Introduction to our IR modelling

LSTM
LIVERPOOL SCHOOL OF TROPICAL MEDICINE

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Background to evolutionary modelling strategies to slow or prevent IR

Most seminal work on IR modelling done in 1980s by (among others)

- **Chris Curtis**
- **Ric Roush**
- **Bruce Tabashnik**
- **Fred Gould**
- **John McKenzie**

Now (thanks to IVCC support) just starting up where they left off…. Use modern computer power particularly for extensive sensitivity analyses

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Example of sensitivity analysis

The use of insecticide mixtures as a strategy to slow IR

- **Curtis, C. F. (1985). "Theoretical models of the use of insecticide mixtures for the management of resistance." *Bulletin of Entomological Research* 75(2): 259-265.**
- **Levick, B., A. South, I.M Hastings (2017). "A Two-Locus Model of the Evolution of Insecticide Resistance to Inform and Optimise Public Health Insecticide Deployment Strategies." PLOS Computational Biology 13(1): e1005327.**

Sensitivity analyses based on these parameter distributions

Table 4. Variables used in the main text, Figures and Tables. Their definitions, the corresponding symbols used in Equations, and their parameter distributions used for sensitivity analysis.

Variable name	Definition	Symbol	Parameter distribution (uniform unless stated)
start_freq_allele1 start_freq_allele2	Starting frequency of resistant allele at locus 1 and 2.	n/a	0.0001–0.1 (log uniform)
exposure	Proportion of female mosquitos exposed to insecticide.	A (Table 1)	0.1–0.9
male_exposure_prop	Male exposure to insecticide as proportion of female exposure.	n/a	0–1
effectiveness_ins1 effectiveness_ins2	Proportion of SS mosquitoes killed after contact with insecticide 1 or 2	φ_A^{SS1}, φ_B^{SS1} (Table 2)	0.3–1.0
dominance_allele1 dominance_allele2	Dominance of resistance at locus 1 and 2	h_A, h_B (Table 2)	0–1
rr_restoration_ins1 rr_restoration_ins2	The ability of the RR genotype to restore the fitness that has been reduced by the insecticide	n/a	0.2–1
correct_mix_deploy	Percentage of insecticide treatment that is deployed correctly.	n/a	0.5–1

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Decision tree….

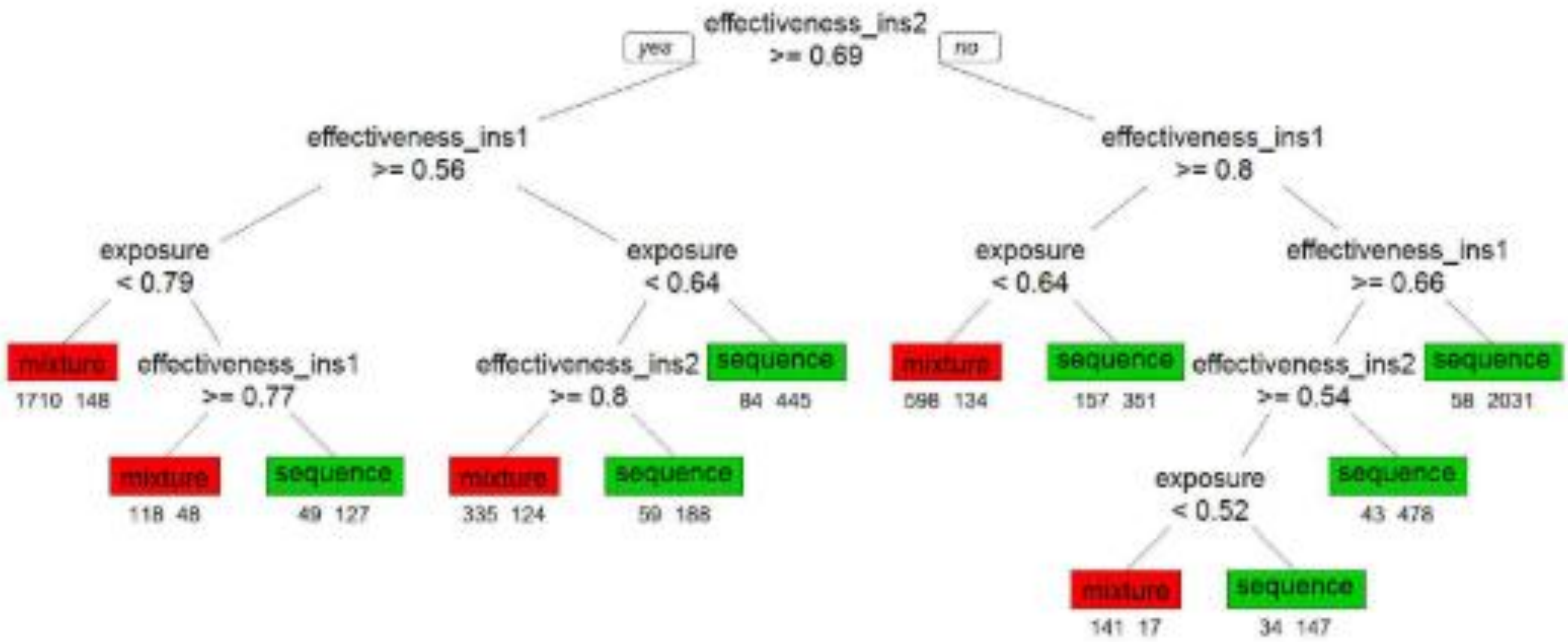

Fig 8. Classification tree from the sensitivity analysis showing under what circumstances sequential deployment is superior to using mixtures, or *vice versa*. The decision nodes indicate whether to move to the left (if the statement is true), or to the right (if the statement is false). The final classification boxes are shaded red if mixtures are the most favoured outcome having followed that decision path, and are shaded green if sequential use if favoured. The numbers below each classification box are the number of simulations in that box favouring Mixture on the left and Sequence on the right. (A) Mixtures are deemed superior to sequential deployment if their time to resistance is longer

Rotations

Widely used in agriculture. Why?

- **Different insecticides for different stages (caterpillar, then adults)… insecticides may differ in their effectiveness against stages.**
- **[if both insecticides applied in a single generation >> equivalent to a mixture]**
- **Reduced environmental impact**
- **Also putative strategy to prevent/slow evolution of IR**

>>>> modelling evidence for this appears weak

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Now modelling rotations

Key questions:

- **How much better are rotations than sequential use… are they always/never better and, if so, under what circumstances?**
- **Fitness costs and/or immigration from refugia are presumably very important in allowing IR to decline when insecticides rotated out of the sequence.**
- **Implementation: rotate every year, second year, third year etc. Can we use cheap one for 3 years, then one year of expensive one, etc?**

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Our objectives

We want to reflect beliefs and policy agendas of the entomology, insecticide deployment and IR-management communities

Need you to guide us about:

- **Key policy/implementation questions**
- **Plausible parameter values**

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