Epidemiological effectiveness of ITNs in the presence of pyrethroid resistance

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Background
Insecticide treated nets (ITNs) have become the primary intervention against malaria vectors, partially because the insecticide, typically a pyrethroid, renders them effective even if holed. Studies have shown that ITNs kill a much lower proportion of host seeking mosquitoes in areas with high pyrethroid resistance compared to areas with susceptible vector populations. The epidemiological implications were examined using the OpenMalaria [1] modelling platform.

Material & methods
We used experimental hut data, where holed nets were tested in Ladi (with pyrethroid resistance) and Malanville (no resistance) [2], to choose parameter values for the effects of holed ITNs on deterrence, pre- and post-landing killing of anopheles mosquitoes. We used older data from elsewhere to estimate values for intact nets [3]. We then evaluated, through simulation, the impact of a mass distribution of ITNs in terms of malaria episodes prevented during the effective life of the net distribution, depending on pyrethroid resistance, and pre-intervention entomological inoculation rate (EIR). The effective life was defined as the number of years that the number of prevented episodes was above half that of the year with the maximum effect.

Results
ITNs reduced the number of episodes relative to the situation without ITNs in the first years after distribution (Fig. 1). The effect then dropped back steeply to above pre-intervention levels, and gradually levelled off.

With low transmission, initially ITNs had as much effect as resistant as for susceptible mosquitoes, but, as ITNs decayed physically and chemically and disappeared, the effect started to wane earlier for resistant than for susceptible mosquitoes.

For higher transmission settings, ITNs were generally less successful in reducing the relative number of episodes. In the first year, ITNs reduced the number of episodes less with resistant than with susceptible mosquitoes, and here also, the effect started to wane earlier for resistant mosquitoes.

The impact was thus negatively related to the EIR (Fig. 2). At a low EIR, with a resistant mosquito population, the impact was 70–80% of that with a susceptible mosquito population (Fig. 3). With increasing transmission levels, the ratio first became worse (as low as 20%), and then levelled off at high EIR levels, depending on mosquito host searching. However, at these high EIR levels, ITNs prevent few episodes, even with susceptible mosquitoes (Fig. 2).

When intact nets were modelled with a higher pre-prandial killing of resistant mosquitoes (blue lines in Fig. 1–3), impact ratios were consistently higher (Fig. 3).

Discussion
Pyrethroid resistance strongly reduces the impact of a mass ITN distribution in settings with medium to high pre-intervention transmission levels. However, intact ITNs still reduce incidence in the first years after distribution in settings with resistant mosquitoes. With low transmission, ITNs still have 80% impact despite strong resistance. In areas with high resistance and high transmission, nets would need to be accompanied by non-pyrethroid based interventions.

Data for intact nets were two decades old and from a different area. The suggested importance of the effects of intact nets on the relative impact calls for hut studies to include both intact and deliberately holed nets. Also, but data for a range of physical net damage, for quantifying the importance of net tear-resistance, increase in relevance as resistance spreads.

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References

Figure 1 - Ratio of annual episodes with an ITN mass distribution to without ITNs
ITNs were distributed to 80% of the people at the beginning of year 6 in settings with susceptible (green), resistant (red), and resistant mosquitoes where intact nets had a higher pre-prandial killing effect (blue). There are 11 lines of each colour in each panel, representing malaria model variants.

Figure 2 - Episodes prevented during the effective life of a mass distribution (impact) of ITNs
The number of prevented episodes was the episode difference with and without ITNs. Values are averages over 14 malaria model variants. Line colours as in Fig. 1.

Figure 3 - Ratio of ITN impact with resistant to with susceptible mosquitoes
Legend as in Figs 1 & 2, except that lines show the ITN impact for a setting with resistant (red), and resistant mosquitoes where intact nets had a higher pre-prandial killing effect (blue), divided by the impact for susceptible mosquitoes.