Health Analytics Workshop

MODELLING NEGLECTED TROPICAL DISEASES IN INDIA

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IIT Bombay, 30 Aug - 1 Sep 2023

DAY 3

Day 3

9:00 am	Review of more complex modelling methods
10:00 am	Reflection on lessons learnt
10:30 am	Dr. Bhupendra Tripathi, BMGF India
11:15 am	Tea break
11:30 am	Prof. Souvik Banerjee, IIT Bombay
12:00 pm	Prof. Mithun Mitra, IIT Bombay
12:30 pm	Prof. Ganesh Ramakrishnan, IIT Bombay
1:00 pm	Closing remarks
1:15 pm	Lunch

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9:00 – 10:00 am

REVIEW OF MORE COMPLEX MODELLING METHODS

More complex models + examples

- Models with time-varying parameters
- Models with dynamic policy
- Age-structured models
- Meta-population models
- Individual-based models
- Models for macroparasites

} combined example

Time-varying parameters

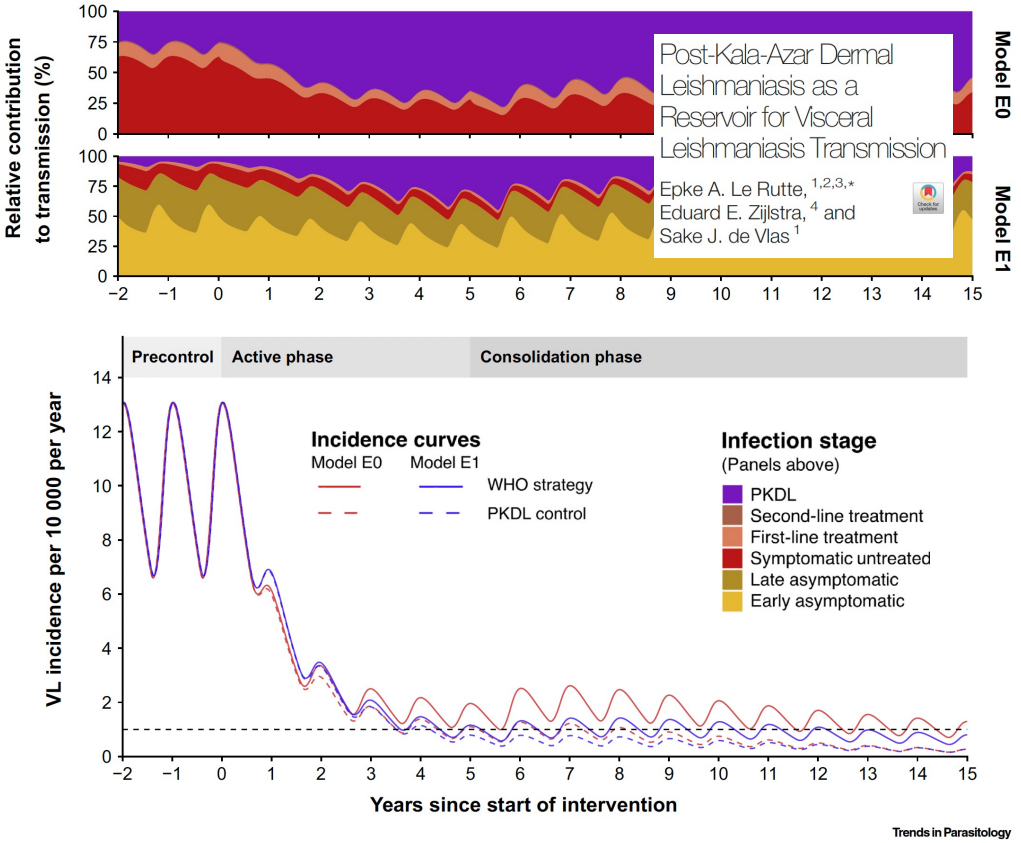
- To simulate changes in policy or context-specific factors over time
  - The model-user defines the variation in parameter values (from outside the model)

- Example code provided in the subfolder “04_Interventions” on Github
  - Start / stop / change in IRS
  - Changes in case detection effort

- Can in principle be applied to any parameter in the model
  - E.g., secular trends in sandfly abundance over the years

Example

- Impact of extra effort to detect and treat PKDL cases in addition to the ”standard” WHO strategy
- Three time periods with different intensity of interventions:
  - Pre-control
  - Active phase
  - Consolidation phase
- Time-varying parameters:
  - Effect of IRS
  - VL case detection rate
  - PKDL case detection rate



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Models with dynamic policy

- The model dynamically updates policy-related parameters based on the state of the population and policy decision-rules that are coded into the model

- Useful to answer questions about whether and how a policy will work out
- Can be very messy and tricky to get working correctly
  - Hard to test and high risk of bugs

- Can be emulated with simpler models (somewhat cumbersome, but also less bug-prone)
  - Run a simulation for an ‘x’ amount of time and assess whether and when the policy decision criterion was reached
  - Re-run the simulation from the point that the criterion was reached, but with different parameters that represent policy action or change

Example

Clinical Infectious Diseases
SUPPLEMENT ARTICLE

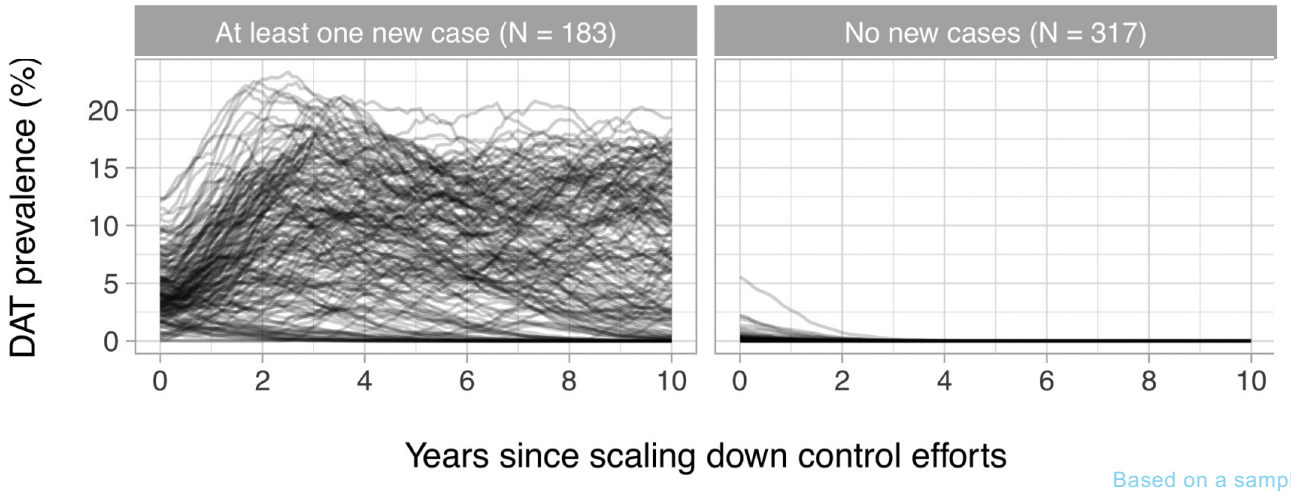
Antibody and Antigen Prevalence as Indicators of Ongoing Transmission or Elimination of Visceral Leishmaniasis: A Modeling Study

Luc E. Coffeng,[1] Epke A. Le Rutte,[1,2,3] Johanna Munoz,[1] Emily Adams,[4] and Sake J. de Vlas[1]

[1]Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands; [2]Department of Epidemiology and Public Health, Swiss Tropical and Public Health Institute, Basel, Switzerland; [3]University of Basel, Basel, Switzerland; and [4]Department of Tropical Disease Biology, Liverpool School of Tropical Medicine, Liverpool, United Kingdom

What happens if control measures are scaled down after reaching the control target? And is it possible to predict whether there will be new VL cases based on population surveys?

- Stochastic model (Coffeng et al. Clin Infect Dis 2021)
- Build a large databank of population states that have just reached the target
- Simulate forward from population states in databank with scaled-down control



Based on a sample of 500 simulations that reached the target

Age-structured models

- For *n* age classes, each compartments in the model has to be an *n*-length array/vector
  - Deterministic implementation possible with partial differential equations
  - But: aging should not be an exponential process!
  - Solution: annual “birthday event” that ages everybody (i.e., move everyone to the next 1-year age bin)

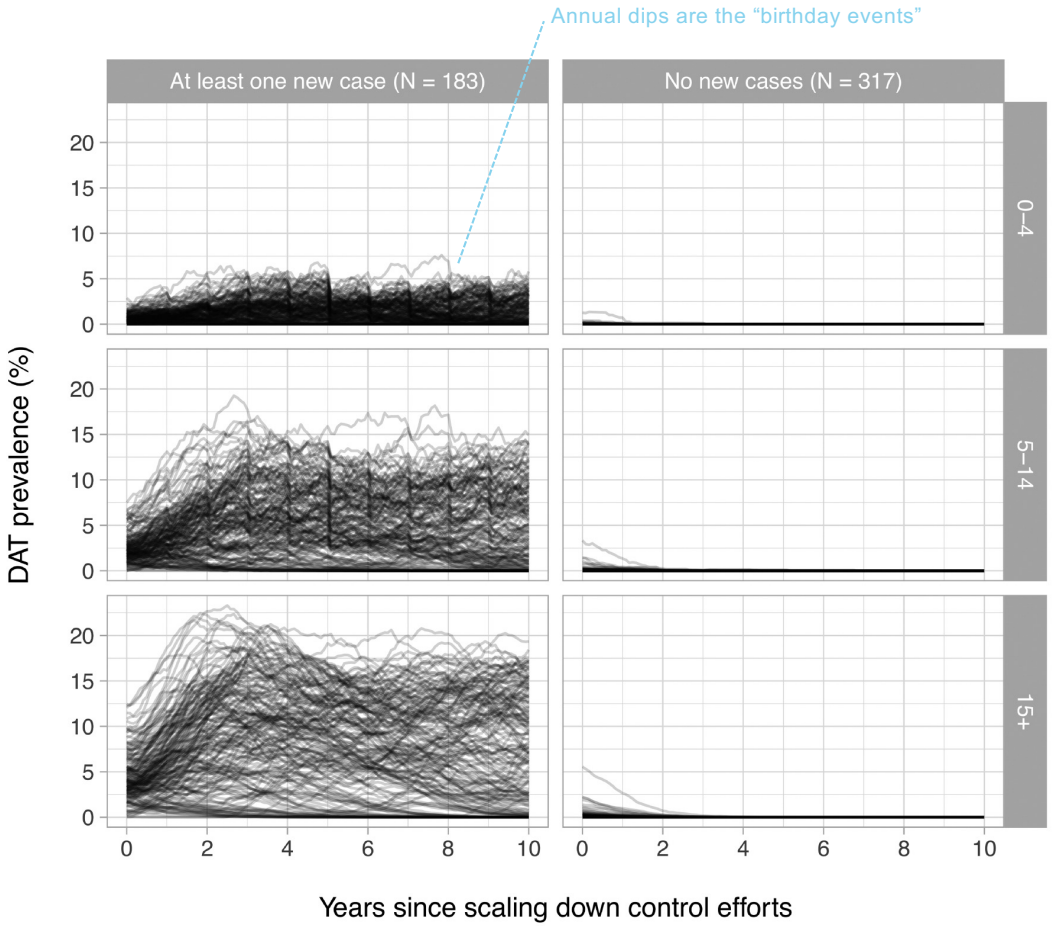
- Requires age-specific data to calibrate
  - Simplest: age-specific mortality rates

- Advantages:
  - More realistic age patterns
  - Heterogeneous mixing of age groups
  - Can answer questions that have an age component (example on next slide)

Example

How informative are surveys in different age groups for prediction of whether there will be new VL cases after scaling down control efforts?

(Coffeng et al. Clin Infect Dis 2021)



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Metapopulation models

- Define *m* clusters that represent distinct but interlinked sub-populations
  - Each cluster has its own local model
  - Add components for mobility and/or transmission between models for local populations

- Can answer questions with a spatially heterogeneous component
  - E.g.: how does a walking VL epidemic behave when control targets have been reached?
  - Requires data or assumptions about connectivity of clusters

- Very few published examples in NTD modelling
  - Leprosy: transmission within and between households (Blok et al. (2015) Adv Parasitol)
  - Onchocerciasis: multiple population clusters that are exposed differentially to multiple vector populations (de Vos *et al.* (2018, 2021) PLoS Negl Trop Dis)

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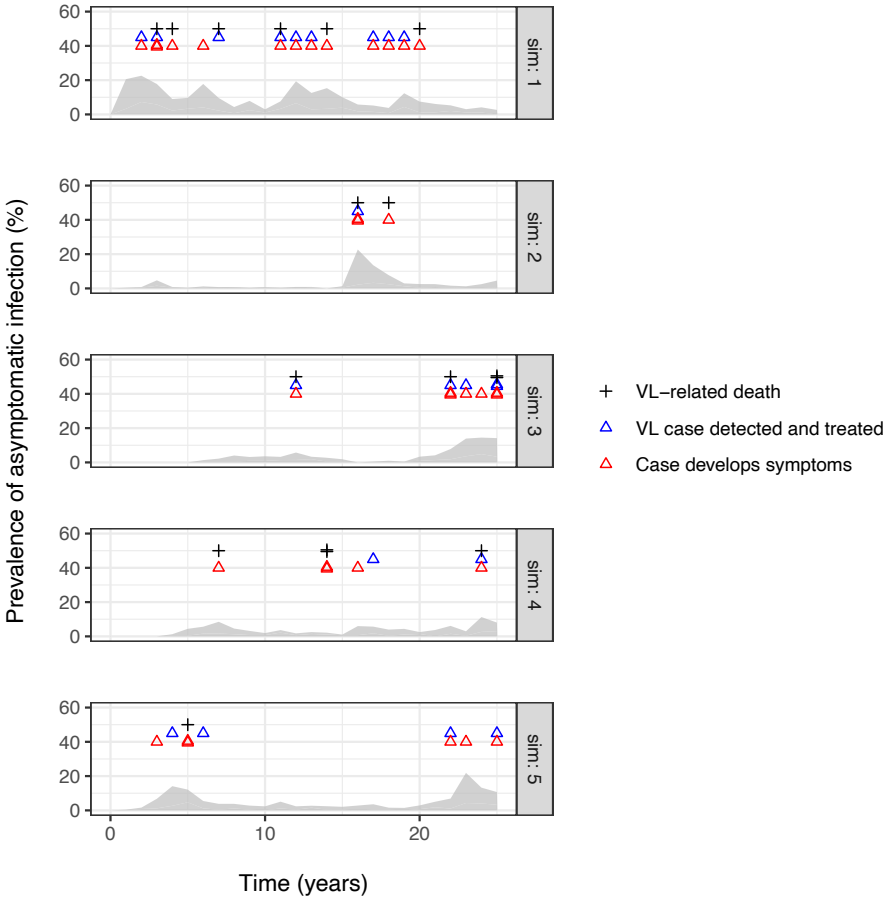
Example (unpublished)

Prototype metapopulation model for VL

- Emulated with existing simple single-community model
- For *m* villages, run *m* parallel simulations
- Every simulation week, interrupt simulations and extract population state, emulate human mobility by shuffling people between villages, and continue simulation
- Extremely simple assumptions about mobility
  - 1/10 individuals per year
  - Here: villages connected in a circle + one direction of mobility (guess which?)



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Individual-based models

Simulation of a population of individuals that each have personal characteristics

- Characteristics are drawn from probability distributions
  - Life-long characteristics (e.g., inclination to participate in MDA)
  - Time until transition to next disease state
  - Any probability distribution is possible; no restriction to exponential or Erlang distributions
- Straightforward to capture multiple strata and multiple sources of heterogeneity

- No elegant mathematical proofs or analytical solutions
- Higher programming effort → longer development time
- Higher computational effort → more resources or time needed for analysis
- Higher risk of bugs or unintended model behaviour → version control and unit testing highly advised

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Models for macroparasites

- Model the density of infection instead of just presence
  - Density is strongly associated with transmissibility and morbidity
  - Parasite density is typically highly heterogeneous across individuals

- Deterministic models exist, but cannot capture many heterogeneities at once
- Individual-based models are widely used within the NTD Modelling Consortium
  - Soil-transmitted helminths (e.g., Coffeng *et al.* 2015 Parasit Vectors)
  - Schistosomiasis (e.g., Graham *et al*. 2021 Infect Dis Model)
  - Lymphatic filariasis (e.g., Stolk *et al*. 2008 Parasitology)
  - Onchocerciasis (e.g., Coffeng *et al.* 2013 PLoS Negl Trop Dis)
- Parasites themselves sometimes modeled as individuals as well (Erasmus MC models)

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Example

What is risk and speed of drug resistance evolving in soil-transmitted helminth (intestinal worm) populations as preventive chemotherapy (PC)? (Coffeng *et al*. in preparation)

- Individual-based modelling of humans, worms in humans, and genes in worms
  - Explicit modelling of life histories
- Simulation of diagnostic test performance and sampling error

- Several mechanisms for how worm genetics (genotype) are linked to drug efficacy (phenotype)

Impact of school-based deworming on hookworm infection prevalence

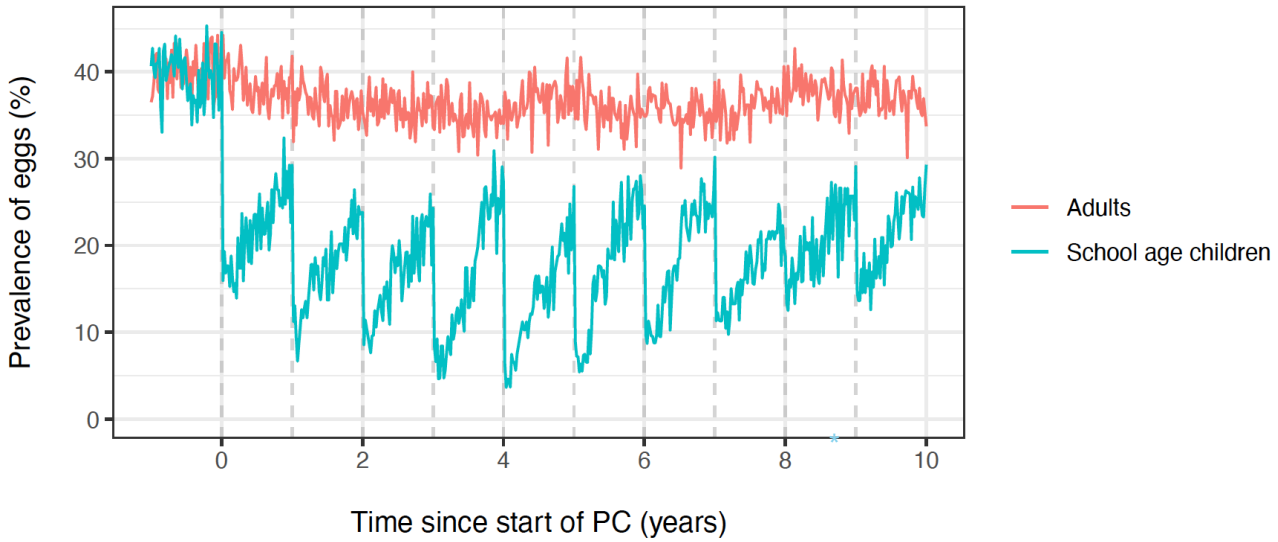

Figure A8: Model-predicted trend in prevalence of eggs in faeces during annual PC (vertical dashed lines) targeted at school age children (age 5-15), implemented at 95% coverage.

* PC = preventive chemotherapy

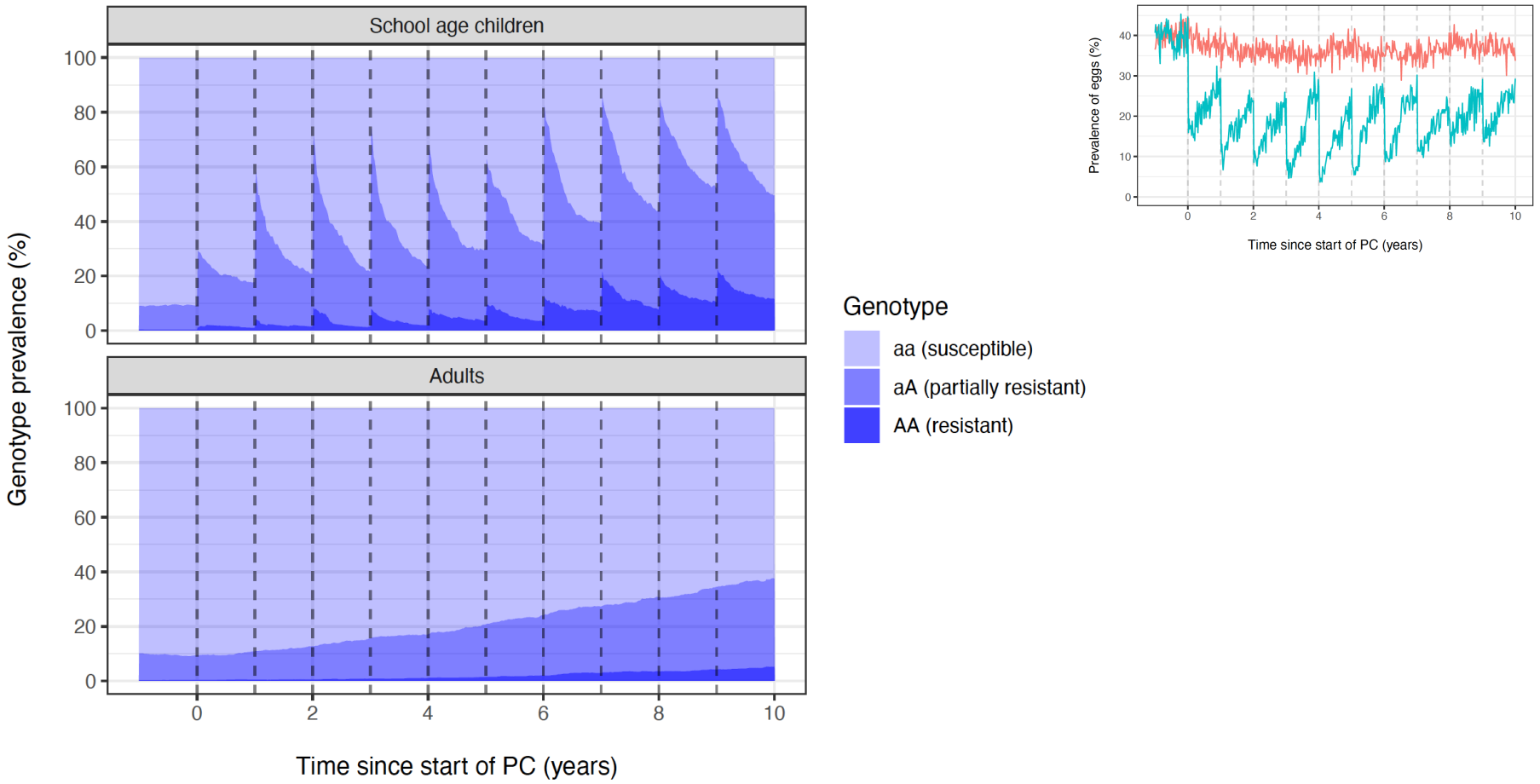

Figure A9: Model-predicted trend in allele frequency during annual PC (vertical dashed lines) targeted at the population of age 2 and above, implemented at 70% coverage.

10:00 – 10:30 am

REFLECTION AND LESSONS LEARNED

COMMON ISSUES CONCERNING THE MODEL

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Why are death terms added to the susceptible compartment?

Total population size is assumed to be constant

Deaths (including the excess deaths) are being replaced by births into S (or the introduction of new individuals)

Why are there two different rates from R to L2?

There are two separate processes:

1) Uninfected individuals (in R) moving to L1 or L2 due to force of infection from sandflies; this rate is a function of the compartment sizes
2) In people who have been infected at some point during their life (i.e., people in R), the immune system may sometimes spontaneously start producing antibodies again in response to residual persistent parasites

THE OTHER MAIN ISSUE

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POMP Installation

Tip: You need to perform some tests to confirm that POMP is successfully installed.
The install.packages() command is not sufficient.

Depending on whether you use Windows, Linux, or MacOS, you may have to install additional software (eg: Xcode for MacOS) or update some of your existing software packages.

The link to instructions + required tests: https://kingaa.github.io/sbied/prep/

(also linked on our Github repository page and the slides of Day 1)

Lessons learnt

- You have hopefully developed (more) appreciation for
  - What models can and cannot do
  - The effort and time it takes to develop models
  - The notion that defining an appropriate model-answerable research question is key
  - Modelling is an iterative process that commonly involves revision of the model and/or research question

- Model development tips:
  - Involve domain experts and stakeholders to inform and review your choices and assumptions
  - Draw a schematic representation to be able to discuss with non-modellers
  - Avoid undetected bugs by performing sense checks
  - In stochastic models, detect and solve bugs by developing a deterministic version of the model in parallel and compare model behaviour

Acknowledgements

NTD MODELLING CONSORTIUM

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LSTM LIVERPOOL SCHOOL OF TROPICAL MEDICINE

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And you for your active participation!

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