Swiss TPH
Swiss Tropical and Public Health Institute
Schweizerisches Tropen- und Public Health-Institut
Institut Tropical et de Santé Publique Suisse

Associated Institute of the University of Basel

Introduction to OpenMalaria

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&

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28 November 2023

Program for the practicals

Swiss TPH

1) Introduction to OpenMalaria
2) Practical 1: How to run a simulation in OpenMalaria
3) Practical 2: How to compare interventions effect in OpenMalaria
4) Practical 3: How to automate the workflow for multiple simulations

What is a mathematical model?

Swiss TPH

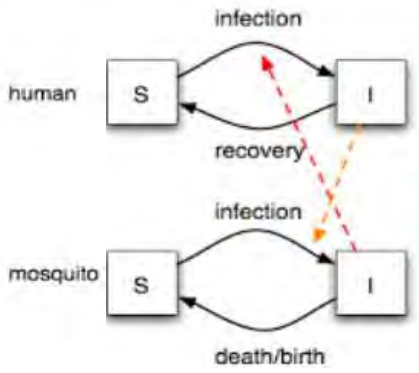
A mathematical model is an abstract description of a system that uses precise language to describe its behaviour.

Transmission, epidemiology, and pathology of malaria

Mathematical equations

Ross Model

S: Susceptible I: Infectious



$$\frac{\mathrm{d}x}{\mathrm{d}t} = mabz(1-x) - \gamma x$$

$$\frac{\mathrm{d}z}{\mathrm{d}t} = acx\,(1-z) - \mu z$$

m: Number of female mosquitoes per human host

a: Number of bites per mosquito per unit time

γ: Recovery rate of humans

μ: Death rate of mosquitoes

c: Probability of transmission of infection from infectious humans to mosquitoes per bite

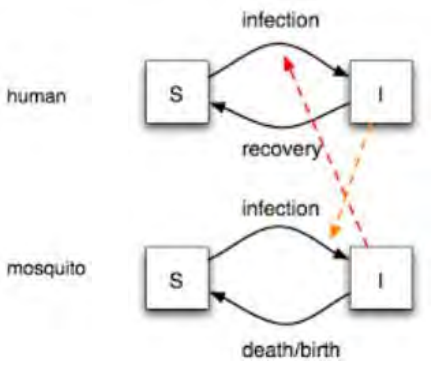
b: Probability of transmission of infection from infectious mosquitoes to humans per bite

Limitations of mathematical models

Swiss TPH

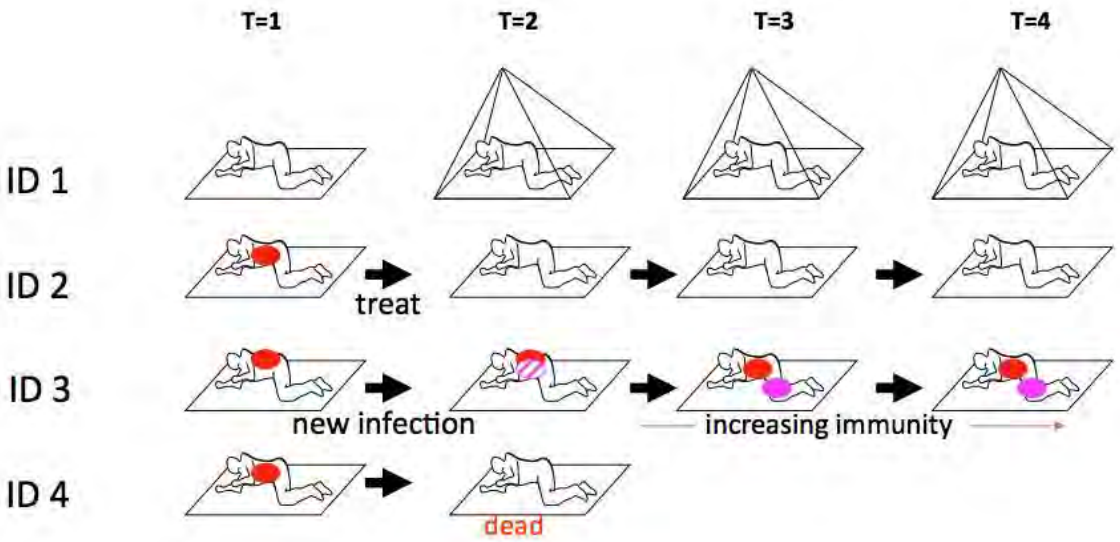
A mathematical model is an abstract description of a system that uses precise language to describe its behaviour.

Ross model:



- Ignores the extent of heterogeneity in many factors between individuals.
- No immunity
- No human morbidity or mortality
- No latent period in humans and mosquitoes
- Ignores stochasticity
- …

Individual-based simulations



- Heterogeneity can be accounted for:
  - Exposure
  - Immunity
  - Symptoms
  - …
- More precisely estimated the impact of interventions on the malaria burden
- Captures more stochasticity

OpenMalaria

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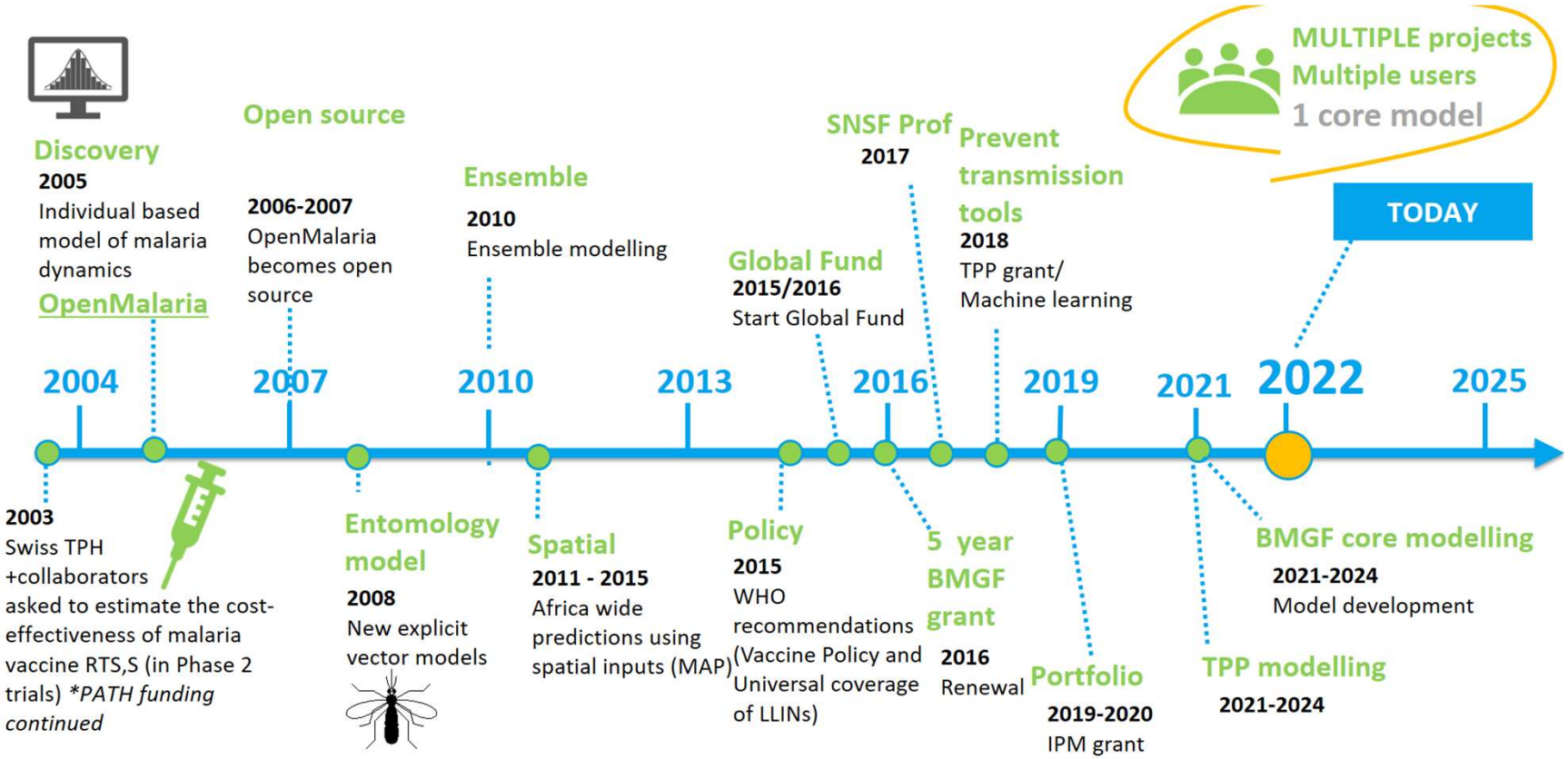
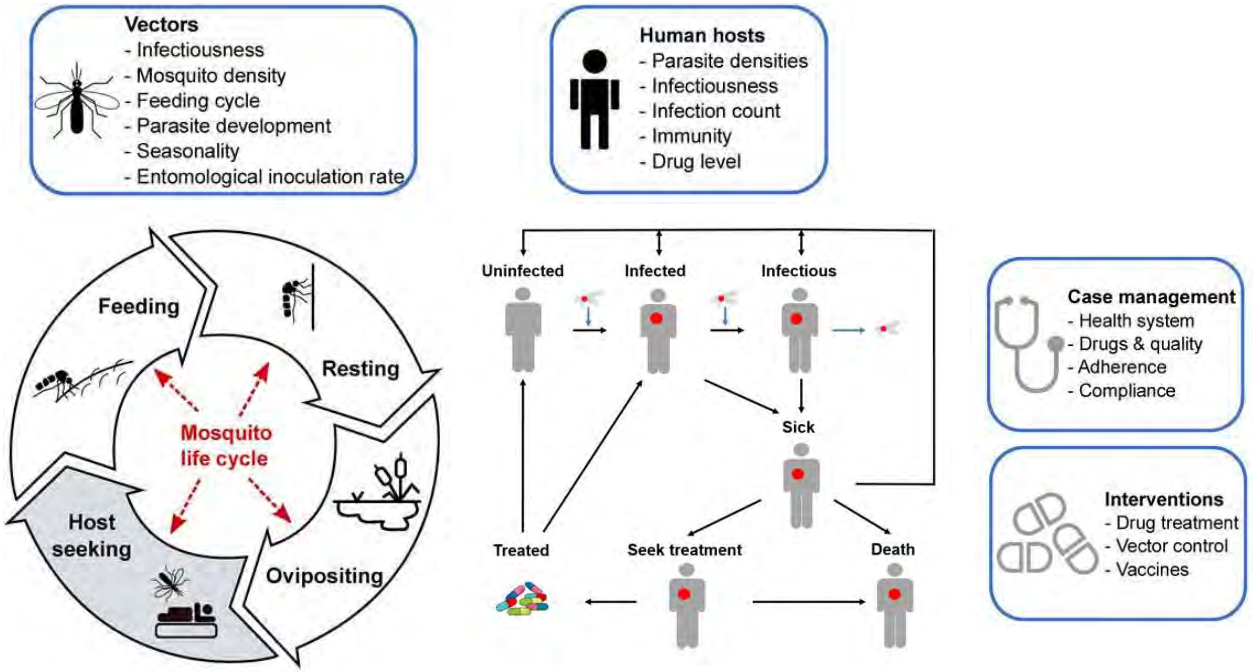


OpenMalaria

Swiss TPH

- OpenMalaria is an individual-based stochastic simulator of malaria epidemiology and control.
- OpenMalaria is composed of multiple model components that run on 5-day time steps.



Entomological model

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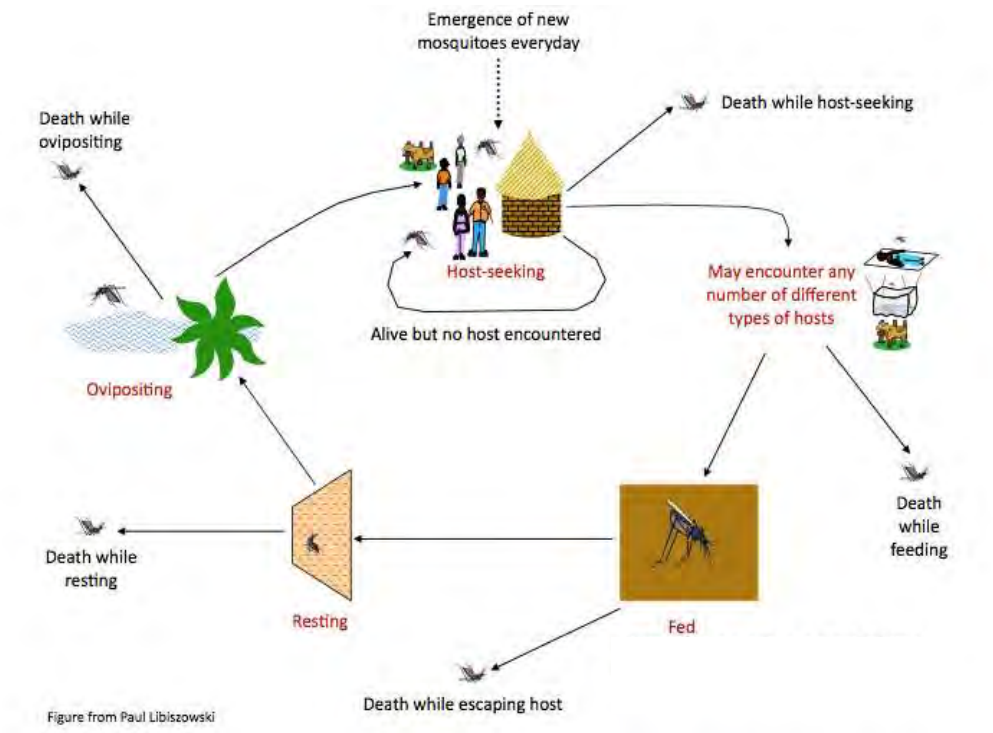
Vector model:



- Model the emergence of mosquitos and the feeding cycle (parameters depend on vector species).
- Three different infectious states of mosquitos based on the probability of getting infected after biting a human and the time for parasite development (extrinsic incubation period ~ 10 days):
  - Susceptible
  - Infected
  - Infectious.
- The number of infectious mosquitos determines the entomological inoculation rate (EIR, the number of infectious bites received by an individual over time).
- Seasonality depends on the emergence rate of mosquitos.

More details: https://link.springer.com/article/10.1007/s11538-011-9710-0

Human model

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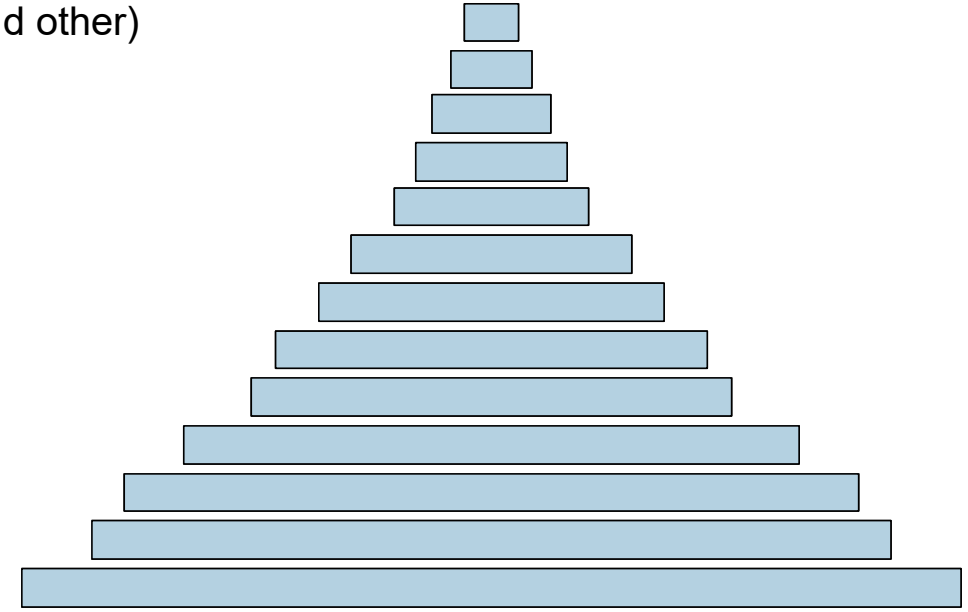
Demography

- Define a **population size** and **age structure** that remain stable across time
- Process:
  1. Remove death (due to malaria and other)
  2. Add birth
  3. Add importation



Human model

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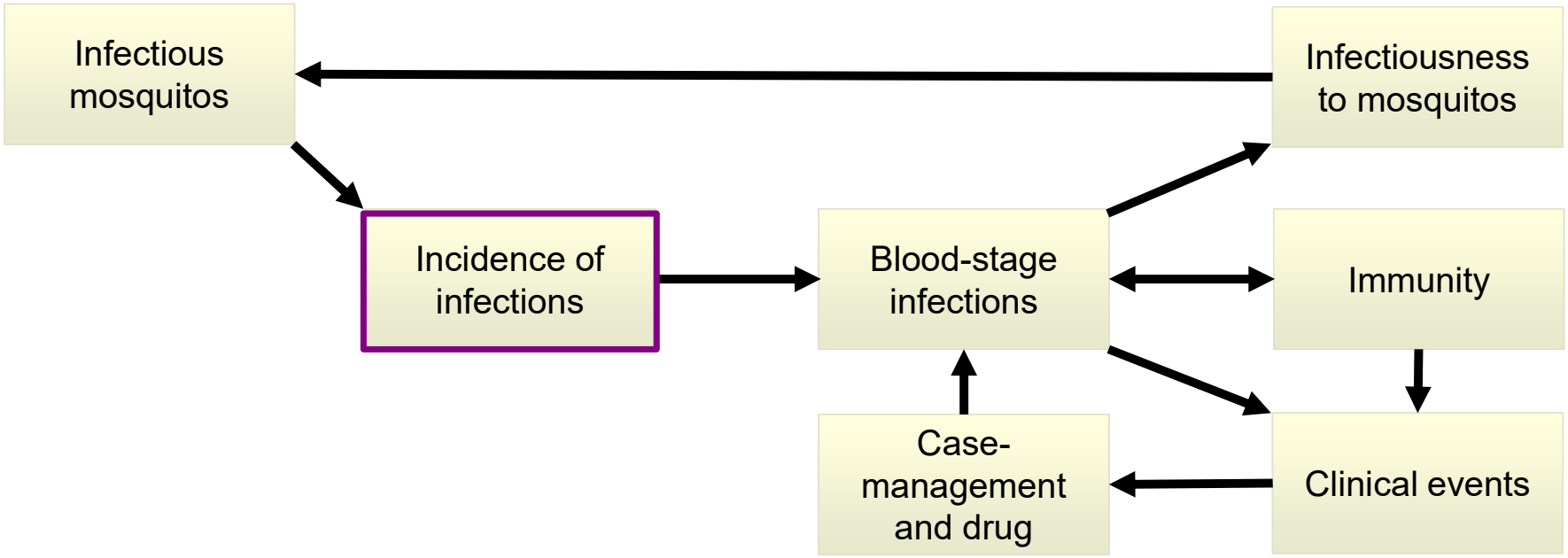
Overview



Human model

Swiss TPH

Incidence of infections

- Translates the EIR to infection in a specific host.
- Depends on:
  - Variation of host availability to mosquitos (based on age)
  - Pre-erythrocyte immunity (based on previous exposure)
  - Poisson distribution.
- Does not account for sporozoites density or number of infected hepatocytes → Success/failure.

Age-adjusted EIR of individual i at time t

$$E_a(i,t) = E_{\max}(t)\frac{A(a(i,t))}{A_{\max}}$$

EIR Aviability to mosqutios

Mean number of potential new blood-stage infection

$$\lambda(i,t) = S_p(i,t)E_a(i,t)$$

Survival function for soprozoite

Number of new blood-stage infection per unit time

$$h(i,t) \sim \text{Poisson}(\lambda(i,t))$$

More details: https://www.ajtmh.org/view/journals/tpmd/75/2_suppl/article-p11.xml

Human model

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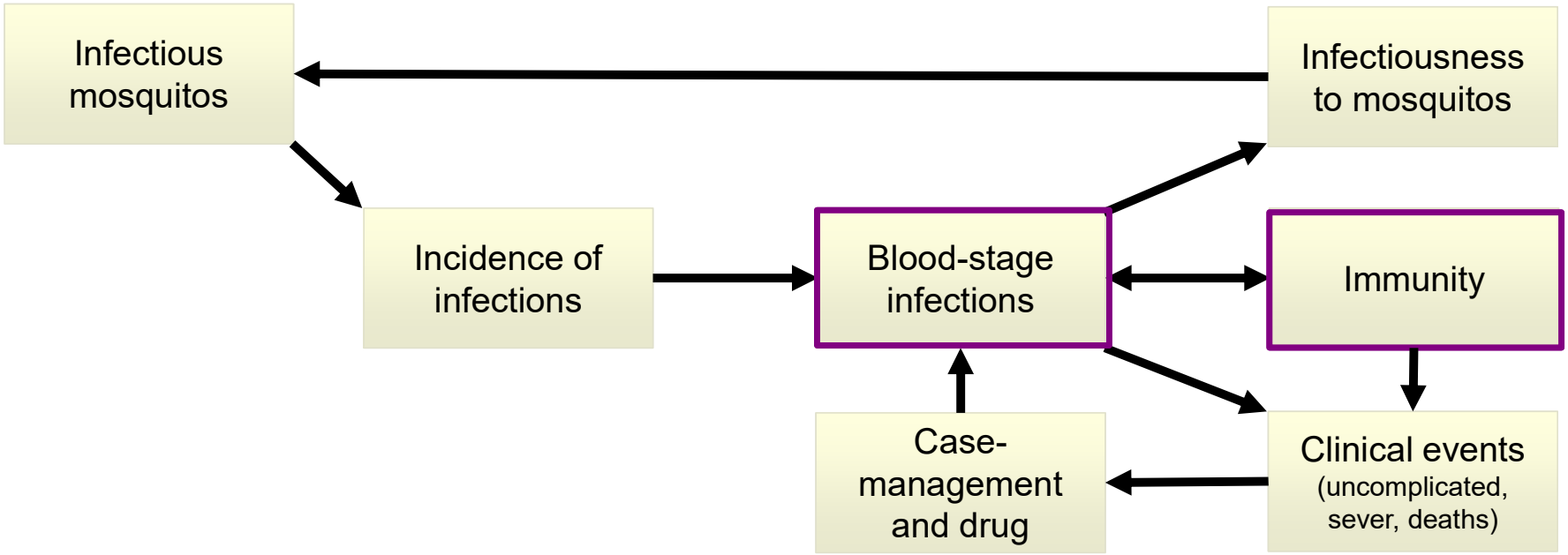
Overview



Human model

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Blood-stage models

- **Two mains options:**
  - **Maire et al. (2006) :**
    - A statistical representation of the parasite densities over time in a naive human (malaria therapy data).
  - **Molineaux et al. (2001):**
    - A mechanistic model of *Plasmodium falciparum* asexual parasite densities.
    - Needed to use PK/PD model and for drug resistance modelling.

Human model

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Blood-stage model - Maire et al. (2006)

- Assumes 15 days between infection and the start of the blood stage.
- Statistical representative description of the parasite density over time of the malaria therapy dataset (MT).
- Immunity reduces total parasite density and depends on:
  - Exposure to asexual blood stage based on the cumulative parasite density
  - Exposure to asexual blood stage based on the number of infections
  - Effect of maternal immunity.
- Allows multiple infections and competition dynamics between them.
- Considers stochastic noise between and within individuals.

Duration of infections (based on MT)

$$\ln\left(\tau_{\max}(i,j)\right) \sim Normal(5.13, 0.80)$$

Expected density at time

$$E(\ln(y(i,j,\tau))) = D_y D_h D_m \cdot \ln\left(y_0(i,j,\tau)\right) + \ln\left(\frac{D_x}{M(t)} + 1 - D_x\right)$$

Simulated density at time t

$$\ln(y(i,j,\tau)) \sim Normal\left(E(\ln(y(i,j,\tau))), \sigma_y^2(i,j,\tau)\right)$$

Immunity

Average density in MT

Effect of concurrent infections

Variation

More details: https://pubmed.ncbi.nlm.nih.gov/16931812/

Human model

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Blood-stage model – Molineaux et al. (2006)

- Mechanistic model fitted to malaria therapy dataset using one day time steps.
- Includes:
  - Intraclonal antigenic variation (model 50 variants)
  - Multiplication factor (vary between variants and hosts)
  - Immune responses: innate + acquired variant specific + acquired variant transcending.
- Needed to use PK/PD model and for drug resistance modelling.

Density of variant i

Number of variant that switch to this variant

$$P_i(t+2)' = \left[(1-s)P_i(t) + sp_i(t) \sum_{j=1}^{v} P_j(t) \right] \times m_i S_c(t) S_i(t) S_m(t),$$

Immune responses

Number of variant that did not switch to another variant

Multiplication factor

More details: journals.cambridge.org/action/displayAbstract?aid=76599

Human model

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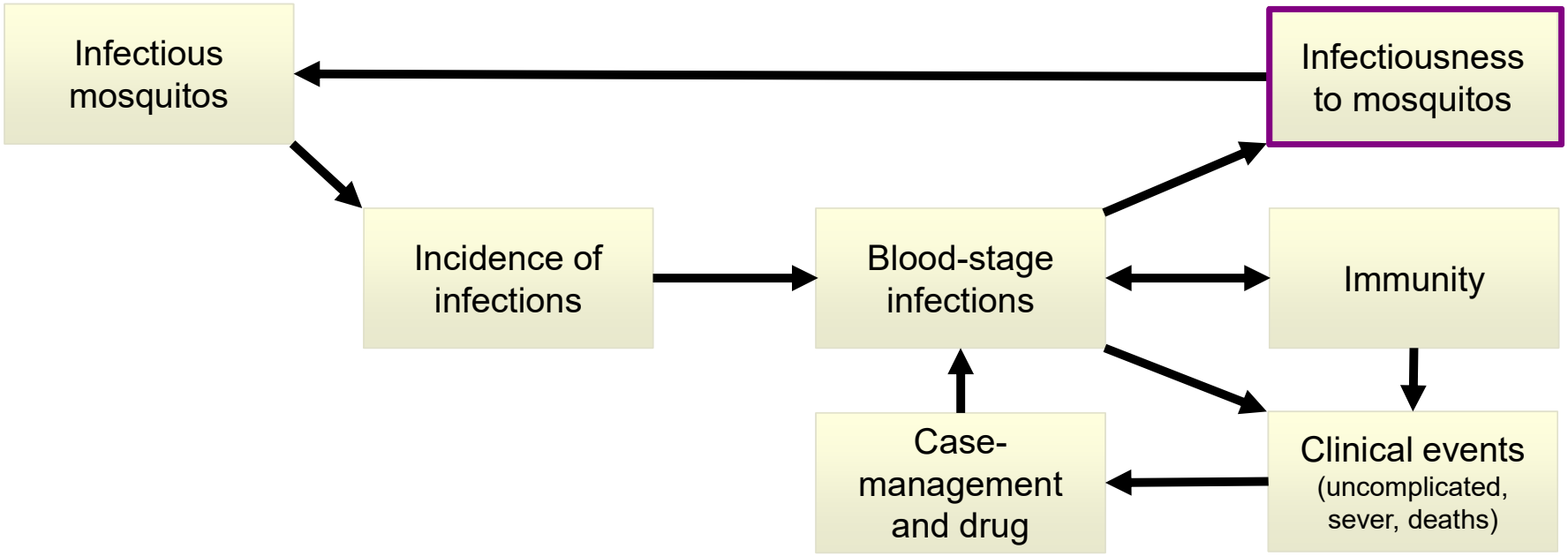
Overview



Human model

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Transmission model

- Links the asexual parasite density to infectivity to mosquitos based on the malaria therapy data.
- Captures delay between parasitaemia and gametocytaemia (10-20 days).
- Mosquitoes need a blood meal containing both male and female gametocytes at a minimum quantity to be infected.

Weighted sum of the asexual parasite densities over last days

$$\Upsilon(i,t) = \beta_1 Y(i,t-2) + \beta_2 Y(i,t-3) + \beta_3 Y(i,t-4)$$

Weight Asexual parasite density

Density of functional female gametocytes in the host blood

$$\ln(y_g(i,t)) \sim \text{Normal}(\ln(\rho \Upsilon(i,t)), \sigma_g^2)$$

Standard deviation

Geometric mean of the ratio of female gametocytes to $\Upsilon(i,t)$

The proportion of mosquitoes that are infected feeding on individual i at time t

$$I_m(i,t) = [\Pr(y_g(i,t) > y_g^*)]^2$$

Density of female gametocytes necessary for infection of the mosquito

More details: https://www.ajtmh.org/view/journals/tpmd/75/2_suppl/article-p32.xml

Human model

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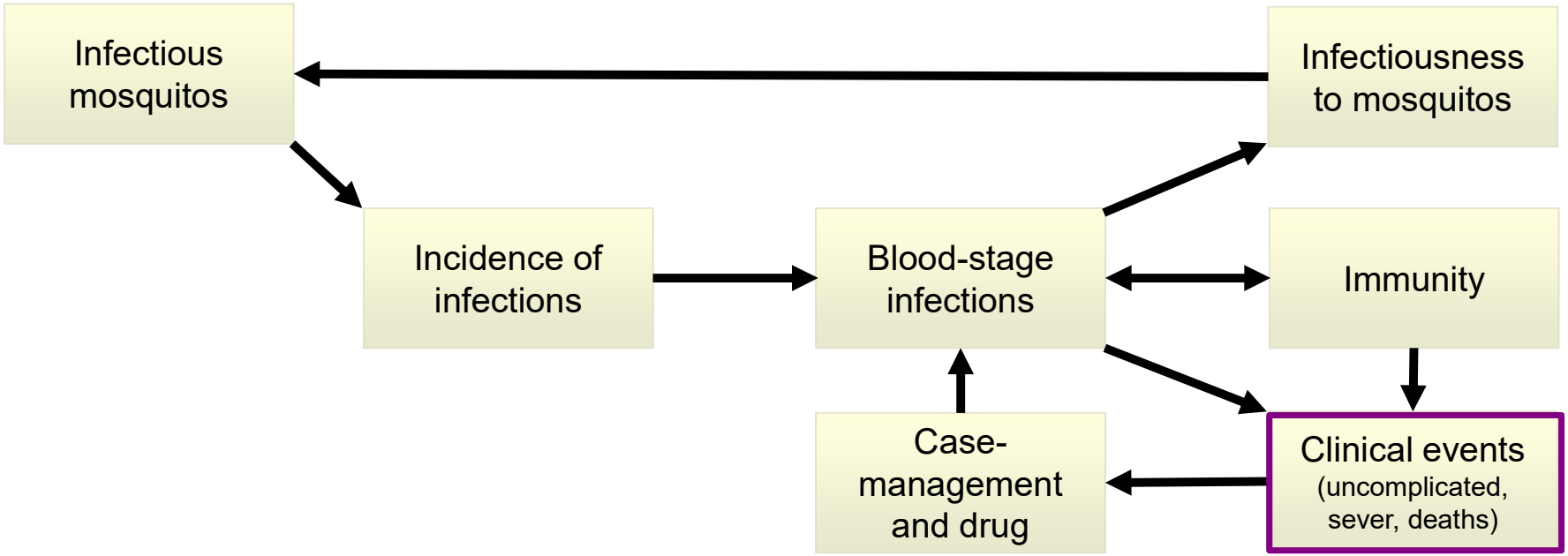
Overview



Human model

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Clinical disease model

- Determines the symptoms and their severity
  - No symptoms
  - Uncomplicated episodes
  - Sever episodes
  - Deaths.

Human model

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Clinical disease model

- Uncomplicated episodes:
  - The probability of an episode depends on parasite density and pyrogenic threshold.
  - The pyrogenic threshold is patients specific and increases with previous exposure to malaria.

Probability that an episode occurs in individual *i*, at time *t*,

$$P_m(i,t) = \frac{Y_{\max}(i,t)}{Y^*(i,t) + Y_{\max}(i,t)}$$

Maximum density during the time interval *t*

Pyrogenic threshold for individual *i* at time *t*

Decay of the threshold

$$\frac{dY^*(i,t)}{dt} = f_1(Y(i,t)) f_2(Y^*(i,t)) - \varpi Y^*(i,t)$$

Function describing the increase of the threshold at high parasite density

Function describing the saturation of the threshold at high parasite density

More Details: https://www.ajtmh.org/view/journals/tpmd/75/2_suppl/article-p56.xml

Human model

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Clinical disease model

- Sever episodes:
  - Sever episodes due to high parasite density.

The probability that a clinical malaria episode in individual i is severe as a result of high parasite density

$$P_{B_1}(i,t) = \frac{Y_{max}(i,t)}{Y^*_{B_1}(i,t) + Y_{max}(i,t)}$$

Critical value

Maximum parasite density measurements during the last time interval

  - Sever episodes due to comorbidities (malnutrition, anemia, bacterial infections) which depend on age.

The probability that a clinical malaria episode occurs in an individual as a result of comorbidity

$$P_{B_2}(i,t) = F(a(i,t))$$

Risk of comorbidities depending on age

More details: https://www.ajtmh.org/view/journals/tpmd/75/2_suppl/article-p63.xml

Human model

Swiss TPH

Clinical disease model

- Death:
  - Direct mortality results from sever episodes of malaria (depends on access to hospital).

Reported number of deaths in hospital

$$Q_c(a) + Q_h(a)$$

Reported number of deaths in community

  - Indirect death due to comorbidity (depends on age).

$$P_{D_2}(i,t) = \frac{Q_D}{1 + \left(\frac{a(i,t)}{a_F^*}\right)}$$

Depend on age

  - Neonatal mortality results from pregnant women infected with malaria (depends on prevalence in pregnant women).

$$\mu_{PG} = \mu_{\max}\left[1 - \exp\left(-\frac{x_{PG}}{x_{PG}^*}\right)\right],$$

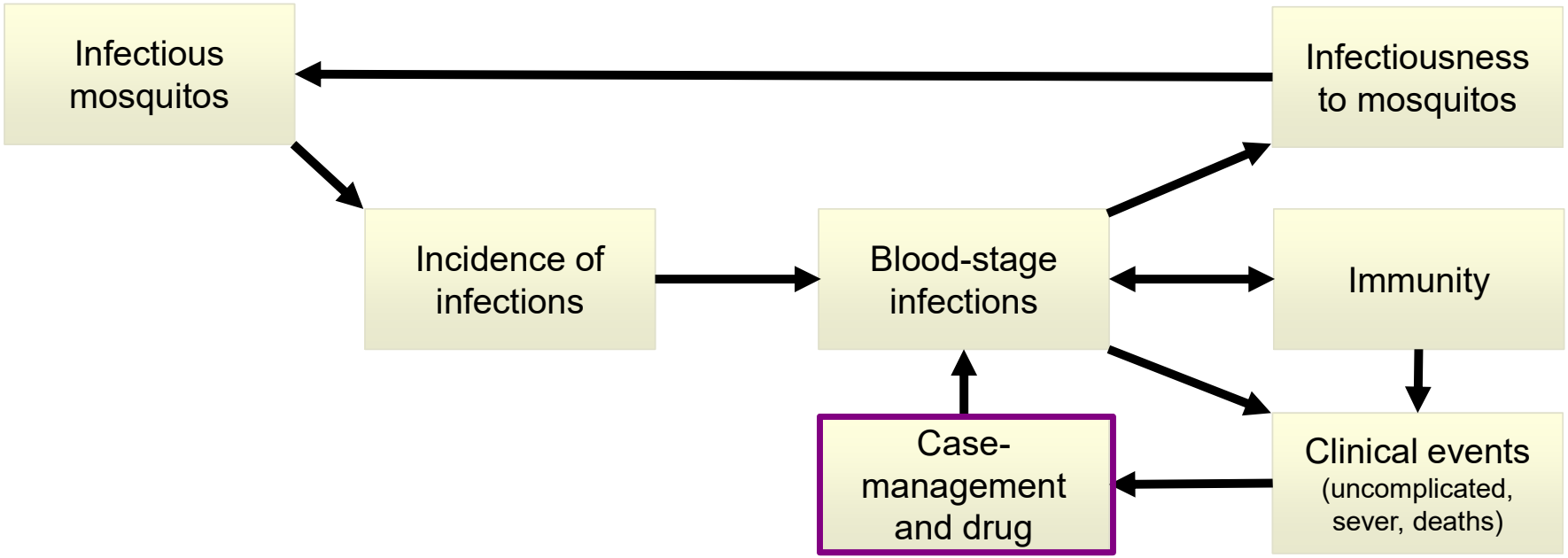
Related to the prevalence in pregnant woman

More details: https://www.ajtmh.org/view/journals/tpmd/75/2_suppl/article-p63.xml

Human model

Swiss TPH

Overview



Human model

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Case management

- Describes the use and access to treatment based on three categories:
  - Uncomplicated malaria with no previous use of treatment (within 35 days) →1st line treatment
  - Uncomplicated malaria with prior use of treatment (within 35 days) → 2nd line treatment
  - Severe malaria.

- The model can consider:
  - Different access to official care for uncomplicated and severe malaria.
  - Different diagnostic tools (vary sensitivity and specificity).
  - Heath system memory (time for which a recurrent bout of illness counts as the same episodes, 35 days).

Human model

Swiss TPH

Drug dynamics

- **Simple treatment model**
  - Define the proportion of infection that are cleared.
  - In patient with treatment failure, the parasite density is not impacted by drug.

Human model

Swiss TPH

Drug dynamics

- **PK/PD model of drug action**
  - **PK**: drug concentration over time (one-/two-/three- compartment models with instantaneous or first-order absorption) depending on dosage regimen (vary with age or weight).

Drug concentration over time (mg/L):

$$C = C_0 \cdot e^{-kt}$$

C_0:	initial drug concentration (mg/L)
t:	time (day)
k:	eliminate rate (1/day)

  - **PD**: killing effect of a drug on the parasite based on the drug concentration.

Drug killing rate at concentration C (1/day):

$$f(C) = \frac{Emax\ Cn}{C^n + EC5^{\ n}}$$

Emax:	Maximum killing rate (1/day)
EC50:	half maximal effective concentration (mg/L)
C:	drug concentration (mg/L)
n:	slope

More details: https://journals.asm.org/doi/pdf/10.1128/aac.01712-10

Human model

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Drug dynamics

- **PK/PD model of drug action**
  - The killing effect of the drug is transformed into a survival factor that impacts the multiplication factors of the parasite within hosts (Molineaux model needed).

Density of parasite at time t+1:

$$P(t+1) = P(t)\, m\, I(t)\, D(t)$$

$P(t)$: Density of parasite at time t

m: Multiplication factors of genotype i

$I(t)$: Probability that parasites escape immune responses at time t

$D(t)$: Probability that parasite escape drug effect at time t

$$D(t) = \frac{1}{exp(intergral(f(C)))}$$

  - Library of PK/PD parameterization: https://github.com/SwissTPH/openmalaria.snippets/tree/master/pharmacology

More details: https://journals.asm.org/doi/pdf/10.1128/aac.01712-10

Limitations of mathematical models

viss TPH

A mathematical model is an abstract description of a system that uses precise language to describe its behaviour.

Ross model:

OpenMalaira:

- Many parameters
- More time to run simulations.

Fitting of OpenMalaria

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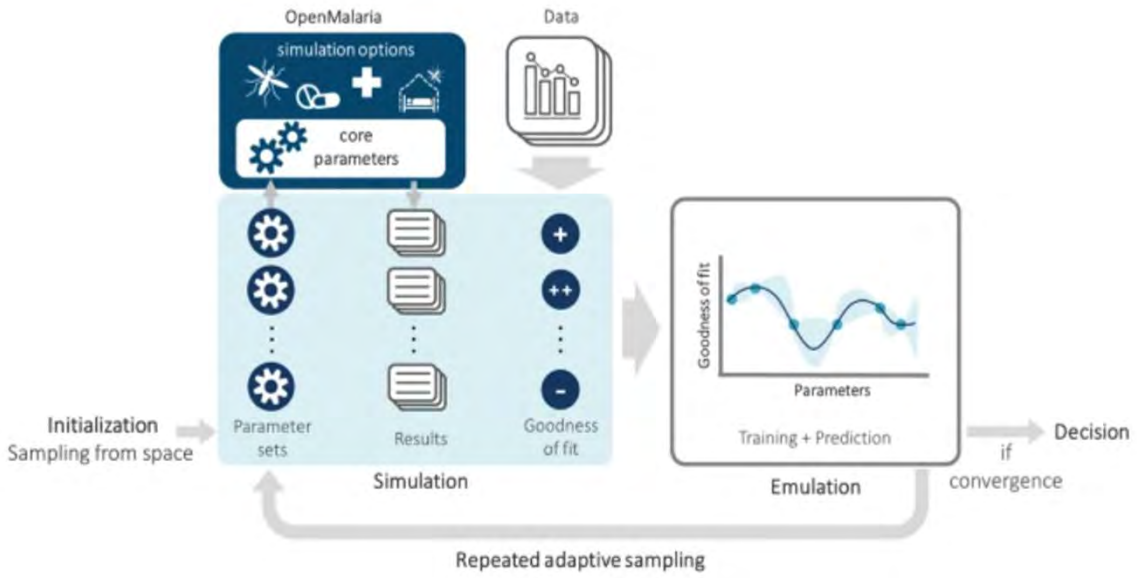
Challenges:

- Core parameters: 23 (e.g. case fatality rate, decay maternal immunity, pyrogenic threshold, immunity acquisition)
- Objectives functions: 11 (e.g. transmission intensity and age pattern of prevalence, incidence)
- Long-simulation time
- Interdependency between the different modules of the model

Single-Layer Bayesian optimisation approaches*



*Reiker et al., 2021

Who knows how to code with R?

Who knows how to code with Python?

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Practical 1: How to run a simulation in OpenMalaria

Thiery Masserey

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Lars Kamber

28 November 2023

How to use OpenMalaria ?

Swiss TPH

1. Model configuration: XML file describing the simulation to run

```
<?xml version="1.0" encoding="UTF-8"?>
<om:scenario xmlns:om="http://openmalaria.org/schema/scenario_43" xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
 <demography maximumAgeYrs="90" name="Zambia 2010 census Southern province " popSize="10000">
  <monitoring name="Change of prevalence" startDate="2000-01-01">
  <interventions name="Vaccine deployment">
  <healthSystem>
  <entomology mode="dynamic" name="Namawala" scaledAnnualEIR="5">  <!-- site specific - pre intervention EIR -->
  <parasiteGenetics samplingMode="tracking">
  <diagnostics>
  <pharmacology>
  <model>
</om:scenario>
```

2. Run the model (C++): command line

3. Obtain the output (survey or continuous)

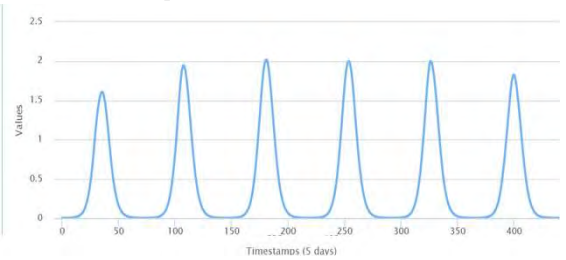
Survey output example:

	Survey	Age group	Output measure	Value
1	1	1	0	158
2	1	2	0	842
3	1	1	3	18
4	1	2	3	246
5	1	1	14	1
6	1	2	14	4
7	1	1	15	0
8	1	2	15	0
9	1	0	36	0.135673

Continuous output:

timestep	simulated EIR
0	0.0694153
1	0.0296148
2	0.0210636
3	0.0130566

4. Post-process the results



XML

Swiss TPH

```
<?xml version="1.0" encoding="UTF-8" standalone="no"?>
<om:scenario xmlns:om="http://openmalaria.org/schema/scenario_45" xmlns:xsi=
    <demography maximumAgeYrs="90" name="Ifakara" popSize="2000">
    <monitoring name="monthly surveys" startDate="1990-01-01">
    <interventions name="GVI example"/>
    <healthSystem>
    <entomology mode="dynamic" name="Namawala" scaledAnnualEIR="20">
     <diagnostics>
     <model>
</om:scenario>
```

https://github.com/SwissTPH/openmalaria/wiki

XML - Demography

Swiss TPH

```
<demography maximumAgeYrs="90" name="Ifakara" popSize="2000">
    <ageGroup lowerbound="0">
        <group poppercent="3.474714994" upperbound="1"/>
        <group poppercent="12.76004028" upperbound="5"/>
        <group poppercent="14.52151394" upperbound="10"/>
        <group poppercent="12.75565434" upperbound="15"/>
        <group poppercent="10.836323739" upperbound="20"/>
        <group poppercent="8.393312454" upperbound="25"/>
        <group poppercent="7.001421452" upperbound="30"/>
        <group poppercent="5.800587654" upperbound="35"/>
        <group poppercent="5.102136612" upperbound="40"/>
        <group poppercent="4.182561874" upperbound="45"/>
        <group poppercent="3.339409351" upperbound="50"/>
        <group poppercent="2.986112356" upperbound="55"/>
        <group poppercent="2.555766582" upperbound="60"/>
        <group poppercent="2.332763433" upperbound="65"/>
        <group poppercent="1.77400255" upperbound="70"/>
        <group poppercent="1.008525491" upperbound="75"/>
        <group poppercent="0.74167341" upperbound="80"/>
        <group poppercent="0.271863401" upperbound="85"/>
        <group poppercent="0.161614642" upperbound="90"/>
    </ageGroup>
</demography>
```

Population size

Proportions of individual in each age group

XML - Monitoring

Swiss TPH

```
<monitoring name="monthly surveys" startDate="1990-01-01">
    <SurveyOptions onlyNewEpisode="true">
      <option name="nHost"/>          <!-- id 0 -->
      <option name="nInfect"/>        <!-- id 1 -->
      <option name="nPatent"/>        <!-- id 3 -->
      <option name="nUncomp"/>        <!-- id 14 -->
      <option name="inputEIR"/>       <!-- id 35 -->
      <option name="simulatedEIR"/>   <!-- id 36 -->
    </SurveyOptions>
    <surveys diagnostic="deterministic">
      <surveyTime repeatStep="5d" repeatEnd="2020-01-01">2000-01-01</surveyTime>
    </surveys>
    <ageGroup lowerbound="0">
      <group upperbound="1"/>
      <group upperbound="2"/>
      <group upperbound="5"/>
      <group upperbound="10"/>
      <group upperbound="15"/>
      <group upperbound="20"/>
      <group upperbound="100"/>
    </ageGroup>
</monitoring>
```

Start date of simulation

Measures of interest
(https://github.com/SwissTPH/openmalaria/wiki/MonitoringOptions)

Start date of the survey

End date of the survey

Frequencies of survey deployment
(d: day, y: year) (snapshot vs aggregated)

Age categories for reporting the measured values

XML – Health system

Swiss TPH

```
<!-- Specify health system parameters here, see: https://github.com/
<healthSystem>
    <DecisionTree5Day name="example name">
        <pSeekOfficialCareUncomplicated1 value="0.30"/>
        <pSelfTreatUncomplicated value="0.0"/>
        <pSeekOfficialCareUncomplicated2 value="0.30"/>
        <pSeekOfficialCareSevere value="0.48"/>
        <treeUCOfficial>
            <treatSimple durationLiver="0" durationBlood="1t"/>
        </treeUCOfficial>
        <treeUCSelfTreat>
            <noTreatment/>
        </treeUCSelfTreat>
        <cureRateSevere value="1.0"/>
        <treatmentSevere>
            <clearInfections stage="blood" timesteps="1t"/>
        </treatmentSevere>
    </DecisionTree5Day>
    <CFR>
        <group lowerbound="0" value="0.09189"/>
        <group lowerbound="0.25" value="0.0810811"/>
        <group lowerbound="0.75" value="0.0648649"/>
        <group lowerbound="1.5" value="0.0689189"/>
        <group lowerbound="2.5" value="0.0675676"/>
        <group lowerbound="3.5" value="0.0297297"/>
        <group lowerbound="4.5" value="0.0459459"/>
        <group lowerbound="7.5" value="0.0945946"/>
        <group lowerbound="12.5" value="0.1243243"/>
    </CFR>
    <pSequelaeInpatient interpolation="none">
        <group lowerbound="0.0" value="0.0132"/>
        <group lowerbound="5.0" value="0.005"/>
    </pSequelaeInpatient>
</healthSystem>
```

Access to treatments

Effect of treatments

Case fatality rate

Probability of sequelae

XML - Entomology

```
<entomology mode="dynamic" name="Namawala" scaledAnnualEIR="20">
    <vector>
        <anopheles mosquito="gambiae_ss" propInfected="0.078" propInfectious="0.021">
            <seasonality annualEIR="24.826144381650714" input="EIR">
            <fourierSeries EIRRotateAngle="0">
                <coeffic a="-0.2072" b="0.8461"/>
                <coeffic a="0.0906" b="-0.0425"/>
            </fourierSeries>
        </seasonality>
        <mosq minInfectedThreshold="0.001">
            <mosqRestDuration value="3"/>
            <extrinsicIncubationPeriod value="11"/>
            <mosqLaidEggsSameDayProportion value="0.313"/>
            <mosqSeekingDuration value="0.33"/>
            <mosqSurvivalFeedingCycleProbability value="0.623"/>
            <availability/>
            <mosqProbBiting mean="0.95" variance="0"/>
            <mosqProbFindRestSite mean="0.95" variance="0"/>
            <mosqProbResting mean="0.99" variance="0"/>
            <mosqProbOvipositing value="0.88"/>
            <mosqHumanBloodIndex value="0.939"/>
        </mosq>
        <nonHumanHosts name="unprotectedAnimals">
            <mosqRelativeEntoAvailability value="1.0"/>
            <mosqProbBiting value="0.95"/>
            <mosqProbFindRestSite value="0.95"/>
            <mosqProbResting value="0.99"/>
        </nonHumanHosts>
    </anopheles>
```

?

EIR

Mosquitos species name

Seasonality
(https://swisstph.github.io/openmalaria/fourier)

Mosquitoes species-specific parameters

XML - Diagnostic

Swiss TPH

```
<diagnostics>
    <diagnostic name="deterministic">
        <deterministic minDensity="40"/>
    </diagnostic>
</diagnostics>
```

Minimum density at which parasite is detected within host

NB: The diagnostic is used to diagnose patients with uncomplicated malaria seeking treatment and for performing each survey.

XML - Parameter

Swiss TPH

```
is proportional to age and/or body surface area. This should not be change unless you have a biologically source. -->
<human>
    <availabilityToMosquitoes>
        <group lowerbound="0.0" value="0.225940909648"/>
        <group lowerbound="1.0" value="0.286173633441"/>
        <group lowerbound="2.0" value="0.336898395722"/>
        <group lowerbound="3.0" value="0.370989854675"/>
        <group lowerbound="4.0" value="0.403114915112"/>
        <group lowerbound="5.0" value="0.442585112522"/>
        <group lowerbound="6.0" value="0.473839351511"/>
        <group lowerbound="7.0" value="0.512630464378"/>
        <group lowerbound="8.0" value="0.54487872702"/>
        <group lowerbound="9.0" value="0.581527755812"/>
        <group lowerbound="10.0" value="0.630257580698"/>
        <group lowerbound="11.0" value="0.663063362714"/>
        <group lowerbound="12.0" value="0.702417432755"/>
        <group lowerbound="13.0" value="0.734605377277"/>
        <group lowerbound="14.0" value="0.788908765653"/>
        <group lowerbound="15.0" value="0.839587932303"/>
        <group lowerbound="20.0" value="1.0"/>
        <group lowerbound="20.0" value="1.0"/>
    </availabilityToMosquitoes>
</human>

<!-- DO NOT CHANGE THE MODEL PARAMETERS BELOW -->
<parameters interval="5" iseed="1" latentp="3d">
    <parameter include="0" name="'-ln(1-Sinf)'" number="1" value="0.050736"/>
    <parameter include="0" name="Estar" number="2" value="0.03247"/>
    <parameter include="0" name="Simm" number="3" value="0.138161050830301"/>
    <parameter include="0" name="Zstar_p" number="4" value="1514.385853233699891"/>
    <parameter include="0" name="gamma_p" number="5" value="2.036925334424484"/>
    <parameter include="0" name="sigma2i" number="6" value="10.173598698525799"/>
    <parameter include="0" name="CumulativeYstar" number="7" value="35158523.311325103044451"/>
    <parameter include="0" name="CumulativeHstar" number="8" value="97.334652723897705"/>
    <parameter include="0" name="'-ln(1-alpha_m)'" number="9" value="2.330310458761937"/>
    <parameter include="0" name="decay_m" number="10" value="2.53106547375805"/>
    <parameter include="0" name="sigma2_0" number="11" value="0.655747311168152"/>
    <parameter include="0" name="Zstar_v" number="12" value="0.916181104713054"/>
    <parameter include="0" name="Ystar2" number="13" value="6502.26335600001039"/>
    <parameter include="0" name="alpha" number="14" value="142601.912520000012591"/>
    <parameter include="0" name="Density bias (non Garki)" number="15" value="0.177378570987455"/>
    <parameter include="0" name=" sigma2 " number="16" value="1.0"/>
    <parameter include="0" name="log oddsr CF community" number="17" value="0.736202"/>
    <parameter include="0" name="Indirect risk cofactor" number="18" value="0.018777338"/>
    <parameter include="0" name="Non-malaria infant mortality" number="19" value="49.5390465999999999"/>
    <parameter include="0" name="Density bias (Garki)" number="20" value="4.79610772546704"/>
    <parameter include="0" name="Severe Malaria Threshhold" number="21" value="784455.599999999976717"/>
    <parameter include="0" name="Immunity Penalty" number="22" value="1"/>
    <parameter include="0" name="Immune effector decay" number="23" value="0"/>
    <parameter include="0" name="comorbidity intercept" number="24" value="0.0968"/>
    <parameter include="0" name="Ystar half life" number="25" value="0.275437402"/>
    <parameter include="0" name="Ystar1" number="26" value="0.596539864"/>
    <parameter include="0" name="Asexual immunity decay" number="27" value="0"/>
    <parameter include="0" name="Ystar0" number="28" value="296.302437899999973"/>
    <parameter include="0" name="Idete multiplier" number="29" value="2.797523626"/>
    <parameter include="0" name="critical age for comorbidity" number="30" value="0.117383"/>
</parameters>
```

Do not change the parameter values of the list of parameter at end of XML

Output

Swiss TPH

Survey output example:

	Survey	group	Output measure	Value
1	1	1	0	158
2	1	2	0	842
3	1	1	3	18
4	1	2	3	246
5	1	1	14	1
6	1	2	14	4
7	1	1	15	0
8	1	2	15	0
9	1	0	36	0.135673

Continuous output example:

timestep	simulated EIR
0	0.0694153
1	0.0296148
2	0.0210636
3	0.0130566

(https://github.com/SwissTPH/openmalaria/wiki/MonitoringOptions)

Swiss TPH

Practical 1 continued: Getting started

November 28th 2023

Thiery Masserey, Lars Kamber, Nakul Chitnis
Swiss TPH, Disease Modelling Unit

Objectives of Practical 1

1. Successfully **run OpenMalaria** on your computer
2. **Download files** for the hands-on session and set up the folder structure
3. Go through first practical script:
    1. Run an OpenMalaria simulation from R/python using a given scenario XML
    2. Read in the output file and plots some results
    3. Make minor adjustment to the XML and rerun the simulations

Swiss TPH

1. Running OpenMalaria

Installing OpenMalaria

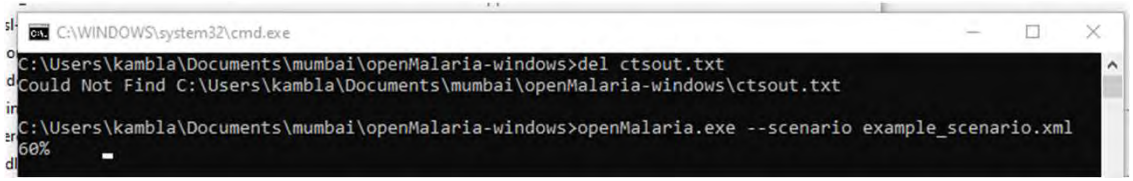
A) Use pre-compiled version

- Download the latest compiled version of OpenMalaria from our GitHub page as a zip archive
  - https://github.com/SwissTPH/openmalaria/releases
  - Extract the archive

B) Compile OpenMalaria on your machine

- Installation instructions can be found on our GitHub wiki
  - https://github.com/SwissTPH/openmalaria/wiki/UserGuide

Check if OpenMalaria runs by double-clicking the file *run-example-scenario.bat* in your OpenMalaria folder (Windows). You should see the following window:



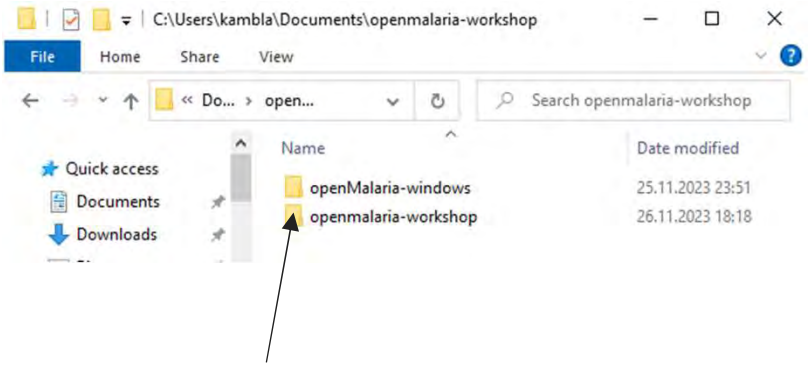
Swiss TPH

2. Setting up the folder structure

Setting up the folder structure for the hands-on session

Create a new folder containing two subfolders:

- Folder containing your running version of Openmalaria
- Folder containing the resources for the hands-on available on Google drive
  - https://drive.google.com/drive/folders/1IGdBK5dWFRCYczMuSTjo9vqbFEtuj7jI
  - We will continuously upload solutions and simulation outputs to the Google drive



Put the practical folders from Google drive into this folder

Swiss TPH
Swiss Tropical and Public Health Institute
Schweizerisches Tropen- und Public Health-Institut
Institut Tropical et de Santé Publique Suisse

Associated Institute of the University of Basel

Practical 2: How to compare interventions in OpenMalaria

Thiery Masserey

&

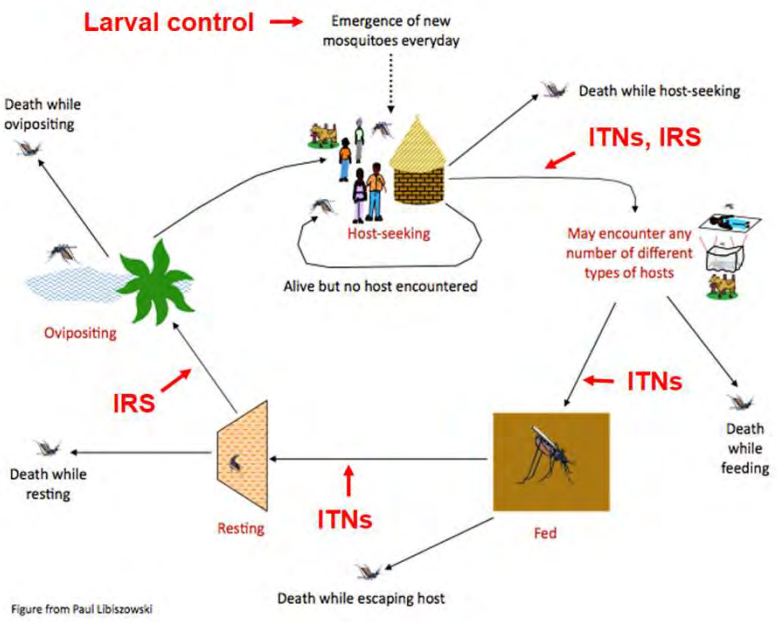
Lars Kamber

28 November 2023

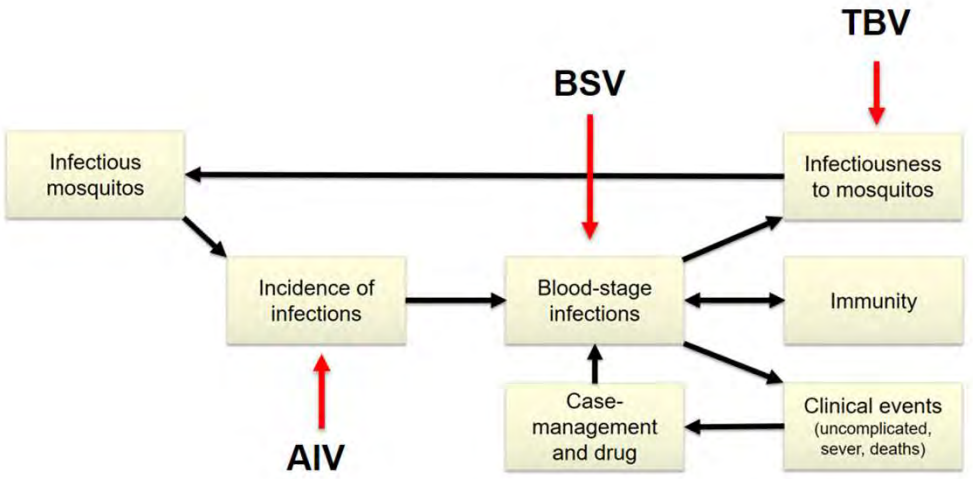
Intervention and OpenMalaria

Swiss TPH

Vector model:



Human model:



- Efficacy can decay over time (half-life and shape functions).
- Variation of efficacy among individuals.

Example of XML parameterisation

Swiss TPH

Pre-erythrocytic vaccine (PEV)

```
<interventions name="interventions">
    <human>
      <component id="PEV_vaccine" name="PEV_vaccine">
            <PEV>
                <decay L="2y" k="1" function="weibull"/>
                <efficacyB value="1.0"/>
                <initialEfficacy value="0.95"/>
            </PEV>
      </component>
         <deployment>
             ...
         </deployment>
    </human>
    <vectorPop>
    </vectorPop>
</interventions>
```

Category of interventions
- human (deploy to human)
- vectorPop (deploy to mosquitos)

Define the name of the intervention
Define the decay of the intervention
Define the variation of efficacy between ind.
Define the efficacy of the intervention

Example of XML parameterisation

Swiss TPH

Insecticide-treated bed nets (ITNs)

```
<interventions name="interventions">
    <human>
        <component id="LLIN" name="LLIN">
            <GVI>
                <decay L="3y" k="1" function="weibull"/>
                <anophelesParams mosquito="arabiensis" propActive="1">
                    <deterrency value="0.5"/>
                    <preprandialKillingEffect value="0.13"/>
                    <postprandialKillingEffect value="0.23"/>
                </anophelesParams>
            </GVI>
        </component>
    <deployment>
            ...
    </deployment>
    </human>
</interventions>
```

Category of intervention (human/vector)
Define the name of the intervention
Define the decay of the intervention
Define the mosquito's specie affected
Define the % of mosquito bites affected
Define the effect of the intervention

Deployment of interventions

Swiss TPH

- **Timed**: mass administration of the intervention to a part of the population (time, coverage, age range, etc.).

```
<interventions name="interventions">
    <human>
        <component id="LLIN" name="LLIN">
            ....
        </component>
        <deployment>
            <component id="PEV_vaccine"/>
            <timed>
                <deploy coverage="0.6" minAge="0.25" maxAge="5" time="2010-01-01"/>
            </timed>
        </deployment>
    </human>
</interventions>
```

Coverage Age group Time

- **Continuous**: Individuals receive the intervention when they reach a specific age.

```
<interventions name="interventions">
    <human>
        <component id="PEV_vaccine" name="PEV_vaccine">
            ....
        </component>
        <deployment>
            <component id="PEV_vaccine"/>
            <continious>
                <deploy coverage="0.8" age="1" />
            </continious>
        </deployment>
    </human>
</interventions>
```

Coverage Age of deployment

Objectives of practical 2

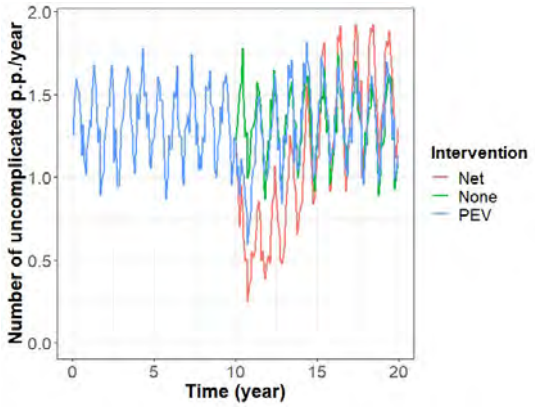
Swiss TPH

Compare the impact of interventions in OpenMalaria:

1) Run three simulations:
   - Control arm
   - ITN arm
   - PEV arm

We will use the same XML as in Practical 1 for the control arm but with:
- Monthly survey
- Only one age group (0-100)

2) Compare the effect of the two interventions on the number of uncomplicated cases (p.p./year)



3) Quantify the impact of the interventions

Interventions	% of cases averted
ITN	Z%
PEV	X%