Exploring the epidemiological impact of insecticide resistance

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(Note: this is ongoing research and is as yet unpublished, so results and conclusions should not be circulated as definitive)

- 1.2 billion LLINs into Africa in last 10+ years
- Documented spread of pyrethroid resistance across the continent
- And yet…….no clear signal of LLIN failure due to resistance

Aim is to illustrate some ongoing research that might help explain why:

(1) Does realistic exposure to nets still cause mortality in highly resistant mosquitoes?

(2) Are there sub-lethal effects of exposure that could disrupt transmission?

(3) How do single exposure events compound across the lifetime of the mosquito?

Lab strains from Vector Control Research Laboratory (VCRL), Johannesburg

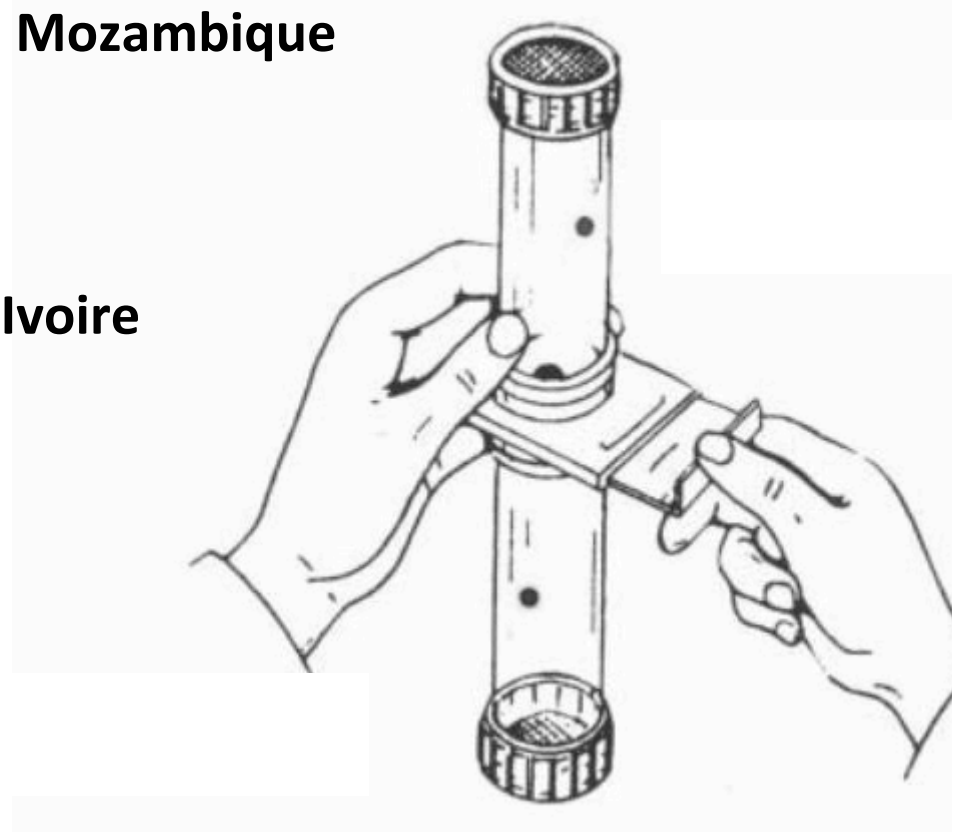
Anopheles arabiensis (SENN-BASE and SENN-DDT)
An. funestus (FUMOZ-BASE and FUMOZ-R)
An. gambiae (TONGS)

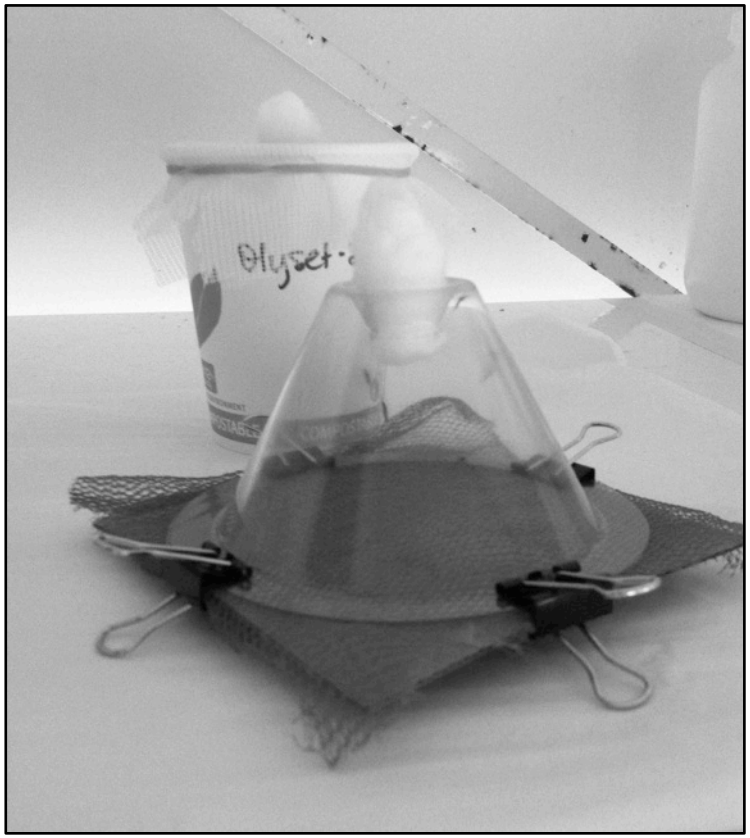
Field strains from CISM, Manhiça, Mozambique

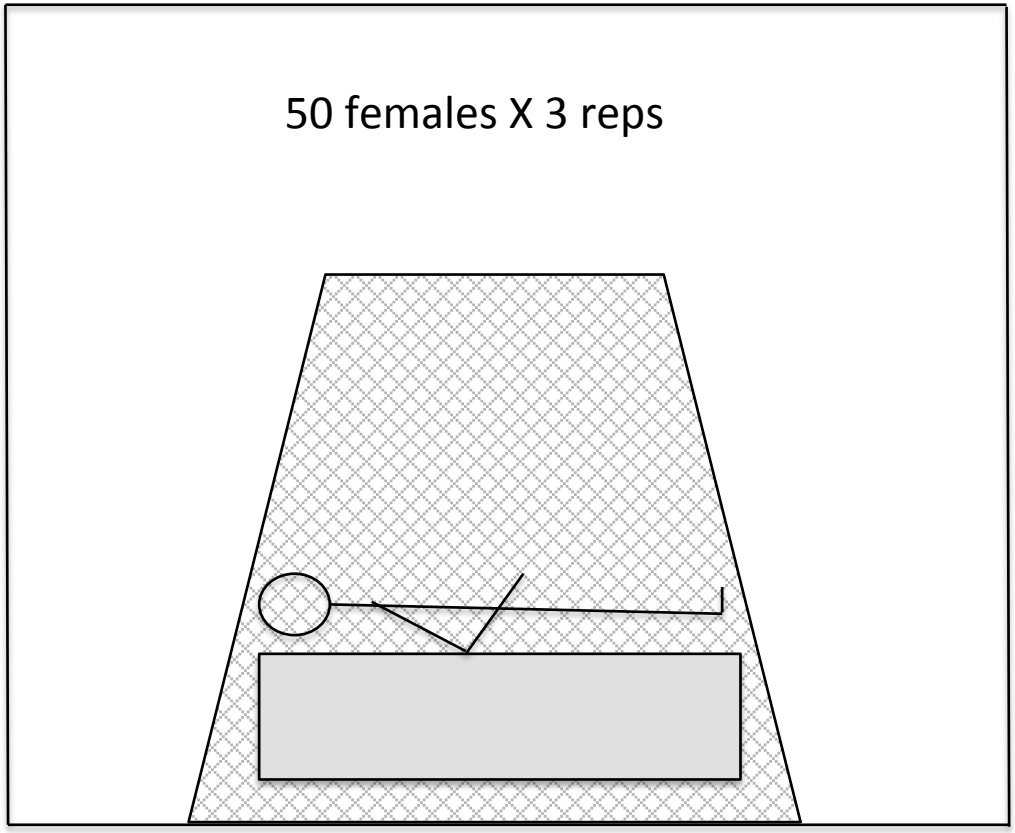
An. funestus

Open field setting in Mbe, Cote d'Ivoire

An. gambiae ss



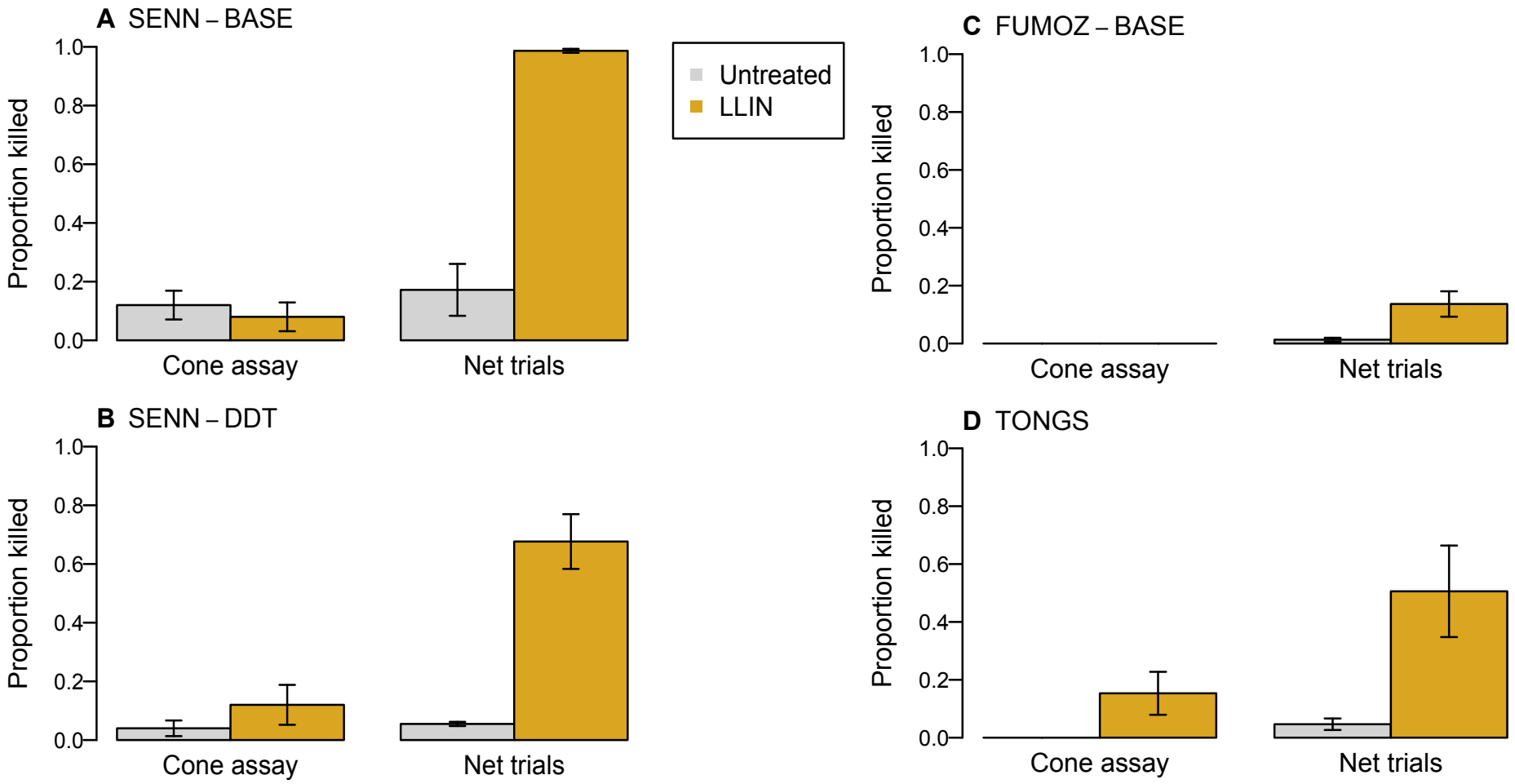


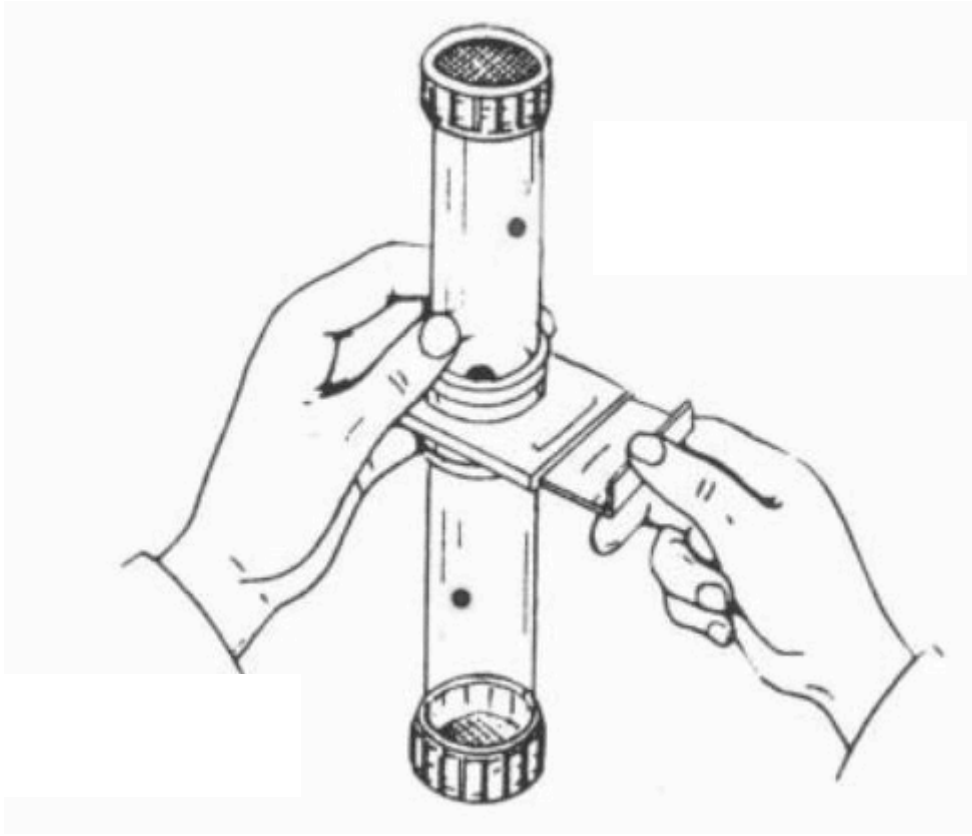


3 minute standard
'forced exposure'

1h free ranging around host
under the same LLIN

Mortality 24h after exposure to LLIN using 3min cone test, or 1h free ranging test

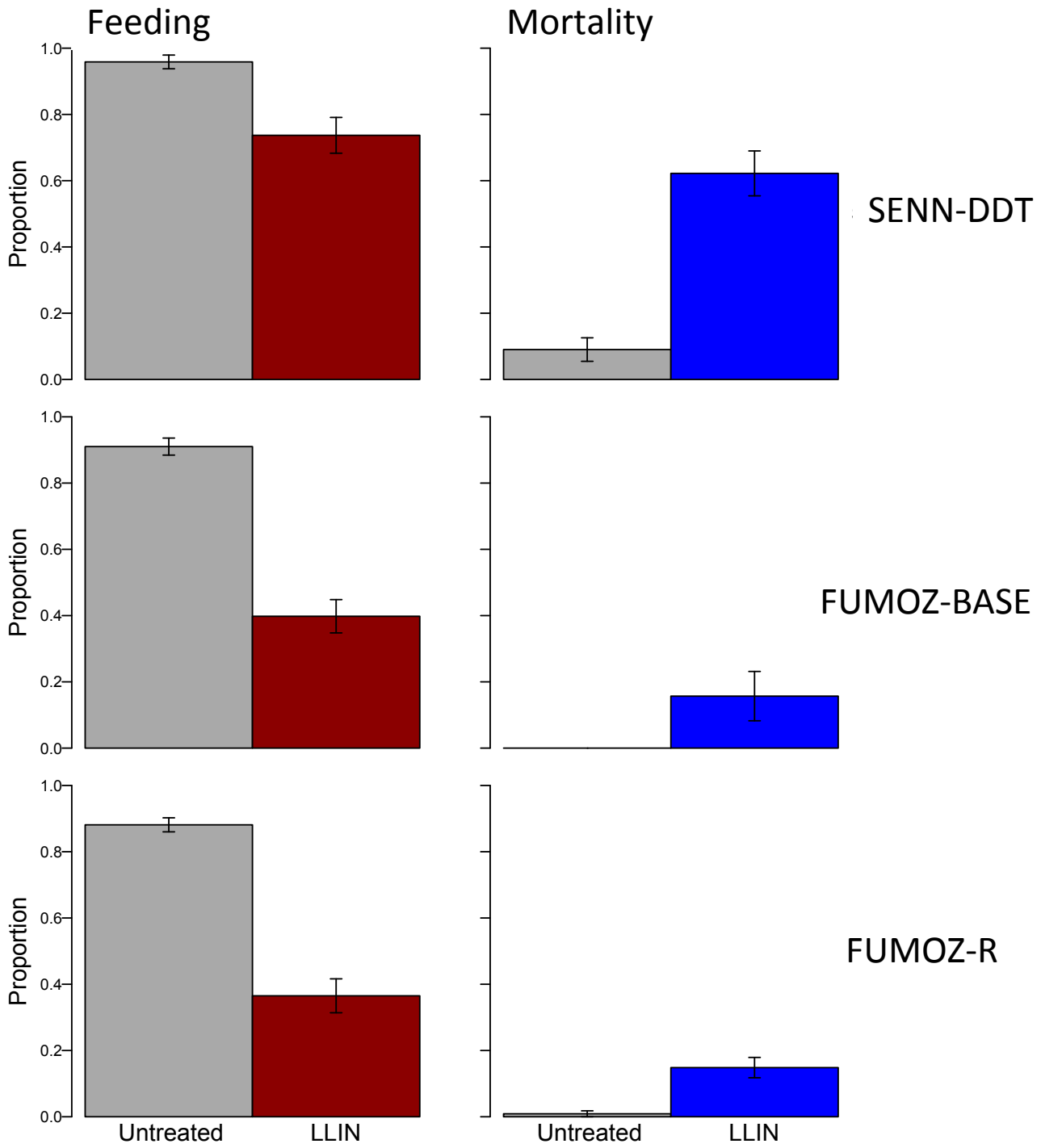


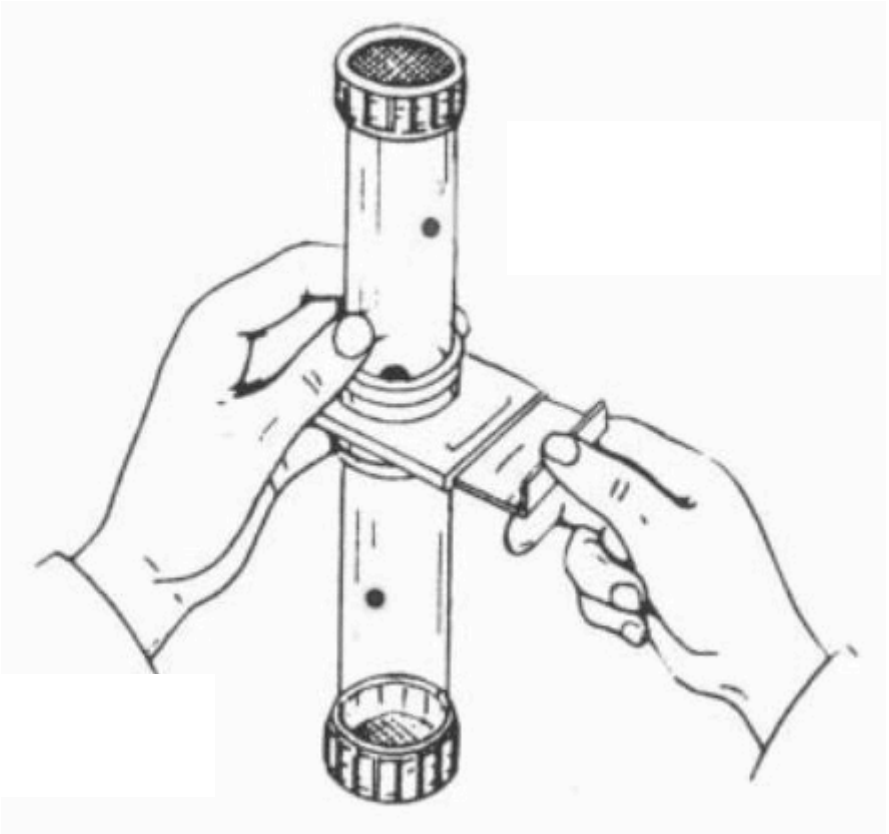


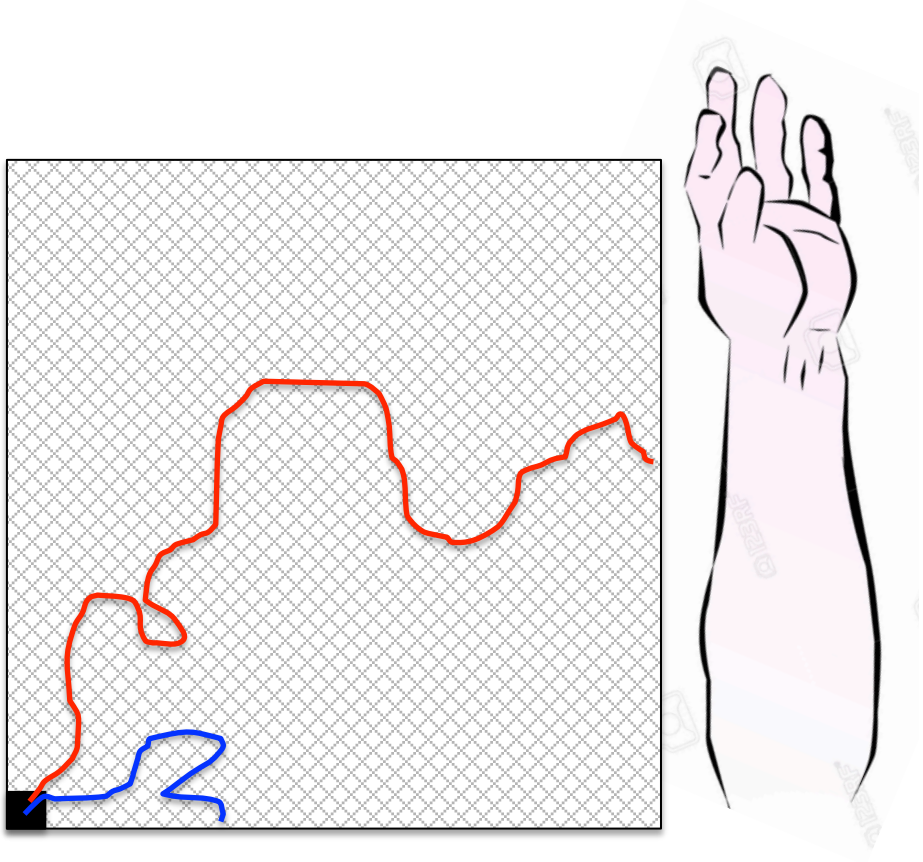
Forced exposure to LLIN using WHO tube

Live (and not knockdown mosquitoes) transferred to cups and offered blood source. Proportion blood fed recorded after 5 min.

Blood feeding and 24h mortality following short-term exposure to LLIN



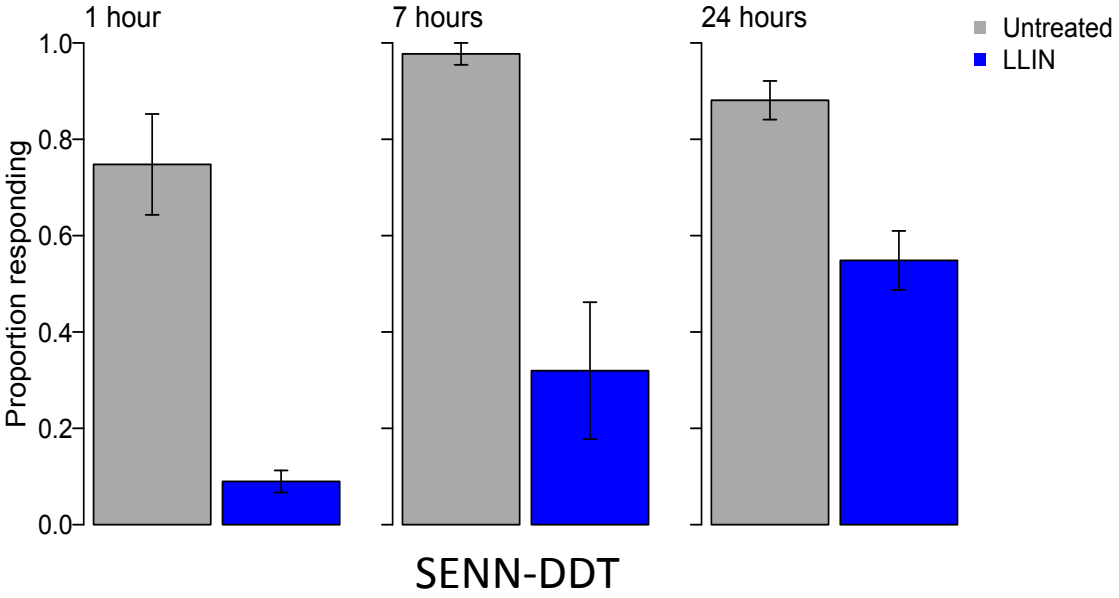




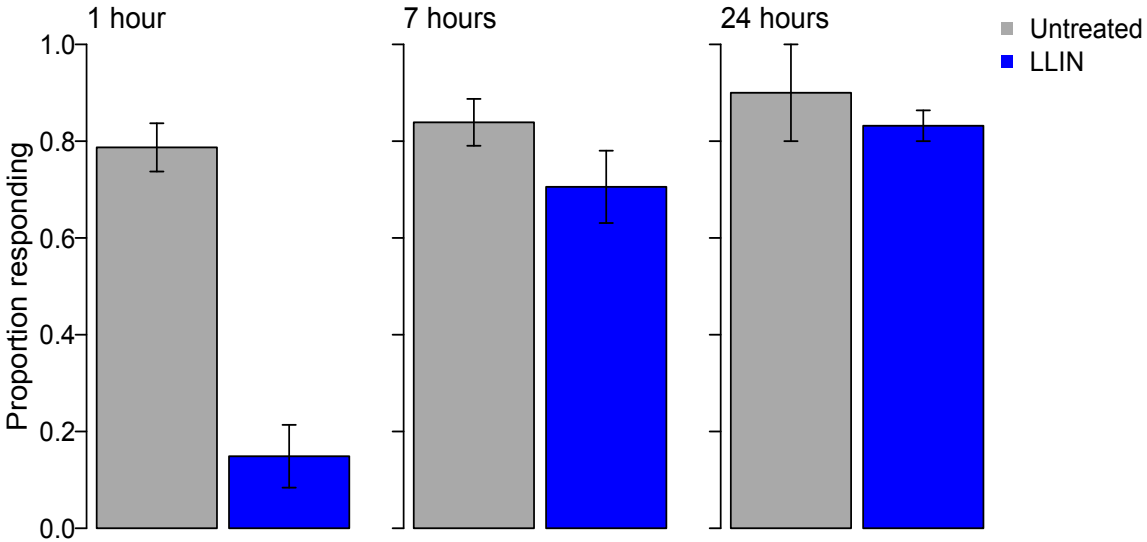
Forced exposure to LLIN using WHO tube

Live (and not knockdown mosquitoes) introduced singly into cage at different time points and proportion recruiting to host recorded.

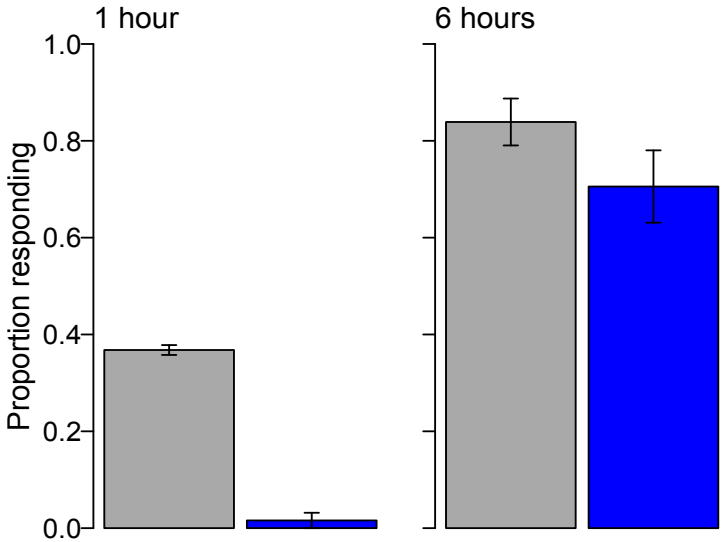
Proportional response to host cues following exposure to LLIN



SENN-DDT

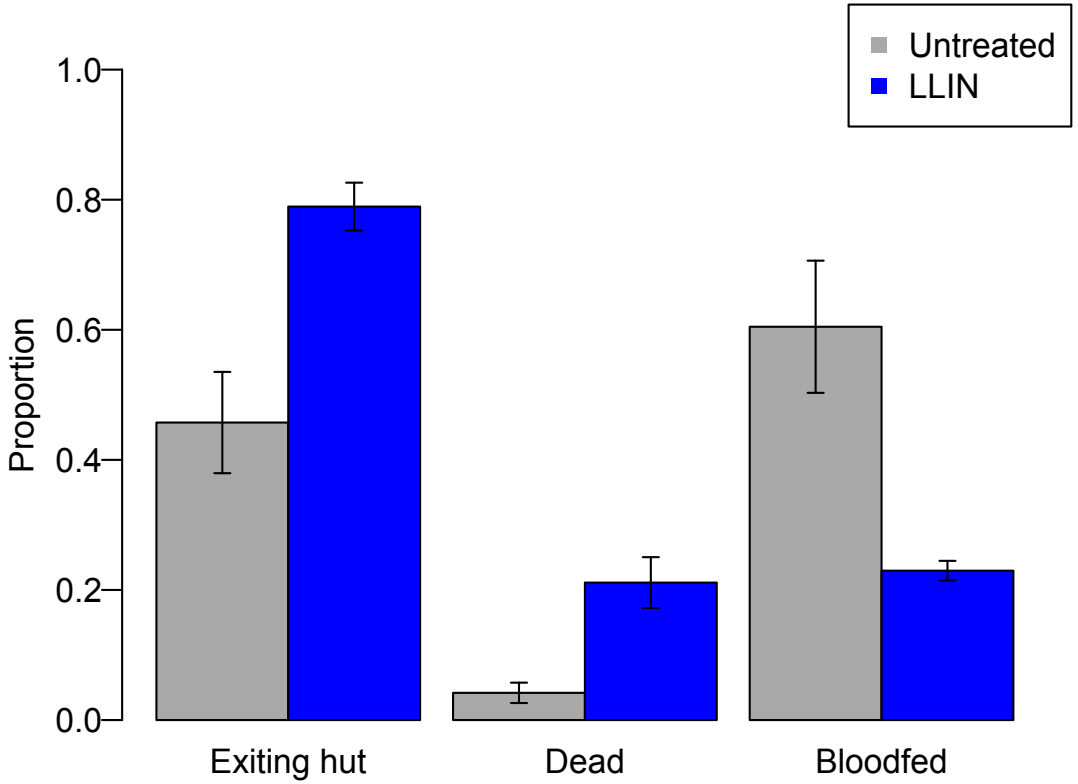


FUMOZ-R



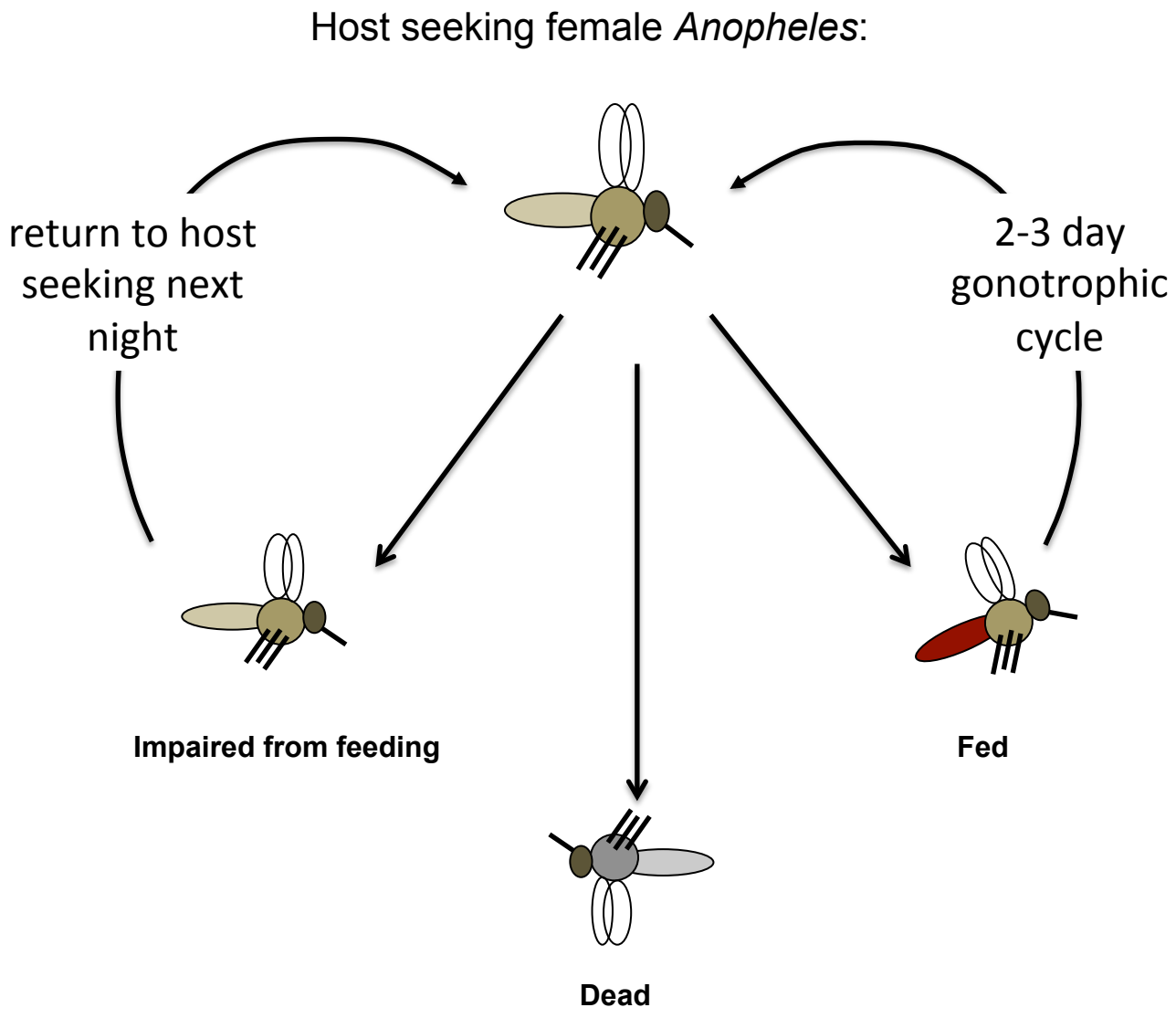
Field caught *An. funestus* (Mozambique)

Experimental hut studies at M'be (Bouake, Cote d'Ivoire) comparing LLIN (Permanet 2) *vs* untreated net



Strain	**Slope** (SE)	**LD_{50}** (95% CI)	**RR_{50}** (95% CI)
KISUMU	1.3 (0.18)	0.0145 (0.0087 - 0.022)	
M'bé	1.9 (0.23)	27.88 (19.18 - 33.62)	1778 (1348.34 - 2345.53)

Feeding cycle model to estimate impact of resistance on transmission potential



Feeding cycle model to estimate impact of resistance on transmission potential

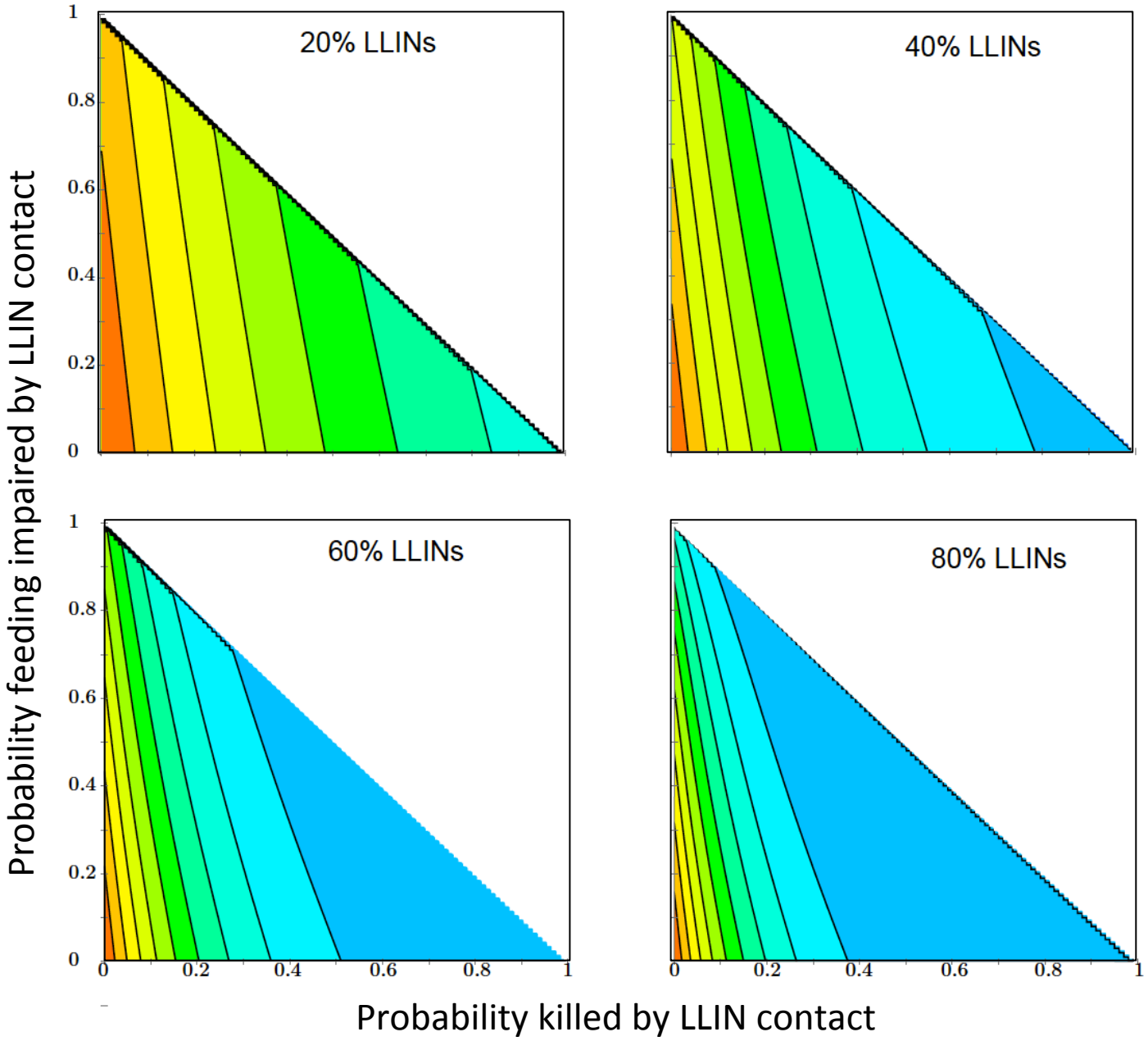
- Average number of infectious bites across the lifetime of a mosquito

- Relative Transmission Potential = the average number of infectious bites across the lifetime of a vector relative to the number of infectious bites if there was no LLIN-related mortality or feeding impairment.

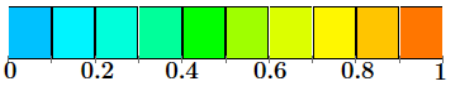
  RTP = 0 as if fully susceptible

  RTP = 1 is equivalent to baseline transmission in the absence of LLINs (or being totally resistant).

Dead



Relative Transmission Potential :



Summary

- Realistic contact with LLINs still causes significant mortality of resistant mosquitoes.

- Even if they don't die, there are effects on feeding and host searching that can last several hours.

- Effects are consistent across species, strains, mechanisms of resistance, lab vs field etc.

- When these effects are compounded across the lifetime of a mosquito, they greatly reduce the functional significance of resistance for transmission.

- However, the effect of resistance increases non-linearly as LLIN coverage falls and/or as impact of the LLIN declines further (could be intensification of resistance or ageing of the LLIN).

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