# Getting started

## Compiling an executable

I have included a pre-compiled executable in the folder "compiled" however it is possible to compile a fresh one directly from the source code contained within the folder "code". The below instructions are based upon the freely available community version of Microsoft Visual Studio, (hopefully it shouldn't be too hard to compile with any alternative preference).

Open Visual Studio. Select "Create a New Project", then select "Empty Project". Give your project a name and a location.

Open the "code" folder and copy and paste it into the directory you have just created.

Within "Solution Explorer" right-click "Source File"->"Add"->"Existing item..."->

Then select "main", so that "main" should now appear within the Solution Explorer. Make sure you have "Release" selected from the top bar where it will have "Debug" as standard (otherwise code will run a lot slower).

Now select "Build" and an executable with the name of your project should appear in your Project's directory (e.g. C:\New\_project\Release\New\_project.exe).

Now copy the .exe to the folder where you wish to run the model (it will require some parameters and additional files to run.

**Running the model**

**Creating a batch file that will run**

The model can be run from the command line but requires at least three arguments. I usually run the model as a batch file - these can be created in a text editor such as 'notepad' in the same way as a text file, saving them as a ".bat" file will then create a batch file that can be run by double-clicking it.

"run\_examples.bat" in the folder "compiled" provides an example of how to run the model, providing as arguments following it:

1)a path to the executable (.exe) a 'root' path for where the model inputs and outputs are located

2)the name of the directory for the user-supplied model parameters

3)a name for the output files, with path to folder if using a separate one.

I recommend this approach (as implemented in "run\_example.bat") - throughout anything that may be customised is italicised.

set root="*path of folder for inputs and outputs*"

set directory="*file name of parameter directory*"

set output="\_location of output folder and name of output file"

.\_name of executable\_.exe %root% %directory% %output%

**The model parameters directory**

All of the user-editable parameters supplied to the executable need to be listed in a text file in the following format

sim\_params "*name of simulation parameters file*"

preg\_params "*name of pregnancy specific parameters file*"

fertility\_rates "*name of pregnancy rates*"

The preg\_params file is set to their posterior medians and probably should be left as "preg\_params.txt" unless the user has refitted the model to additional data. The "fertility\_rates" file is a 7 by 20 matrix of age (7 age\_categories between 15-49) and parity-dependent fertility rates. These can be calculated readily from population-based surveys but are more important for calculating overall burden and otherwise the results within the manuscript are not particularly sensitive to this so I have only included rates from the Malawi 2012 DHS survey in rural areas (so approximating those in the Malawian ISTp trial).

The main file of interest is likely to be the one where users can alter the key aspects of the simulation - currently "sim\_params.txt" - see below for current options..

**Simulation parameters file**

Here I have included all the main simulation parameters you need to define a setting, an intervention to look at and output options. These are as follows (most relevant ones are italicised), often these have error messages coded for the user if misspecified so if the model isn't working it is usually worth checking the .cout file (see later description of what this is):

***EIR***: Entomological Innoculation rate in the general population (should be greater than 0 but typically values between 0.1 and 1000 are likely to be most relevant)

**ft**: Fraction of symptomatic cases treated (values 0-1)

**num\_women**: number of life-courses outputs are averaged over (higher the number implies lower stochastic variability)

**intervene\_imm**: A bit of an esoteric one, a switch to decide if the intervention affects the acquisition of pregnancy-specific immunity: if it takes a value of 0 ANC-based interventions do not interfere with the development of immunity (two versions of each pregnancy is run, one to get the exposure in the absence of intervention in order to acquire immunity, one to look at the impact of immunity)- as this is most reflective of implementing a new intervention this is what I used for this analysis. Otherwise if set to 1, when infections are prevented by prophylaxis women develop lower immunity - for the casual user I recommend sticking to the default 0.

***strategy***: An important one, strategy at ANCs in second trimesters onwards : 0 is no intervention, 1 is IPTp (using **IPT\_drug**, 2 is ISTp (providing **IST\_drug** to those who test positive), 3 is a hybrid strategy where women are tested at the first visit in second trimester, given **IST\_drug** if positive, **IPT\_drug** if negative and are then all provided **IPT\_drug** in future visits regardless of infection status, 4 is the equivalent strategy but where the hybrid approach is repeated at all future visits as well.

**IPT\_drug**: the drug used if strategy involves presumptive treatment (currently drug\_1)

**IST\_drug**: the drug provided to test-positive women if strategy involves testing (currently drug\_1)

***drug\_efficacy\_1***: the probability drug\_1 clears an ongoing infection (currently set to 0.82 reflecting high quintuple SP resistance"

***drug\_half\_life\_1***: the days post administration at which 50% of women in which drug\_1 has previously been effective no longer are protected (currently set to 7 reflecting high quintuple SP resistance)

**drug\_efficacy\_2**: the probability drug\_1 clears an ongoing infection (currently set to 0.99 reflecting an highly effective ACT)

***drug\_half\_life\_2***: the days post administration at which 50% of women in which drug\_2 has previously been effective no longer are protected (currently set to 28 reflecting DHA-P, for AL this will be about 11)"

**drug\_shape\_x**: the shape parameter of the weibull distributed duration of prophylaxis, these have been set to 8 for both drugs to give a curve that maintains protection post administration to near the half-life in most women but then decaying rapidly after the half-life which is likely to be more realistic than a more typically used exponential distribution with a much longer tail (unrealistically high probability of full protection between visits even for short half-lives)

**efficacy\_previous\_failure\_deduction**: the impact upon drug efficacy that failing to clear an infection has upon the probability it will be cleared the next time round (can be between 0-1, default is a 50% reduction in efficacy)

***perfect\_test***: Useful for thinking about potential of an hs-RDT: if this is set to 1 (rather than 0) it allows the user to over-ride the in-built model of RDT sensitivity to define a notional "perfect test" with a uniform sensitivity

***perfect\_sens***: Defining what the sensitivity of this idealised test could be

**first\_tri\_visit**: A switch as to whether women visit in the first trimester

**first\_tri\_visit\_time**: The timing in gestation of this visit (needs to be between 0 and 84 - i.e. 0-12 weeks)

***first\_tri\_rdt***: 0:no intervention, 1:same sensitivity as adults in the general population, 2:sensitivity defined as **perfect\_sens**. If treated women are given **IST\_drug**.

**ANC\_x**:A switch as to whether women are given the intervention at ANC visit x - NB additional visits can be added (e.g. "ANC\_7") but these need to be provided with corresponding ANC\_time\_x (and good practice to keep in chronological order, though think it might still work ok...), these parameters are not affected by whether a first trimester visit took place

**ANC\_time\_x**: Day of gestation ANC visit x takes place (between 84-280 - i.e. 12-40 weeks)

***summary***: Whether the user want a summary of outputs across gravidity classes or just the timeline

**output\_beg\_x**: The lower bound of a gravidity category (e.g. if 0 then includes primigravidae, 1 includes secundigravidae etc.)

**output\_end\_x**: The upper bound - if the same as the lower bound then just include one gravidity, if set to -1 this reflects no upper bound on gravidity included (i.e. output\_beg\_x 0, output\_end\_x -1 reflects all gravidities)

There can be as many gravidity categories as desired in any order (e.g. one could have 0-1, 2-4,5+ and then all gravidities as categories x=1:4) but just needs to care to define these sequentially (ie. no x=(1,2,4) without a category 3 etc..)

**Altering simulations on the command line**

Any parameter can be altered in the **sim\_params** folder but often it is more convenient to alter on the command line, this can be done by providing a list of sets of two arguments - the name parameter you want to overwrite and the new value you wish it to take - returning to our previous example:

.\_name of executable\_.exe %root% %directory% %output% strategy 1 first\_tri\_visit 1

will change the simulation from no intervention to IPTp-SP, with an additional visit in the first trimester (see "run\_examples.bat" for other examples)

**Interpreting outputs**

At the path where you specified the output file to appear there will be either two or three files say you gave the output nae "output\_name":

**output\_name.cout** A file that records all the options you supplied for the run: those that were contained within the parameters files and those modified on the command line. It also may contain useful error messages if you don't get the output you were expecting

**output\_name.txt** A file with a timeline of the prevalence throughout pregnancy.

The "Day" column refers to day of gestation after conception.

"peri\_infected\_x\_y" refers to the prevalence of peripheral infection between gravidities x and y inclusive,

"plac\_infected\_x\_y" refers to the prevalence of appreciable sequestered placental parasitaemia (i.e. would be defined as 'active infection' if still present by placental histology at delivery). There should be columns for each gravidity category defined.

**output\_name\_summary.txt** This will only appear if the user sets the "summary" simulation option to 1. This will provide the following summary statistics for each gravidity category ("Grav\_cat" provides detail of what each category represents):

*prop\_peri*: proportion of women who experience peripheral infection at any point during pregnancy

*prop\_plac*: proportion of women who experience placental infection at any point during pregnancy

*average\_plac\_duration*: Average duration of placental infection in days (includes women who had 0 days exposure)

*prop\_fail\_clear*: proportion of women with an infection at first ANC that goes uncleared (all infections if strategy =0)

*prop\_newly\_infected\_clear*: proportion of women who are newly infected after their first ANC visit (to evaluate need for better prophylaxis)

*average\_new\_infections*: average number of new infections after first ANC visit in second trimester (including those with no new infection)

*LBW\_risk*: the proportion of women with malaria-attributable LBW deliveries. NB This only appears for strategy 0 (with or without first trimester testing) as the impact of clearing placental infection later in pregnancy is not sufficiently well characterised.