MINT – Malaria INtervention Tool

Tool to guide malaria control decision making

User Guide

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Version 1

Accompanying publication:

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CONTENTS

1. BACKGROUND

1.1 What is the problem?

Insecticide treated bed nets (ITNs) and indoor residual spraying of insecticides (IRS) have been the key vector control tool for malaria in the past 20-years. Mosquitoes that transmit malaria are becoming increasingly resistant to the pyrethroid insecticide that forms the active ingredient of the traditional bed nets distributed on mass across malaria-endemic countries (1). Resistance to other insecticides is also increasing (2,3). In response, the global community has been developing novel vector interventions to mitigate for the diminishing protection provided by pyrethroid only long-lasting ITNs (pyrethroid LLINs).

1.2 What are the benefits of the tool?

These novel interventions have contrasting public health impact given the characteristics of the local mosquito population, the level of disease and history of control interventions. Decisions on which product to use are complicated by the cost of different interventions vary from day-to-day so that the most cost-effective intervention to deploy will also change continually and differ between locations. This poses a challenge for decision makers with limited budgets tasked with protecting communities from malaria.

1.3 What can the tool do?

Version 1 of this vector control decisions tool is designed to help National Malaria Control Programs explore the most cost-effective current World Health Organisation (WHO) recommended ITN and IRS products for falciparum malaria control. Local human, mosquito and cost data are used to characterise the setting of interest (we refer to this setting as a region or zone in the tool). The tool then summarising the impact of different vector control interventions used in the region and calculates the cost effectiveness of each of the intervention packages. A maximum budget can be set to help determine the most appropriate and affordable intervention for that particular region according to local goals.

1.4 What the model cannot do?

No model is as good as high-quality local surveillance data which should be collected and used to inform future policy. Predictions are made using average entomological and epidemiological data from throughout Africa so may not be representative of all settings. For example, IRS efficacy is thought to vary according to the type of wall material which will vary from site to site (4,5). These differences and uncertainties should be considered in any decision-making process. Similarly, predictions from the model are only as good as data used to parameterise them, so the better the local data the better the predictions are likely to be. Simplifications have been made (for example, in the range of endemicity settings that are explored) so individual estimates of impact and cost-effectiveness will be different from reality. Nevertheless, the relative difference between intervention options is likely to be more consistent and predictions of impact have been shown to adequately reflect changes in malaria prevalence observed in the field (see main manuscript).

1.5 What sized area should be considered?

A region is defined as a management unit which has similar characteristics. This could be an administration unit or province. IRS is very focal and usually completed in a smaller region of a larger province or district. The model assumes that IRS is applied at random to the population so, it is more appropriate to separate regions into IRS regions or non-IRS regions for this assessment and adjust population size accordingly.

1.6 Where can it be found?

The online tool can be accessed free online

https://mint.dide.ic.ac.uk/

Key definitions

Intervention Class – World Health Organization classification for a new set of malaria vector control interventions which have the same entomological model of action. To form a new intervention class new products require epidemiological evidence of benefit over standard-of-care from two cluster randomised control trials

ITN – Insecticide treated mosquito net where the durability of the product is undetermined

LLIN – Long-lasting insecticidal net. An ITN which has proven durability i.e. the lethal time until less than 50% of the initial mortality induced is at least 2 years.

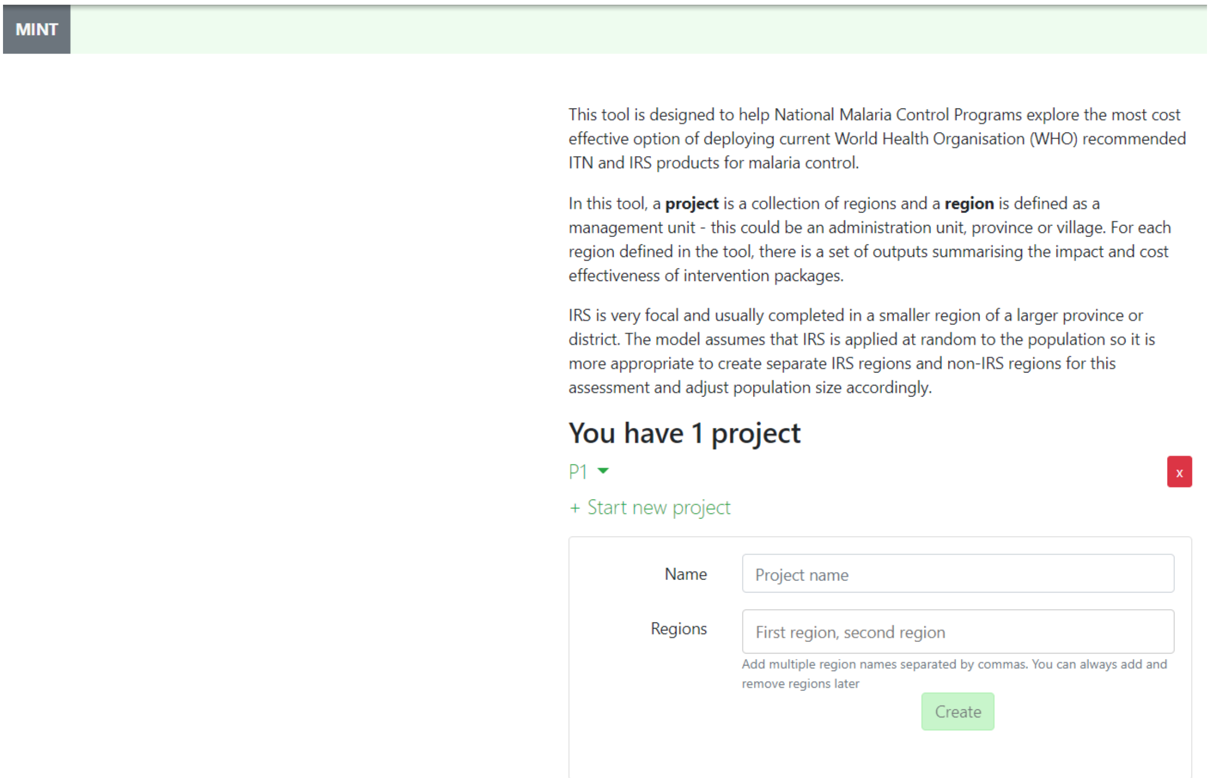
Pyrethroid LLIN – LLIN containing pyrethroid insecticide only. Widely used since 2000 this class of interventions is now showing signs of diminished efficacy in areas with highly pyrethroid-resistant mosquitoes.

Pyrethroid-PBO ITN – mosquito nets which contain pyrethroids and the synergist piperonyl butoxide. A new WHO-declared intervention class for mosquito nets that kill host-seeking insecticide-resistant mosquitoes by neutralising the enzymes responsible for pyrethroid resistance; epidemiological value has been demonstrated by the first-in-class product when compared to the public health impact of pyrethroid-only nets in two RCTs (10,11) though their long-term durability in the field is presently unclear.

All model assumptions are outlined in the attached manuscript other than the variables outlined below which the user is able to define.

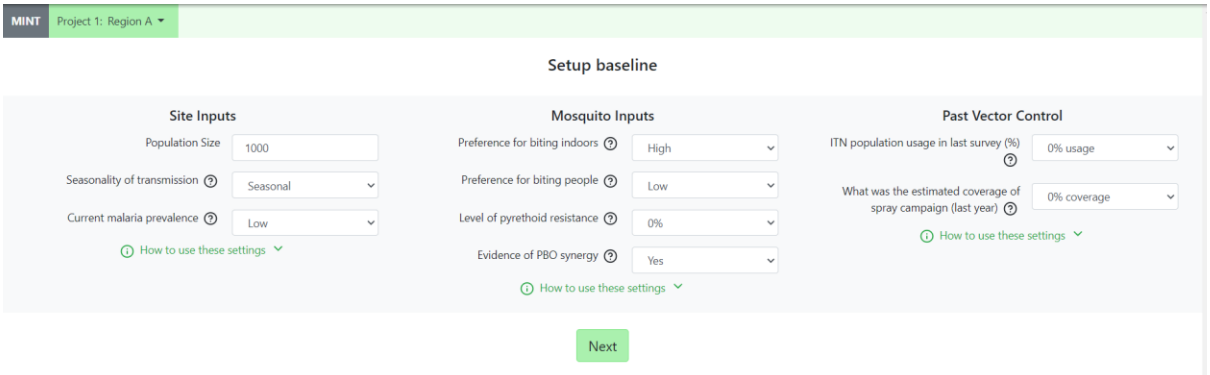
2. STEP-BY-STEP USER GUIDE

The online tool allows multiple projects to be created.



The user can choose a name for the project and define the different regions present. In this tool, a region is defined as a management region. The tool identifies the impact and cost-effectiveness of different vector control intervention combinations given the current situation for the location. For each region, the tool is described in separate input sections;

2.1 Setup baseline



The user can enter the appropriate information to set up the baseline scenario that best represents the region. The region of interest is summarised using a limited number of key characteristics. Numbers are currently limited for computational reasons though these are set to expand to include a greater range of scenarios. The user selects characteristics most representative of the current situation based on recent local data. All inputs can be approximations though users are encouraged to experiment with multiple values to understand how different factors influence the optimal decision. The information buttons can be pressed to provide additional help to fill in the form.

2.1.1 Population size

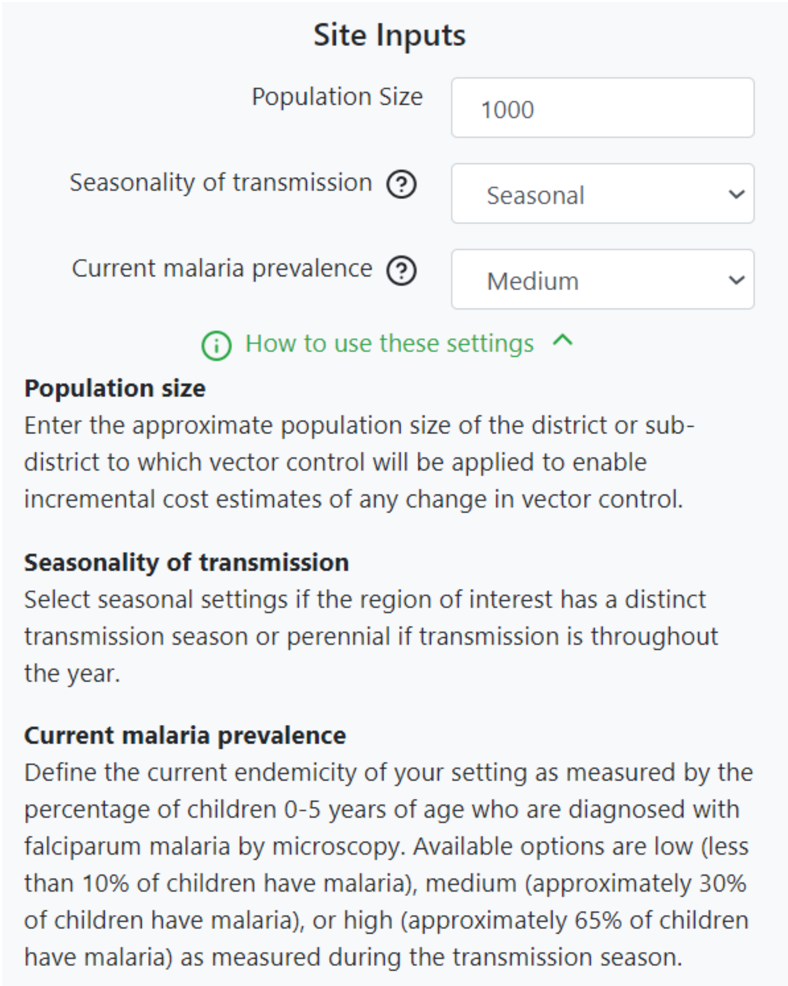
Enter the approximate population size of the district or sub-district to which vector control will be applied. This is only necessary if estimates of the overall budget and impact are needed. Otherwise default levels left.

2.1.2 Seasonality of transmission

Select the *seasonal* settings if the region of interest has a distinct transmission season, or *perennial* if transmission is throughout the year.

2.1.3 Current malaria prevalence

Define the average current endemicity of the setting as measured by the percentage of children under 5-years of age who are diagnosed with *falciparum* malaria by microscopy. Available options are *low*, approximately 5% of children under 5 are malaria positive (use this option for zones where less than 10% of children have malaria); *medium,* approximately 30% of children have malaria (use this option for any scenario with 15 – 45% of children positive for malaria); or *high*, approximately 65% of children have malaria (use this option for any scenarios where malaria prevalence in children under 5-years old is above 50%) as measured during the transmission season.



Values chosen should represent the 'average mosquito' transmitting malaria throughout the year within the zone. If multiple vectors are present, then the characteristics should be weighted towards the dominant vector species. For example, consider a location where two mosquito species A and B are present and are caught throughout the year at a ratio of 3:1 (i.e. Species A = 75%, Species B = 25%). If species A exhibited high levels of resistance with bioassay survival of 80% whilst species B was completely susceptible then the overall level of resistance should be 60% (0.75*0.8 + 0.25*0).

2.1.4 Preference for biting indoors

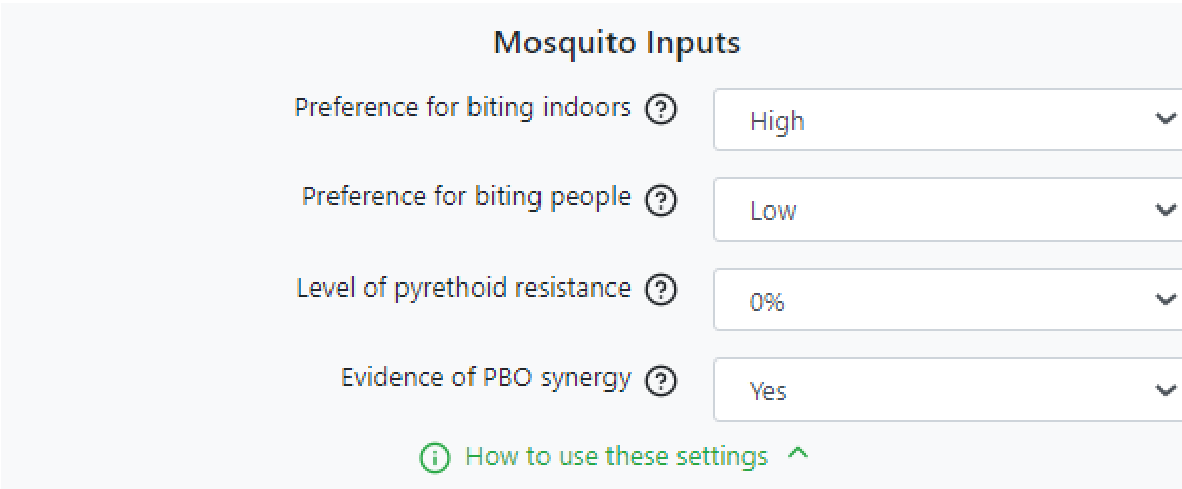
Mosquitoes may show differing propensity to bite people when they are indoors. This depends on both mosquito biting behaviour and when people go indoors. Details for calculating this quantity can be found in (6). A value of *High* indicates ~97% bites taken when people are indoors, whilst selecting *Low* represents 79% bites taken when people are indoors.

2.1.5 Preference for biting people

Mosquitoes show different preference for biting humans relative to other animals (often referred to as the human blood index) (7). A *high* value for the preference for biting people corresponds to ~92% of mosquito bites that are taken on humans prior to introduction of interventions whilst a *low* value equates to ~74% of all bites taken on humans.

2.1.6 Level of pyrethroid resistance

Mosquito survival in 24-hour WHO discriminatory dose bioassays; 0% indicates all mosquitoes die and are susceptible to the pyrethroid insecticide in ITNs. 100% indicates all mosquitoes survive and are resistant to the pyrethroid insecticide in ITNs. Estimates should be adjusted taking into account mortality in the control (unexposed) mosquitoes (8,9).

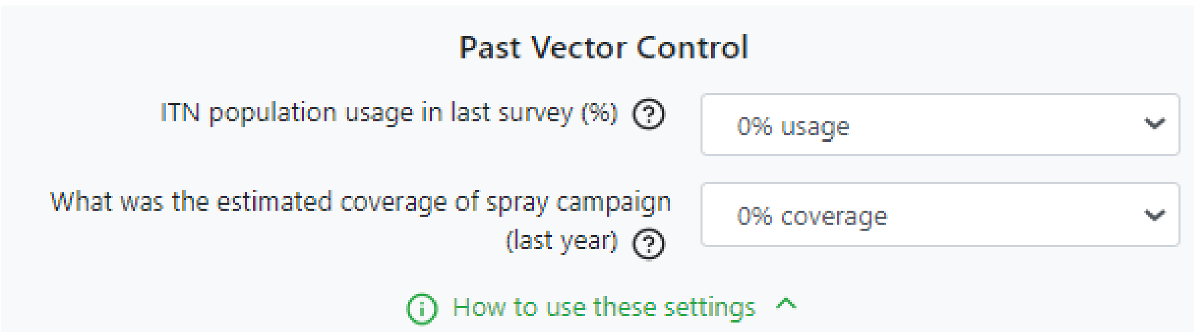


2.1.7 Evidence of PBO synergy

If there is evidence that PBO (piperonyl butoxide) synergises pyrethroid insecticide or that metabolic mechanisms contribute resistance in the local mosquito population then we can select 'Yes' and the pyrethroid PBO ITN will be expected to perform well relative to the pyrethroid LLIN under scenarios with pyrethroid resistance

2.1.8 Past Vector Control

The endemicity of a setting is determined by the mosquito ecology, community activities and environment but also the historic pressure from interventions that are controlling malaria transmission. This information needs to be provided for the zone for both ITNs and IRS.



2.1.9 ITN population usage in last survey (%)

This can be estimated from Demographic Health Surveys or other surveys on net use completed in this zone.

2.1.10 What was the estimated coverage of the recent spray campaign

Please choose the option that best represents the percentage of homes sprayed within the zone during the last IRS campaign. Select option from the drop-down tab. If spraying has never been implemented, please select 0% option.

We will demonstrate a scenario that has:

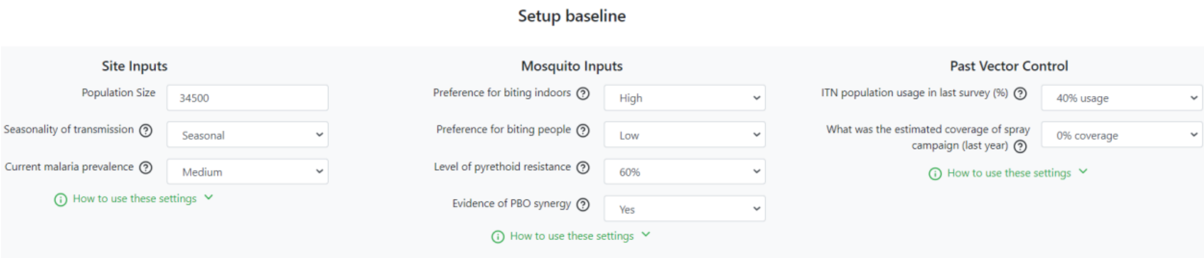
- ✓ a population of 35,400 people,
- ✓ seasonal transmission with approximately 30% prevalence in children under 5 years of age.

Mosquito behaviours are:

- ✓ highly endophilic,
- ✓ less anthropophilic, and;
- ✓ approximately 60% of mosquitoes are shown to be surviving exposure to a discriminatory dose bioassay (60% pyrethroid resistance).
- ✓ There is evidence of PBO synergy - so that we would expect pyrethroid-PBO ITNs to perform advantageously to pyrethroid LLINs in this scenario.

Historically:

- ✓ about 40% of the community have been using mosquito nets, but;
- ✓ no IRS has been used in the region.



2.2 Set up interventions

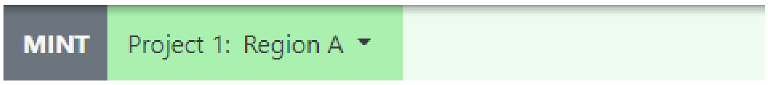
After clicking on the 'next' tab, on the left of the screen, the user can enter the expected ITN use moving forward, and explore the option of including IRS.

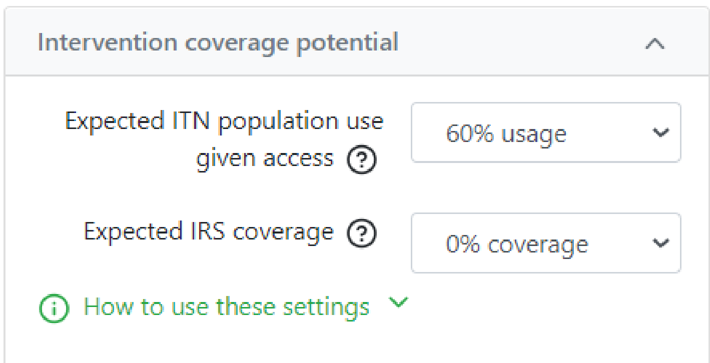
2.2.1 Expected ITN usage

User enters the expected ITN usage (of any net type: pyrethroid LLIN or pyrethroid-PBO ITN) of people in the community after mass distribution given the procurement and distribution assumptions made in 2.2. This will determine the intervention efficacy over the next period and should be based on what usage was achieved after the last mass campaign (and can be assessed by local or Demographic Health surveys). Only one net type is implemented across the zone and the model assumes there is a loss of ITN use over time since the mass campaign. This loss accounts for both the waning efficacy of the active ingredient and the waning adherence to ITN use.

2.2.2 Expected IRS coverage

Indoor residual spraying can be added to a region instead of, or in addition to, ITNs (of any type). Houses to receive IRS are selected at random (irrespective of ITN ownership) and IRS coverage estimates represent the percentage of the population living in houses with IRS. Care should be taken interpreting results as IRS is often highly clustered within small geographical areas. The model predicts the impact of a long-lasting IRS product (for example Actellic 300CS or Sumishield) where spraying is repeated annually prior to the peak of the transmission season (if seasonal setting selected in 2.1.2).





2.3 Procurement and distribution

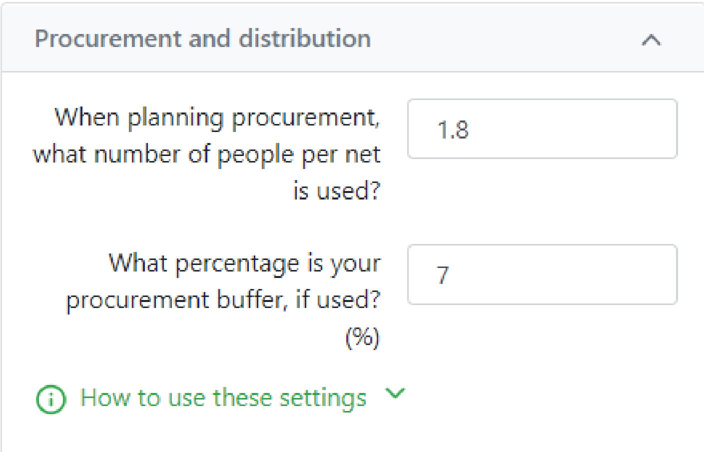
The delivery of nets and sprays is conducted differently in each country. Please answer the following questions so that the price estimates for impact can be augmented appropriately.

2.3.1 When planning procurement, what number of people per net is used?

The default estimate of 1.8 people per net is most commonly cited as the number used for planning mass distributions of nets. Please change as necessary.

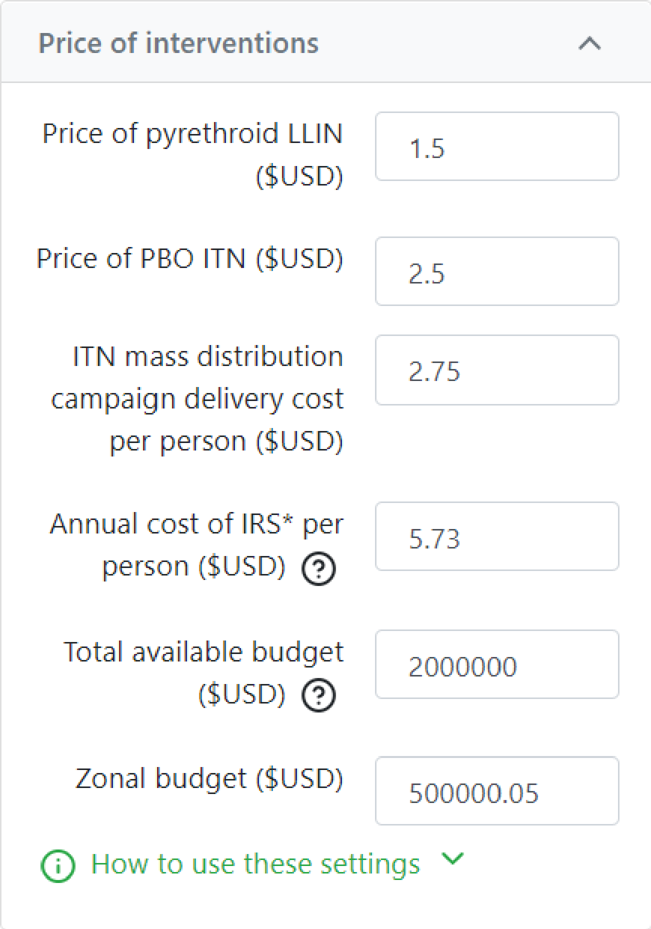
2.3.2 What percentage is your procurement buffer, if used?

When mosquito nets are procured, there is a buffer to ensure there is not a short fall. Please indicate your estimate here. This is used to adjust cost estimates. The default is 7%.



2.4 Price of interventions

The price of different vector control interventions will vary over time, according to the size of orders and specifications. Here quoted prices can be defined by the user in $USD. For simplicity, it is assumed that there is a linear relationship between cost and population coverage, we do not consider inflation in this version of the tool. Costs of the product and of its delivery are separated.



2.4.1 Price of pyrethroid LLIN ($USD)

Price per pyrethroid-only LLIN. The default is set at $1.5 USD.

2.4.2 Price of pyrethroid-PBO ITN ($USD)

Price per pyrethroid-PBO ITN. The default is set at $2.5 USD.

2.4.3 ITN mass distribution campaign delivery cost per person ($USD)

Cost to deliver nets to each person (equivalent for each ITN type). Enough nets are provided to match the number of people per net and (2.2.2) the procurement buffer (2.2.3).

2.4.4 Price of IRS product per person (annual $USD)

The price per person of long-lasting IRS product averaged for each year. Include the average cost for both the IRS product and implementation of IRS. If different IRS products are used in different years, please average the product costs and provide an annual cost per person protected by IRS (in $USD).

2.4.5 Total budget ($USD)

The total budget for the zone for the next 3-year period. This is required to assess the most feasible intervention options for the zone.

At any point, the user can click on the setup baseline option at the top of the page and alter the inputs as useful.

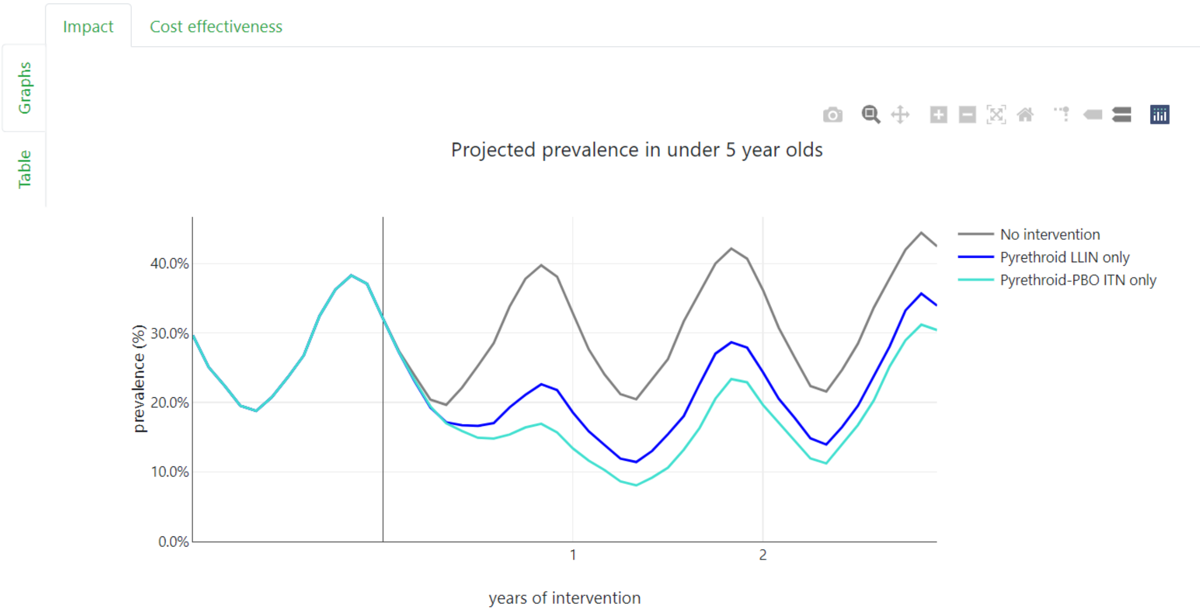
3 INTERPRETATION

There are 4 outputs tabs in the tool. The:

(1) Impact
(2) Cost-Effectiveness
(3) Summary Impact Table
(4) Summary Cost-Effectiveness Table

3.1 *Impact* graphs

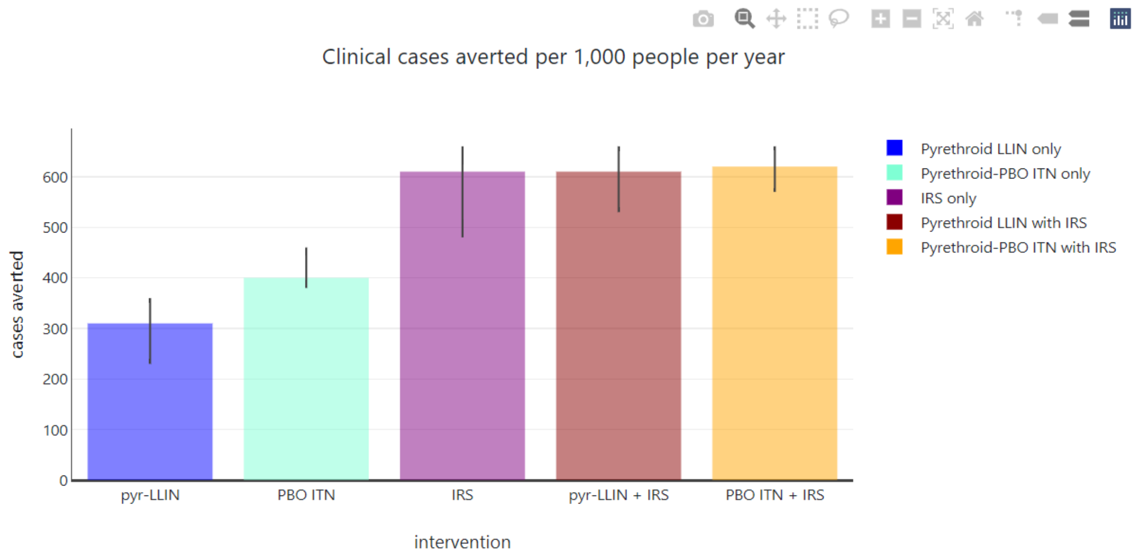
The Impact tab shows the estimated prevalence in the zone over time, and the cases averted per 1,000 people across the 3 years since implementing an intervention package.



Top panel – Predicted changes in prevalence of malaria in children <5 years of age (diagnosed by slide positivity) given an intervention package introduced at time 0 (vertical grey line). Lines show either:

- Do-nothing scenario – No additional vector control interventions. Prevalence may rise as impact of previous interventions (if used) are lost (grey);
- Pyrethroid-only LLINs distributed in a mass campaign at time zero (blue);
- Pyrethroid-PBO ITNs distributed in a mass campaign at time zero (green);
- Annual IRS campaign with no additional ITN distribution (purple);
- Annual IRS campaign plus pyrethroid-only ITNs distributed in a mass campaign at time zero (dark red), or;
- Annual IRS campaign plus pyrethroid-PBO ITNs distributed in a mass campaign at time zero(orange).

The lines for IRS will only show if IRS cover is selected to be > 0%.



Lower panel, barchart showing the number of clinical cases averted per 1,000 people averaged over 3 years for the different intervention packages outlined above (relative to the 'do-nothing' scenario).

The impact figures present the different intervention scenarios for the specified zone without considering cost.

Hovering the cursor over the figures will show absolute estimates and uncertainty for the impact of the strategies.

3.2 *Impact Table*

All data presented in the *Impact* figure is summarised in the *Summary Impact Table* tab. This format allows different summary measures to be examined over the three-year time period. Table can be ordered according to the users metric of preference by clicking on the arrows on the different columns.

Interventions: The ITN and IRS combination used for the scenario.

Net use (%): The percentage of people predicted to use an ITN the previous night following a mass campaign.

IRS cover (%): The percentage of people sleeping in an IRS protected home.

Prevalence under 5 yrs: Yr 1 post intervention: The prevalence in children under 5 years old 1 year after the intervention package is implemented (percentage, detected by microscopy).

Prevalence under 5 yrs: Yr 2 post intervention: The prevalence in children under 5 years old 2 years after the intervention package is implemented (percentage, detected by microscopy).

Prevalence under 5 yrs: Yr 3 post intervention: The prevalence in children under 5 years old 3 years after the intervention package is implemented (percentage, detected by microscopy).

Relative reduction in prevalence in under 5 yrs (%): The relative efficacy of the investigated intervention package against the 'do-nothing' scenario at 3-years after switching to the alternative interventions.

Cases averted (all-age) across 3-yrs since intervention: The absolute number of clinical cases averted given the population size inputted and relative to the 'do-nothing' scenario.

Mean cases averted (all-age) per 1,000 people per year (across 3-yrs since intervention): The mean number of clinical cases averted annually per 1,000 people per year relative to the 'do-nothing' scenario.

Relative reduction in clinical cases (across 3-yrs since intervention) (%): The percentage-efficacy of the intervention package against reducing the number of clinical cases relative to the 'do-nothing' scenario.

Mean cases per person per year (averaged across 3-yrs since intervention): The predicted number of clinical cases per person.

Hovering the cursor over the values in the table will show absolute estimates and uncertainty for the impact of the strategies.

3.3 *Cost effectiveness* Graphs

The Cost effectiveness tab shows the estimated total cost in USD per intervention strategy over 3-years against the expected total number of cases averted per 1,000 people across 3-years (top panel).

The red horizontal dashed line is showing the maximum budget determined by the user for the zone (if provided). Interventions above this line would therefore be considered out of budget so the point furthest to the right beneath this line would indicate the most cost-effective strategy (if no red line is shown the y-axis scale does not intercept this value).

In the scenario demonstrated, the cost-effective strategy within budget would be to use pyrethroid-PBO ITNs, but this may change were the net usage altered or were the different ecologies and assumptions made about the region to be adjusted.

Points show the best estimate for predicted impact whilst the horizontal lines from these points indicate uncertainty in intervention impact driven by the statistical analysis of the interventions (Nash et al. in submission; Sherrard-Smith et al. in submission). Colours denote the different intervention strategies and match those outlined above (and see legend). Uncertainty in costs are not provided in version 1.

Summary information provided by the user indicates the expected ITN usage and IRS coverage to be achieved in the zone. Altering these would alter the cost-effectiveness and the user is encouraged to explore this feature.

3.4 *Cost effectiveness Table*

The cost effectiveness table provides the numbers for the different measures projected by the model. As with the impact table the different intervention packages can be ordered according to the different metrics by clicking on the arrows in each column (to order them by that measure).

Interventions The ITN and IRS combination used for the scenario.

Net use (%): The percentage of people predicted to use an ITN the previous night following a mass campaign.

IRS cover (%): The percentage of people sleeping in an IRS protected home.

Mean cases averted per 1,000 people per year (averaged across 3-yrs since intervention): The predicted number of clinical cases per 1,000 people averted by the intervention package relative to the continuation of the 'do-nothing' scenario.

Total costs $USD: The total cost in USD expected for the product procurement and implementation for the intervention package to cover a 3-year period of protection.

Cost per case averted: The cost in USD per case averted relative to the 'do-nothing' scenario.

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