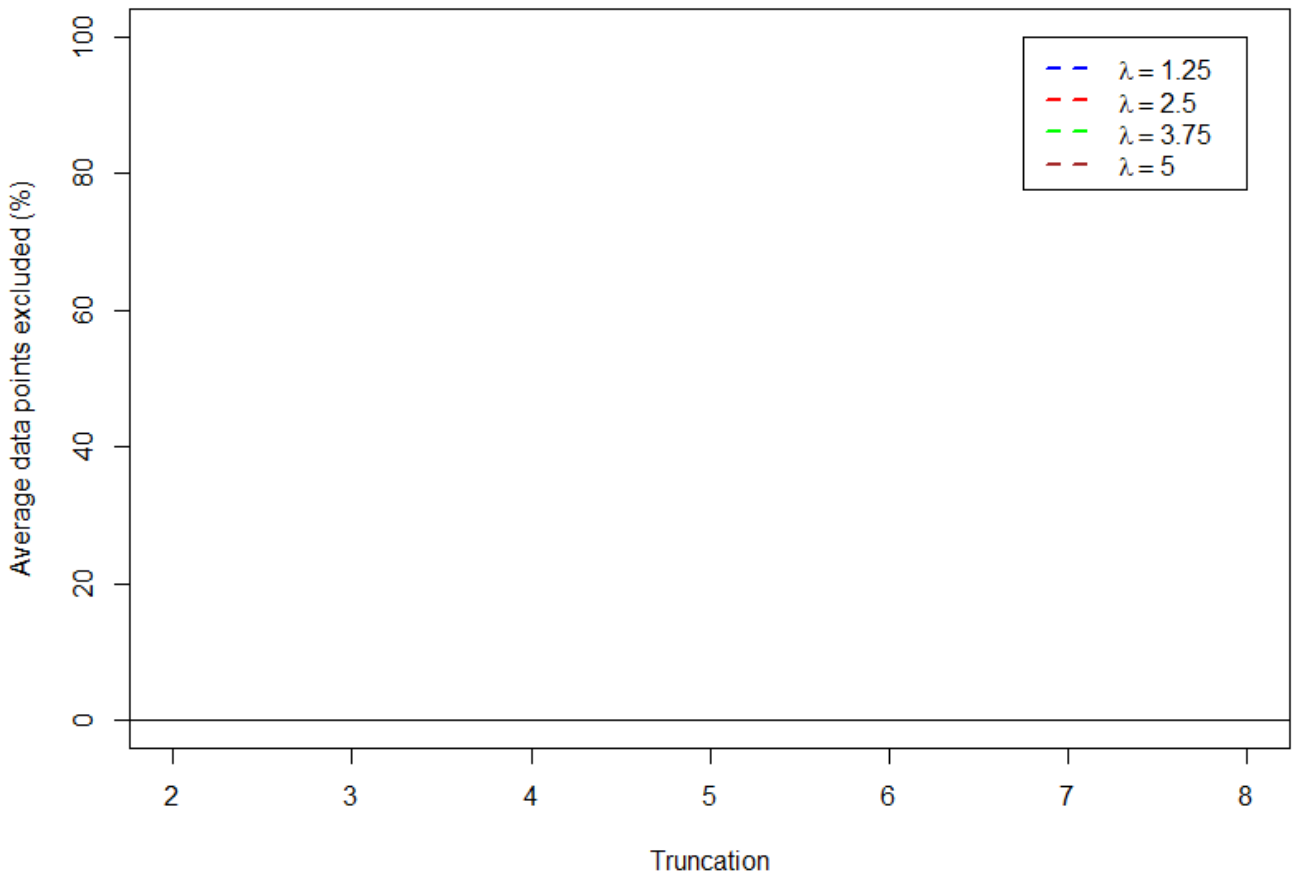

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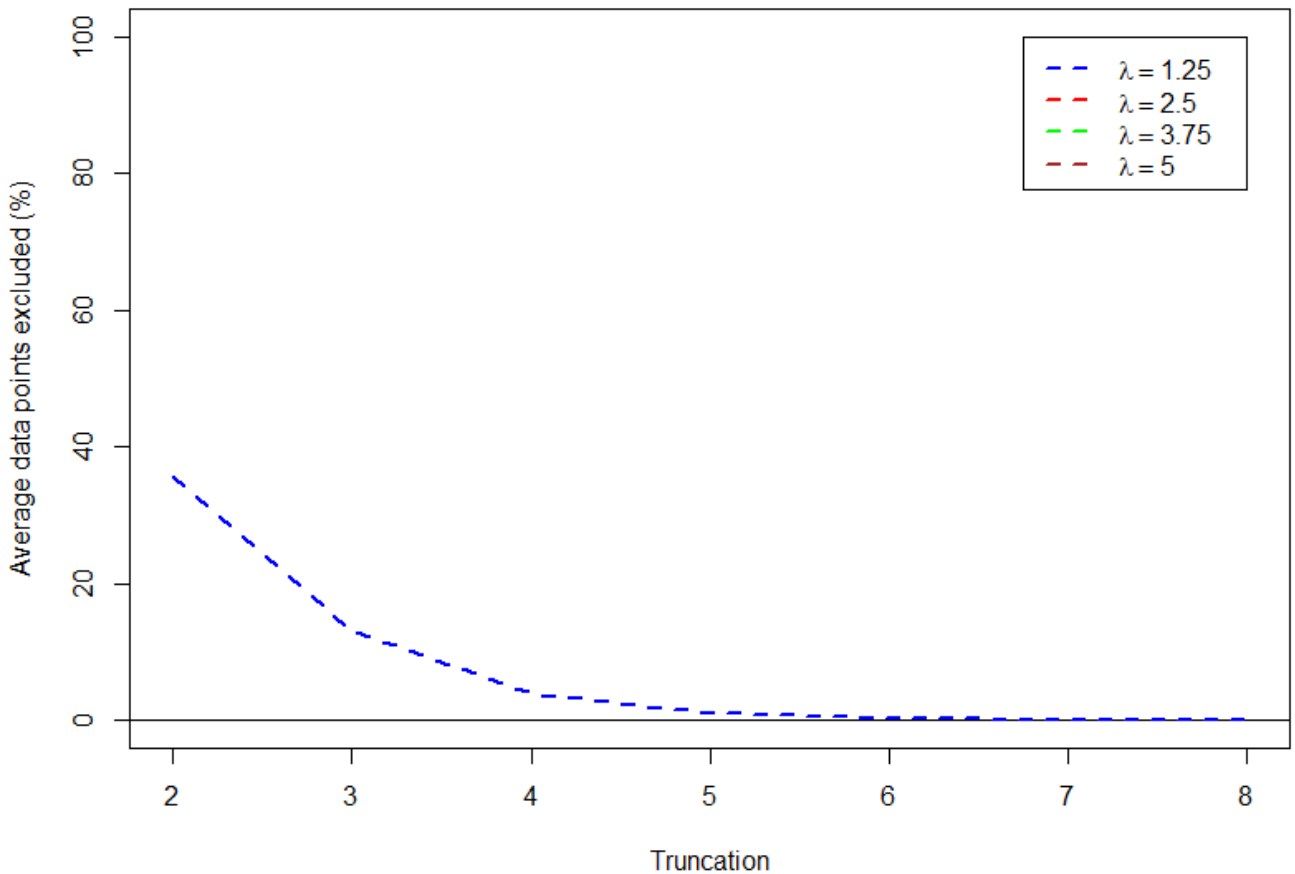

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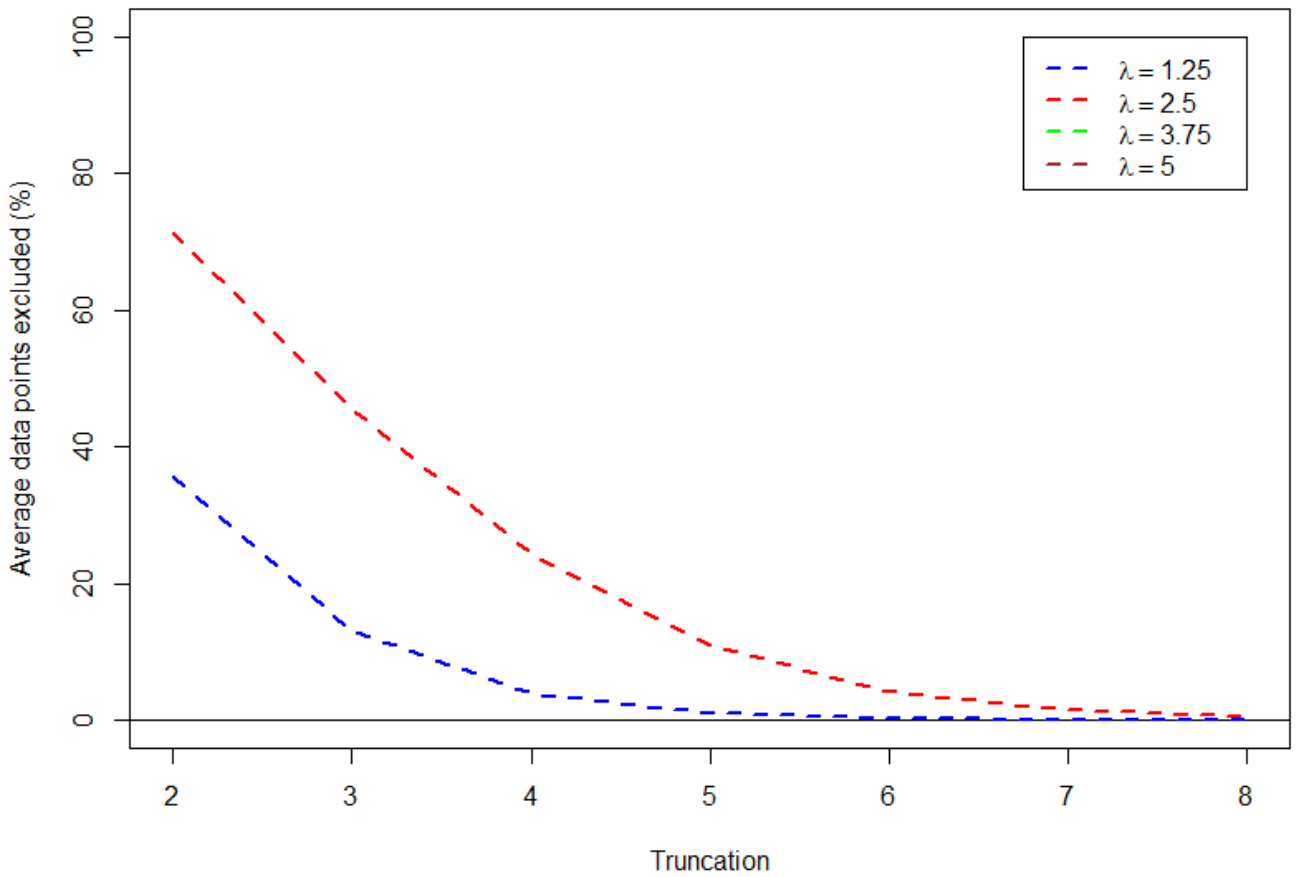

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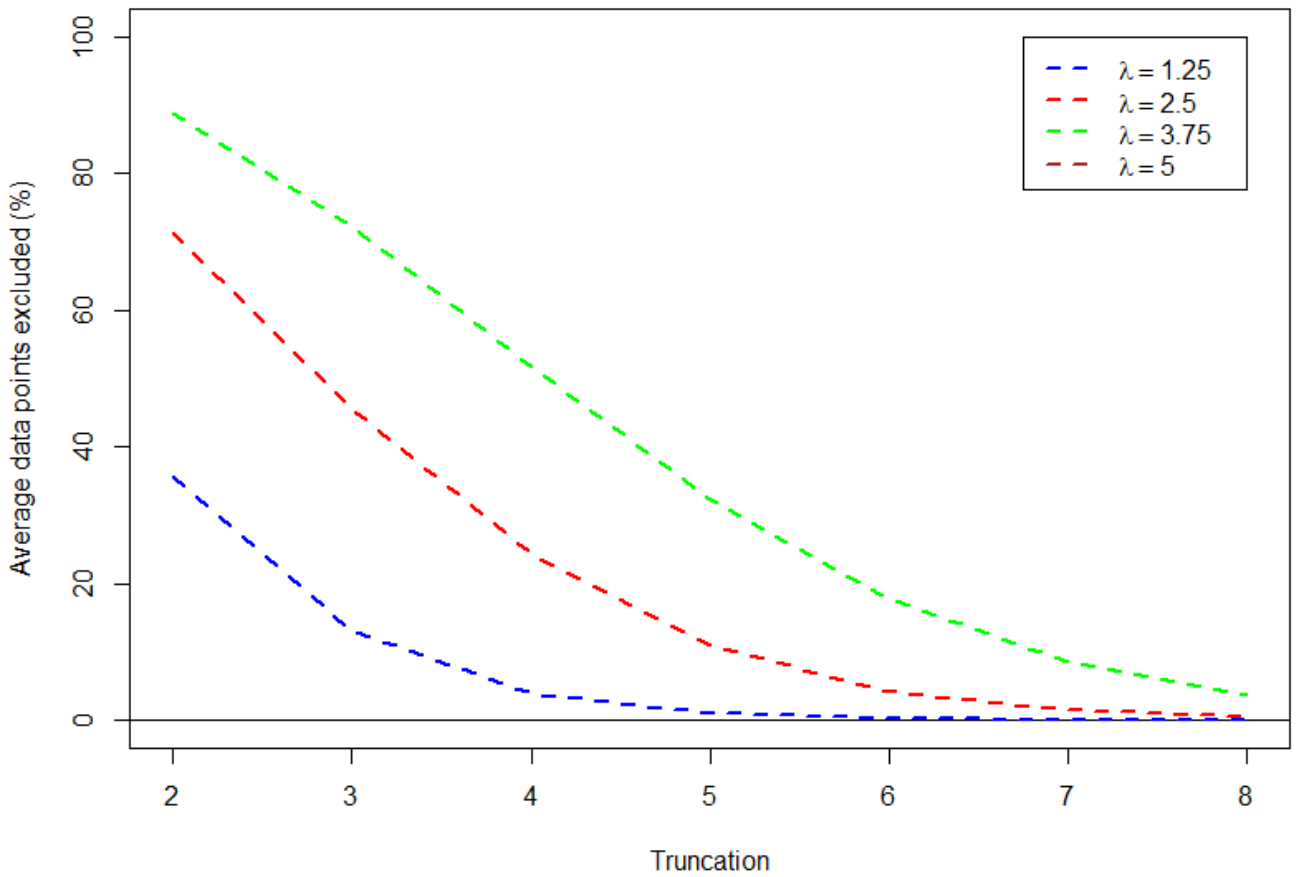

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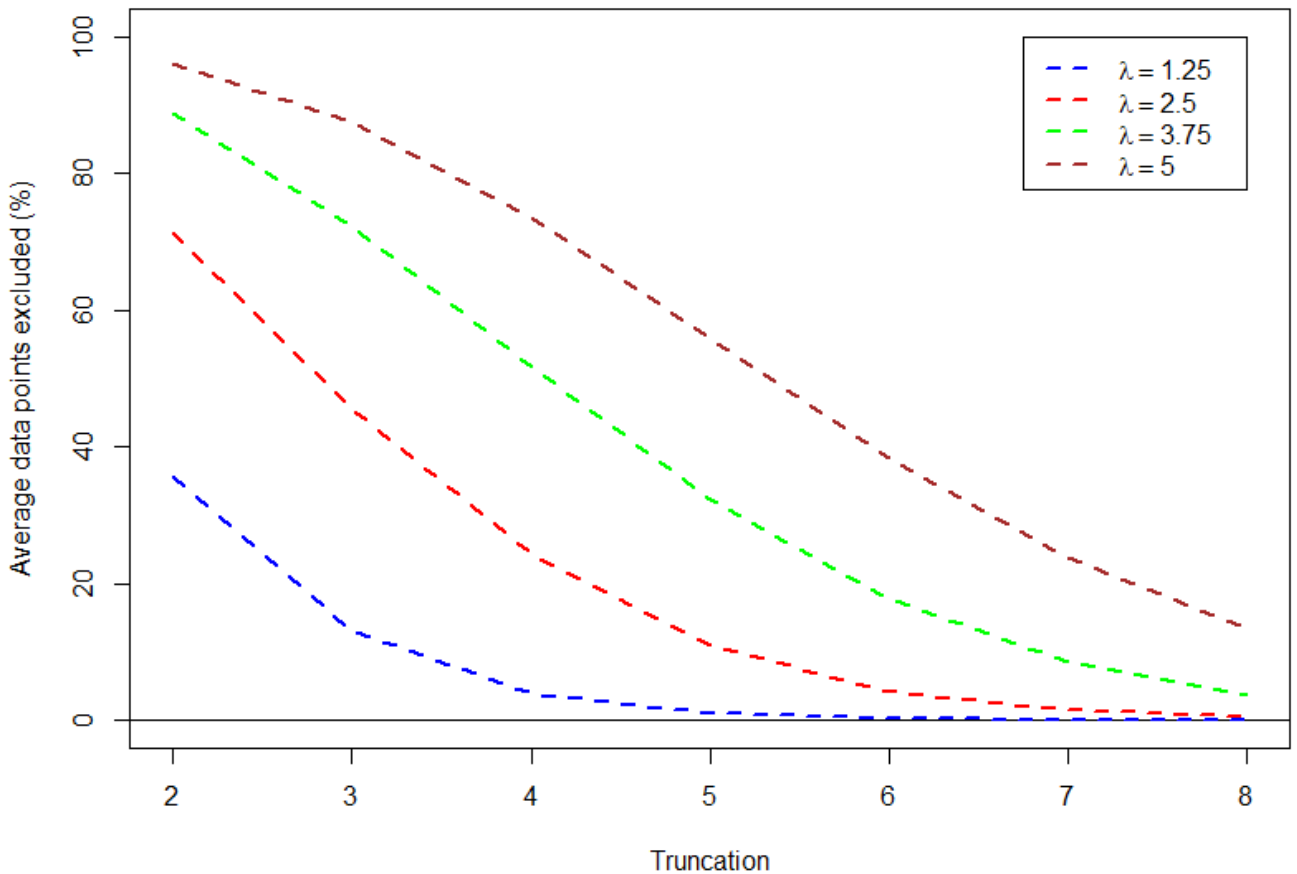

Effect of truncation on events realised from a Poisson distributed outcome

The Power simulation

$$P(Y = y; \lambda; y \leq T) = \frac{e^{-\lambda}\lambda^{y}}{y!} \left\{ \sum_{z=0}^{T} \frac{e^{-\lambda}\lambda^{z}}{z!} \right\}^{-1}, \qquad y = 0, 1, 2.....$$

The Power simulation

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PMF of untruncated Poisson distribution

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Point of truncation

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CDF over range of allowable values

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Point of truncation

$$\lambda = e^{\beta_0 + \beta_{Trt} \times Trt + c_i}$$

1 for ATSB and ITN
0 for ITN

The Power simulation

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PMF of untruncated Poisson distribution

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Random effect capturing cluster variability

1 for ATSB and ITN
0 for ITN

$$c_i \sim N(0, \sigma_c^2)$$

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Power:
Proportion of simulated samples where ATSB has signifcant effect

Results

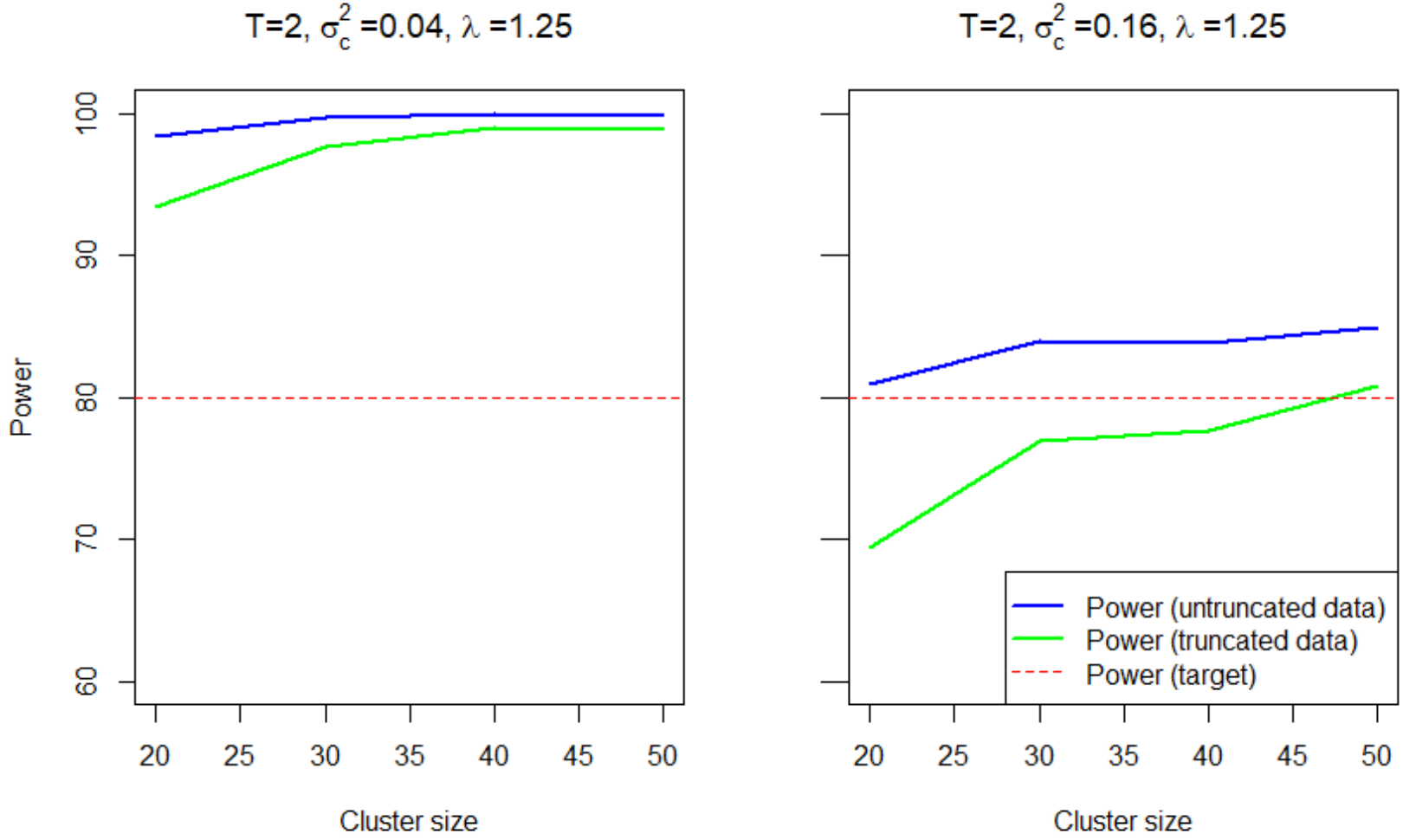

Figure 1: *Statistical power for 50 clusters associated with low and moderate correlation for the number of malaria episodes in a year truncated at T= 2*

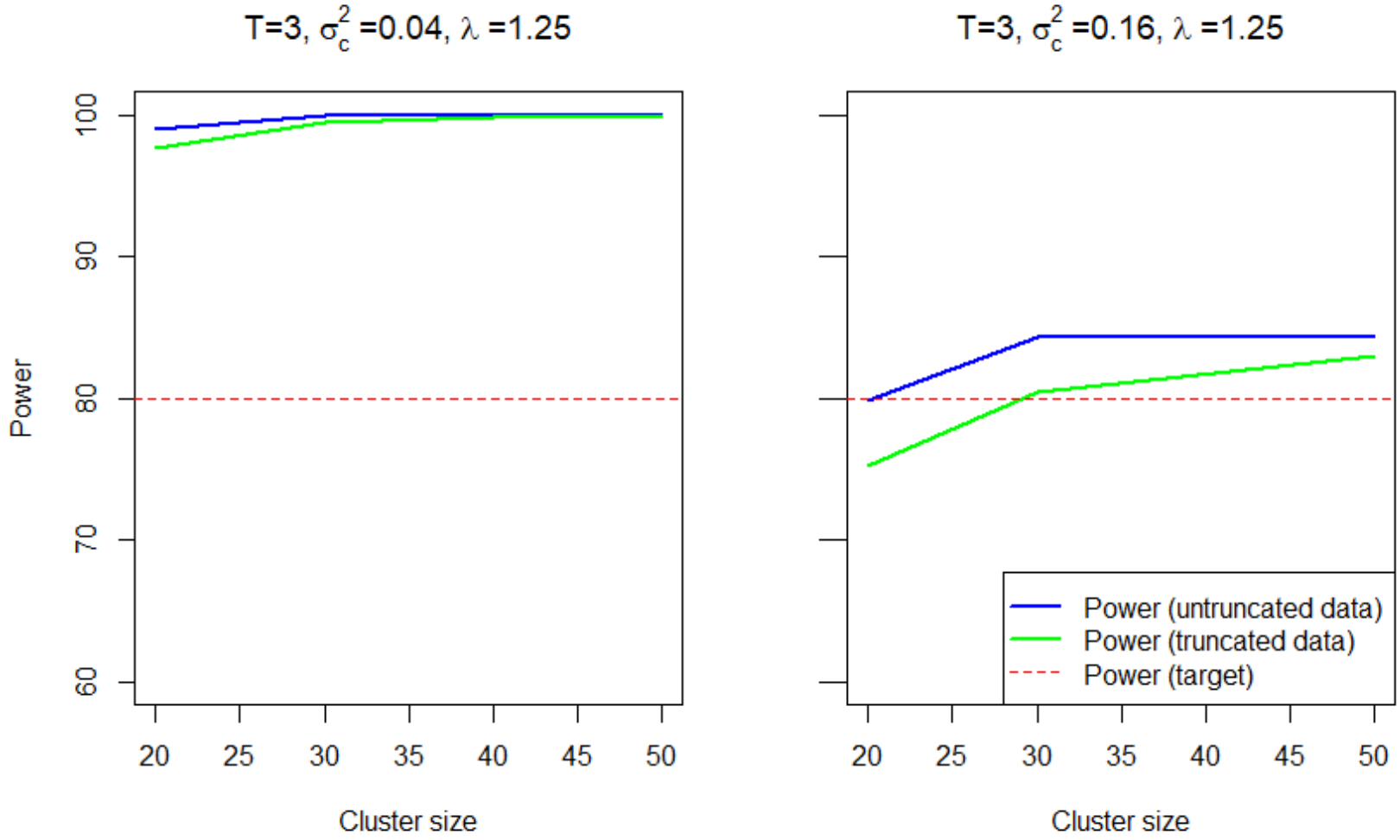

Figure 2: *Statistical power for 50 clusters associated with low and moderate correlation for the number of malaria episodes in a year truncated at T= 3*

Conclusion

Findings

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- Truncation had an adverse effect on power

Take home message

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Take home message

- **Truncation should always be considered in power calculations**

Acknowledgements

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Azra C Ghani
Keith J Frazer

Amy Racine
Samer Mouksassi

References

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