Models of Insecticide Resistance Evolution; narrowing the gap to field data.

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Models of insecticide resistance evolution

Our models are research tools

Uncertainty in model structure and input data

Potential to address operational questions in future

Useful for us to know what the operational questions are
Insecticide use strategies

Sequence
use until resistance threshold reached

Rotation

Mixture

Mosaic

Insecticide 1, 2
RESEARCH ARTICLE
A Two-Locus Model of the Evolution of Insecticide Resistance to Inform and Optimise Public Health Insecticide Deployment Strategies

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Abstract
We develop a flexible, two-locus model for the spread of insecticide resistance applicable to mosquito species that transmit human diseases such as malaria. The model allows differential exposure of males and females, allows them to encounter high or low concentrations of insecticide, and allows selection pressures and dominance values to differ depending on the concentration of insecticide encountered. We demonstrate its application by investigating the relative merits of sequential use of insecticides versus their deployment as a mixture to minimise the spread of resistance. We recover previously published results as subsets of
Our models

- Resistance to each insecticide coded by one gene
- Resistance already present at low frequencies
- Standard population genetic methods
- Most relevant to new active ingredients
- Flexibility to include cross resistance but not yet done
Genotypes

Alleles
Susceptible (S) or Resistant (R)

1 insecticide : 3 genotypes SS SR RR

2 insecticides : 9 genotypes
main model inputs

Exposure proportion of insects exposed to insecticide

Effectiveness proportion of susceptible (SS) insects killed by exposure to insecticide

Resistance restoration ability of resistance (RR) to restore fitness when exposed to insecticide

Cost of resistance decrease in fitness of resistance (RR) insects not exposed to insecticide

Dominance determines fitness of heterozygotes (SR)
Fitness calculation for each genotype in each generation for one insecticide

- not exposed to insecticide
- exposed to insecticide

- dominance
- resistance cost
- effectiveness
- resistance restoration
- dominance

fitness or survival

SS, SR, RR genotype
solid lines = Mixture
dashed = Sequence
Low effectiveness of insecticide 1: sequence slows evolution of resistance to both.

High effectiveness of insecticide 1: mixture slows evolution of resistance to both.

Mechanism: Higher effectiveness of insecticide 1 in right panel speeds up evolution to itself in the mixture but slows down evolution of resistance to the partner.
Levick, South, Hastings (2017) … that depends.

10,000 runs
sequences vs rotations

Preliminary work shows little difference between them in terms of slowing evolution of insecticide resistance.
sequences vs rotations
no costs of resistance or refugia

Sequence

Rotation

key:

insecticide in use
Costs of resistance cause resistance to decline when an insecticide not in use

Sequence

Rotation

key:

insecticide in use
Untreated areas (refugia) and dispersal also lead resistance to decline when insecticide not in use

**Sequence**

**Rotation**
Larger refugia, more dispersal and more insecticides can lead to resistance staying lower for longer

**Key:**
- **areas connected by migration**
- **insecticide in use**

- **insecticide1**
- **insecticide2**
- **insecticide3**
- **insecticide4**
Early results

No simple answer to whether mixtures, sequences or rotations are ‘better’

1. Very effective insecticides are needed to favour mixtures
2. High exposure of less effective insecticides favours sequences
3. Little difference between sequences and rotations

Model user interfaces:
Mixtures : https://andysouth.shinyapps.io/resistmixseq/
Rotations : https://andysouth.shinyapps.io/resistrot/
Have a screenshot of rotations UI just in case online ones don't work.
END
Figure 1. Selection within, and outside of, the normal response of an insect population. Selection within the normal distribution of insecticide tolerance at a concentration indicated by broken line (A) results in the survival of a large number of individuals. These individuals show a marginally enhanced tolerance to insecticide after selection (distribution A'). When repeatedly applied to the same population, such doses of insecticide select for several different resistance traits of minor effect that act cumulatively (polygenic resistance). Selection outside of the normal distribution of tolerance (concentration indicated by the line B) results in the selection of rare mutations that have a major effect within single genes (monogenic resistance). Such mutants show a tolerance distribution (distribution B').

The genetics and genomics of insecticide resistance

Richard H. ffrench-Constant, Phillip J. Daborn and Gaelle Le Goff