Mixtures for Insecticide Resistance Management: Exploring Dosage, Cross Resistance, And Pre-Existing Resistance.

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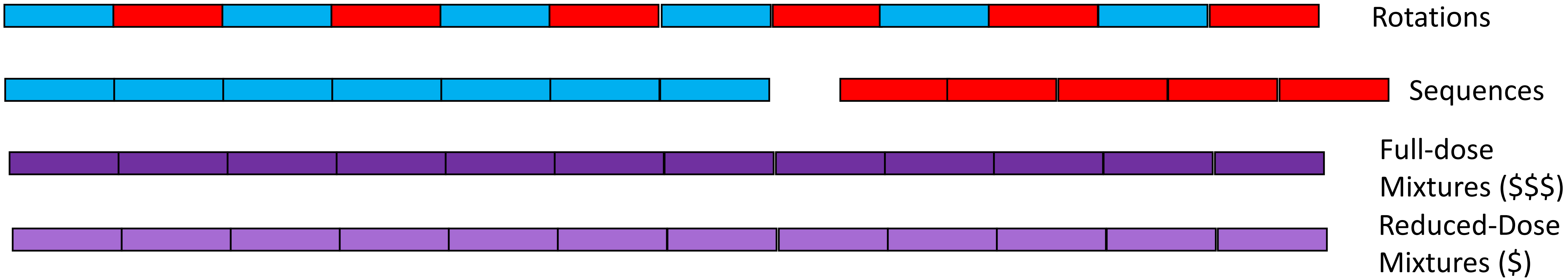
Intro: Insecticide Resistance and Vector Control

- Insecticides are the main tool to control vector-borne diseases: Long lasting insecticide-treated nets (LLINs) & IRS Indoor Residual Spraying (IRS)
- Evolution of insecticide resistance (IR) → Insecticide Resistance Management (IRM).

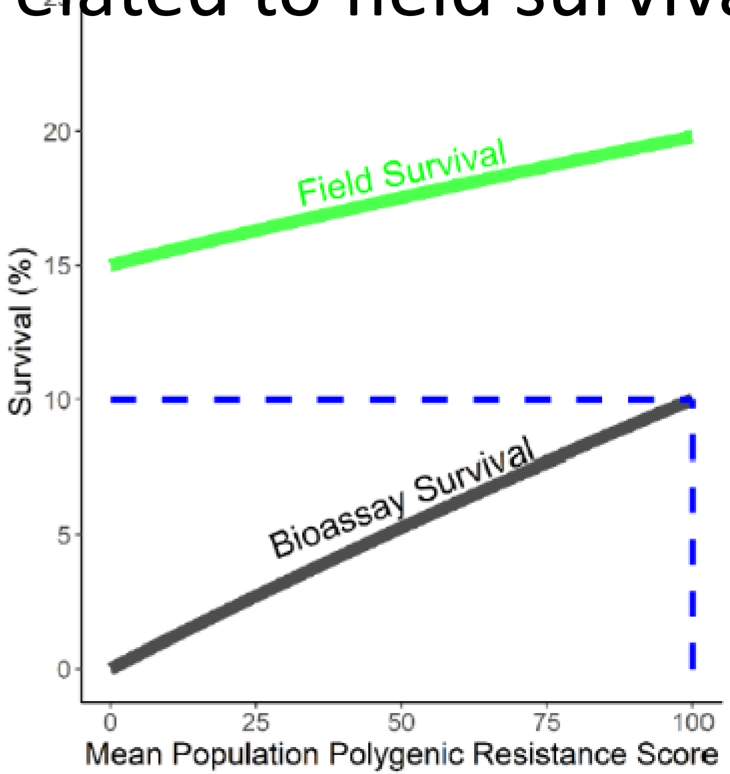


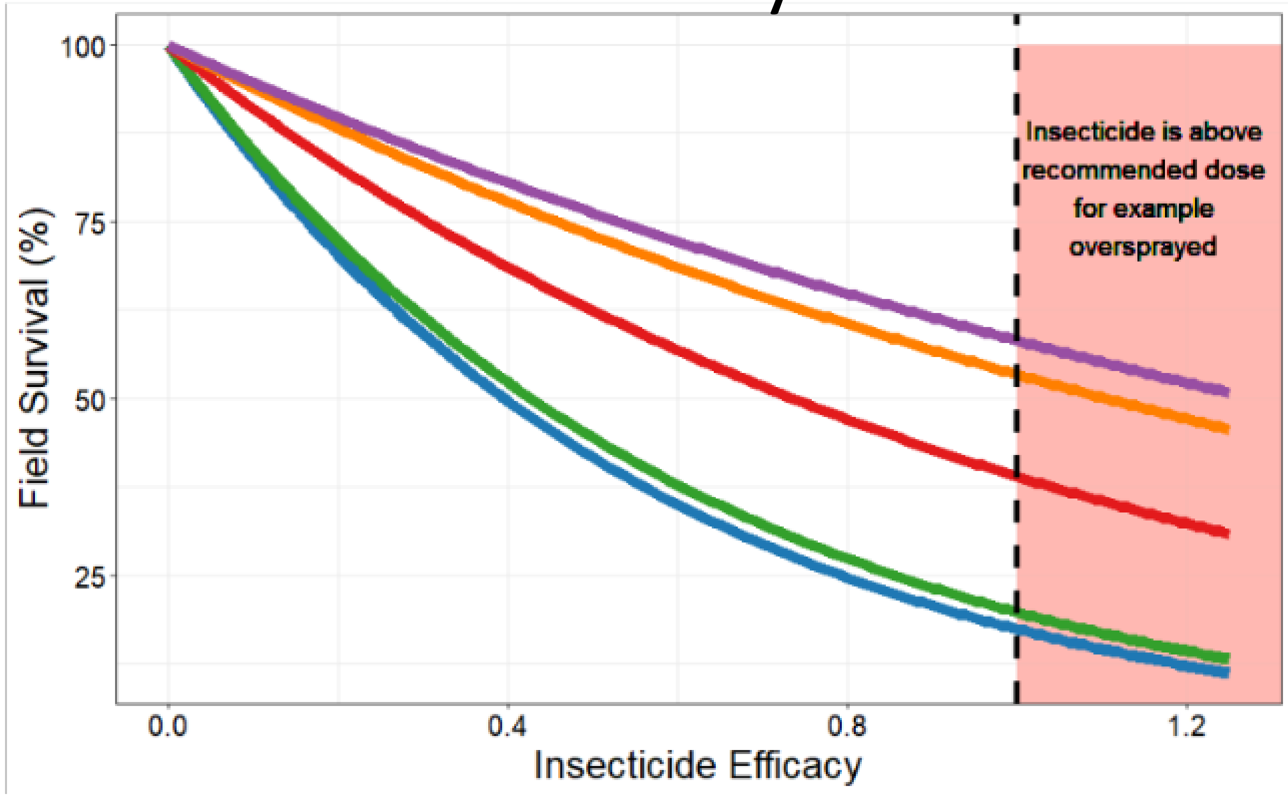
- Most models assume monogenic resistance [SS, RS, RR].
- What if we assume polygenic resistance [many genes]?

Model Overview 1: Quantifying Resistance

Need to quantify the “amount of resistance” → “Polygenic Resistance Score”[1] → classically quantitative trait → measurable in bioassays.

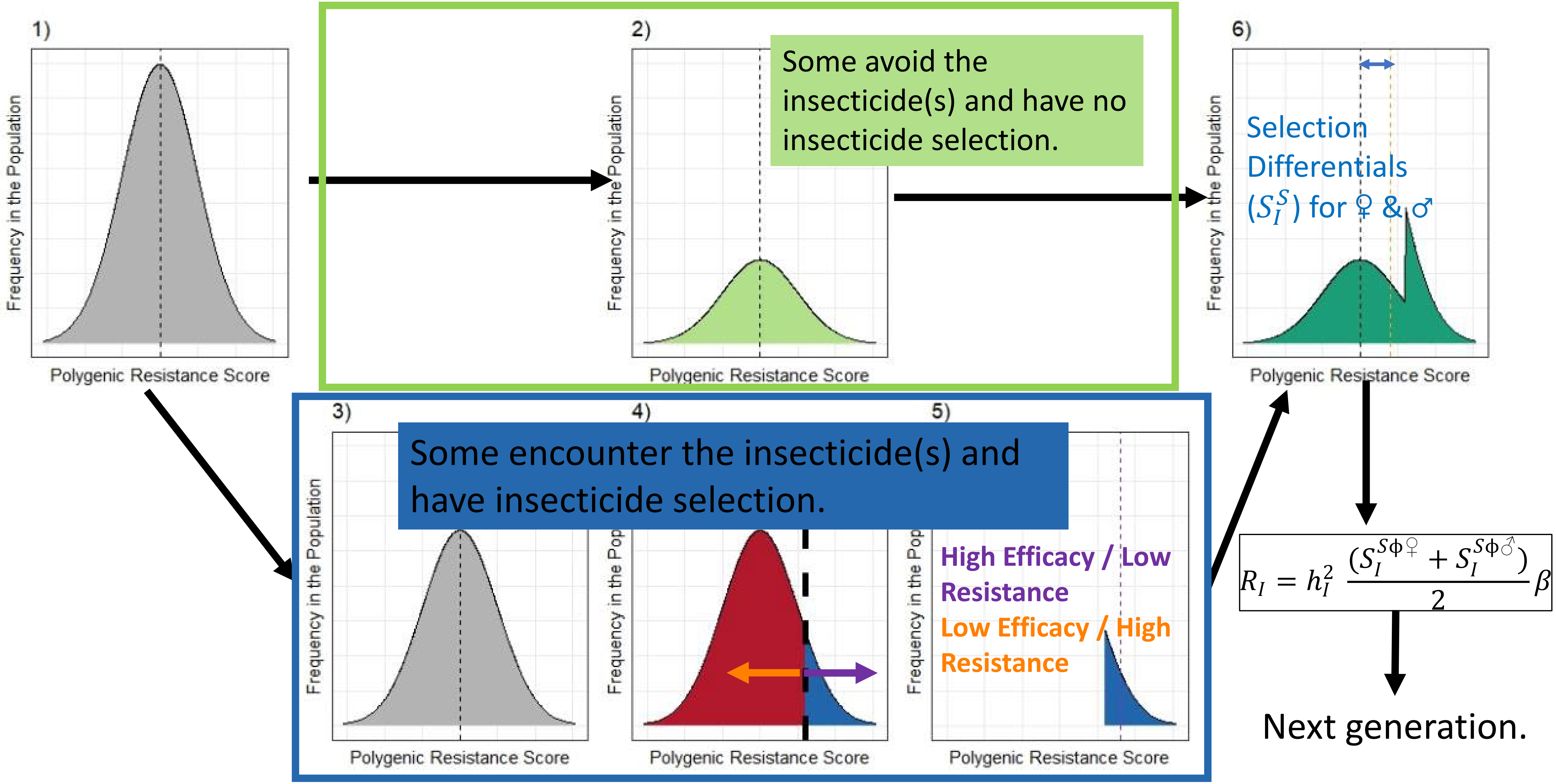
Bioassay survival is related to field survival → Then convert to allow for insecticide efficacy.



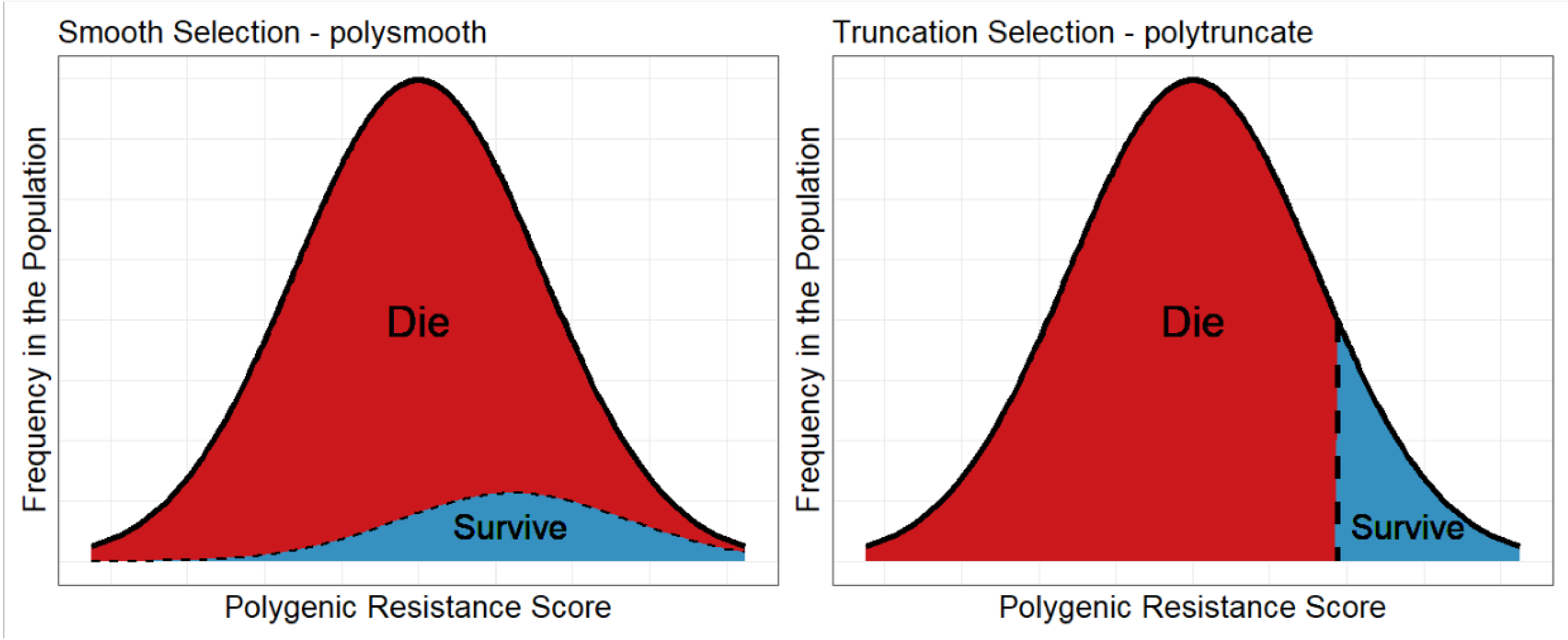


1. Hobbs, N. P., Weetman, D., Hastings, I. (2023). Insecticide resistance management strategies for public health control of mosquitoes exhibiting polygenic resistance: A comparison of sequences, rotations, and mixtures. *Evolutionary Applications.*

Model Overview 2: Selection Process



Model Overview 3: Implementing Selection



Will be showing results from both approaches grouped together.

Simulation Design: Initial Resistance and Dosing

Current next generation (mixture) LLINs are pyrethroid + novel insecticide → how does this impact the mixture effectiveness?

Deployment Strategy
Novel Insecticide Monotherapy
Pyrethroid Insecticide Monotherapy
Mixture (Full Dose): 100% Efficacy
Mixture (Half-Dose): 75% Efficacy
Mixture (Half-Dose): 50% Efficacy

X

Resistance to the Pyrethroid (Bioassay Survival %)
0
10
50
80

X

Ecological/ Biological Parameter Space:

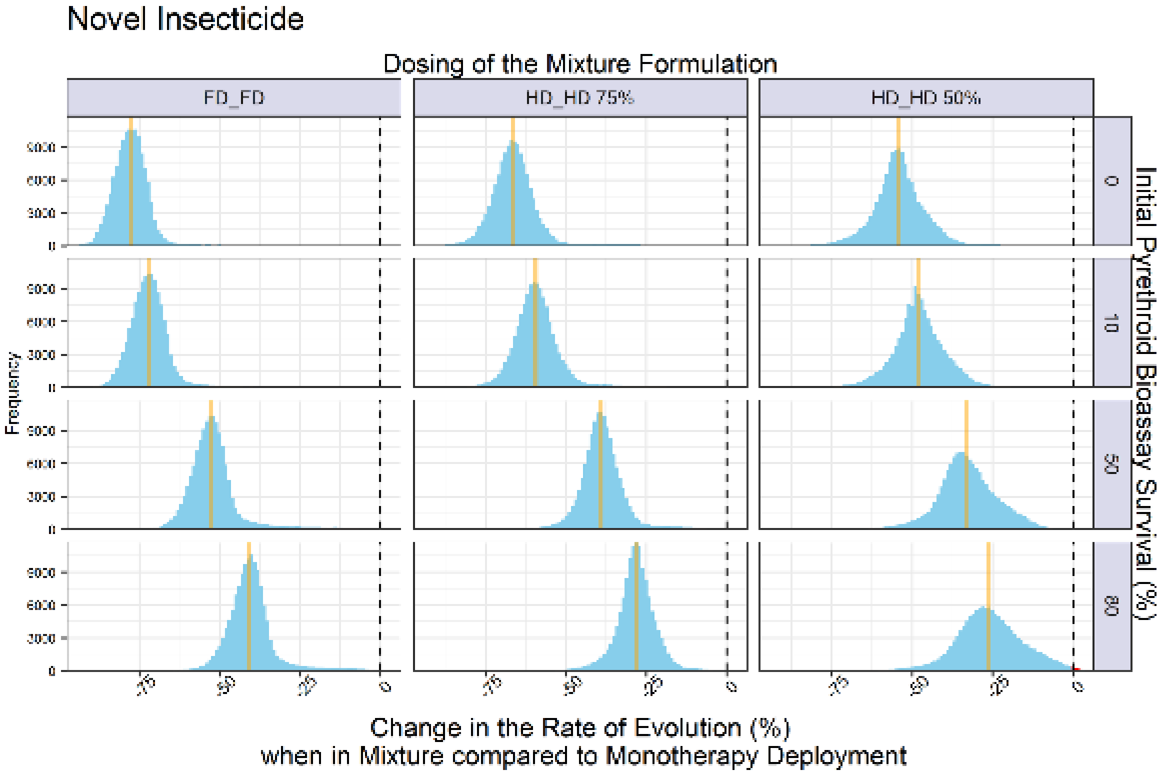
e.g.: Heritability, Encounter Rates, Dispersal, Coverage.

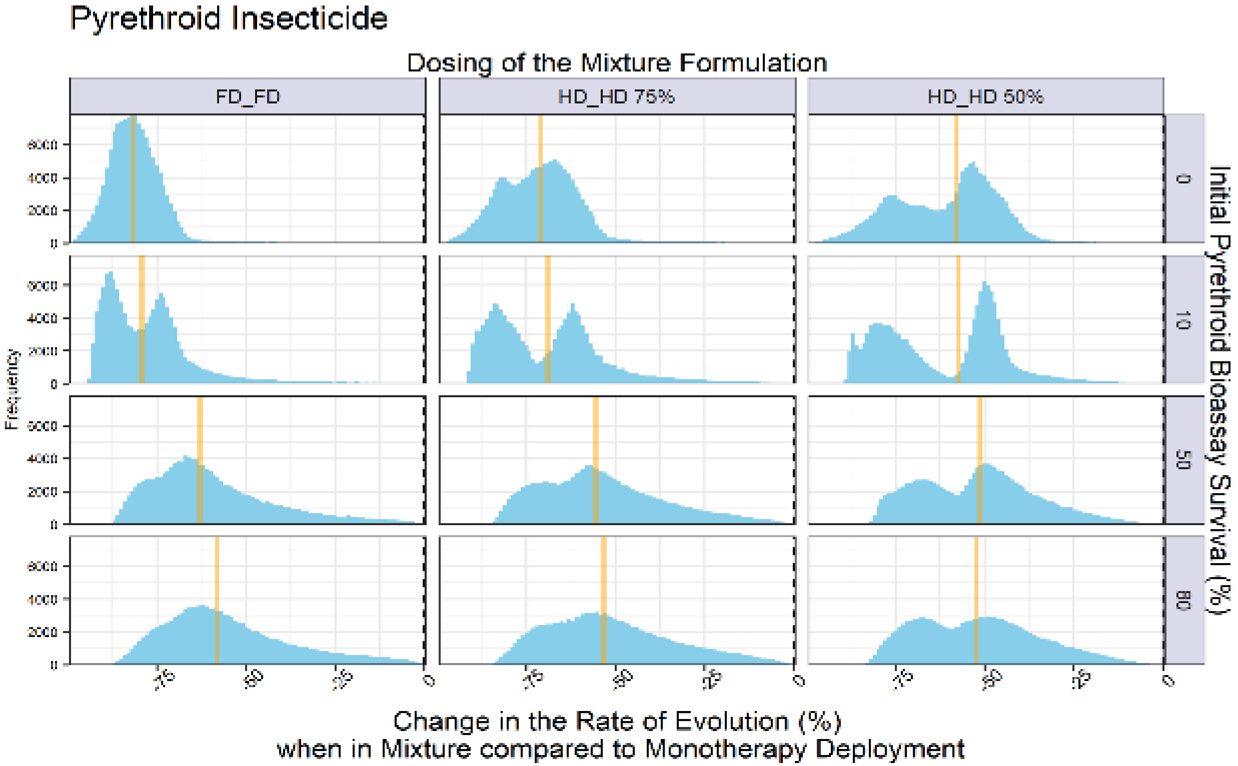
↓

Outcomes:

Change in Novel in Mixture vs Novel Monotherapy & Change in Pyrethroid in Mixture vs Pyrethroid Monotherapy after 20 years continuous deployment.

Results: Initial Resistance and Dosing





Benefit of novel in mixture decreases if:

- Resistance to pyrethroid increases.
- Dose of the mixture decreases.

Benefit of pyrethroid in mixture decreases if:

- Resistance to pyrethroid increases.
- Dose of the mixture decreases.

<u>Policy Implication:</u>

Early deployments of mixtures most effective (IRM); but IRM least needed.

Hobbs et al., unpublished.

Median Value

Simulation Design: Cross Resistance and Dosing

Cross resistance is implemented in the model as a simple correlated response[1] : $R_J = h_J^2 \frac{(s_J^S + s_J^S)}{2} + \alpha_{IJ} R_I$

Deployment Strategy
Rotation [i → j → i → j →…]
Mixture (Full Dose): 100% Efficacy
Mixture (Half-Dose): 75% Efficacy
Mixture (Half-Dose): 50% Efficacy

X

Cross Resistance (α_{IJ})
-0.5 to 0.5

X

Ecological / Biological Parameter Space:

e.g.: Heritability, Encounter Rates, Dispersal, Coverage.

↓

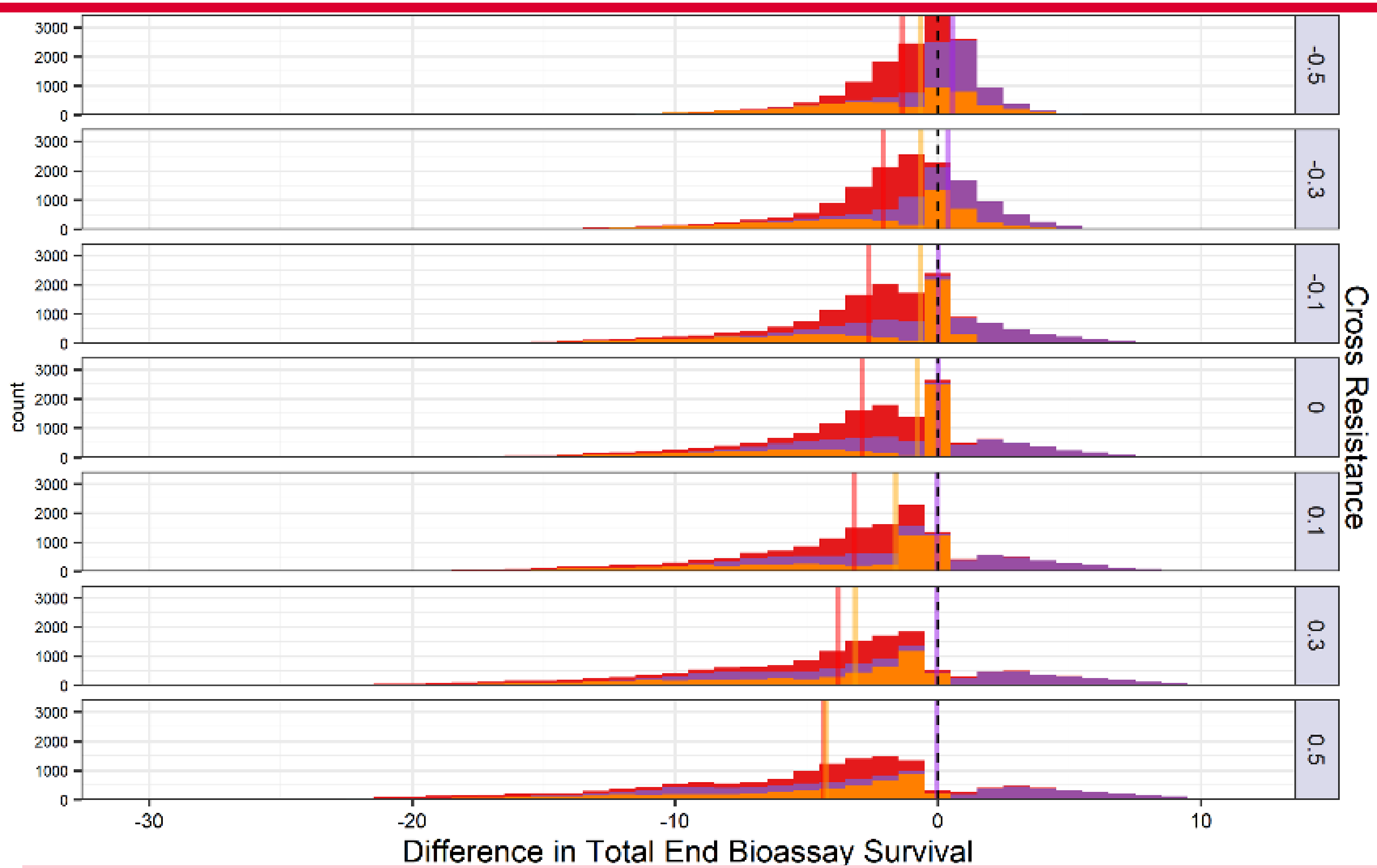
Outcome:

Total Resistance Rotation vs Total Resistance Mixture after timeframe of ~20 years.

Caveat: all insecticides start at 0% bioassay survival [easiest to implement cross resistance under this scenario]

1. Hobbs, N. P., Weetman, D., Hastings, I. (2023). Insecticide resistance management strategies for public health control of mosquitoes exhibiting polygenic resistance: A comparison of sequences, rotations, and mixtures. *Evolutionary Applications.*

Results: Cross Resistance and Dosing



Mixture (Full Dose): 100% Efficacy

Mixture (Half-Dose): 75% Efficacy

Mixture (Half-Dose): 50% Efficacy

- Half-Dose (50% Efficacy) often worse than deploying insecticides in rotation.
- Full-Dose Mixtures >> Rotations when positive cross resistance.

Policy Implication:

- Maintaining high doses of insecticides in mixture important.

Hobbs et al: unpublished

Conclusions

- Implementing IRM before high levels of resistance is important. Greatest benefit when it is least needed/required.
- Maintaining high doses in mixture important.
- Cross resistance a bigger issue for rotations (monotherapies) than mixtures (unless reduced dose).

Acknowledgements

Ian Hastings
David Weetman

Vector Informatics and Genomics Group @ LSTM

LSTM
LIVERPOOL SCHOOL OF TROPICAL MEDICINE

MRC Medical Research Council