A new perspective on the application of mosquito repellents

Great effort is expended in understanding the effect of malaria control interventions on the *Plasmodium* parasite and its anopheline mosquito vector. However, no intervention will work unless it is properly used, and human behaviour is not always carefully considered during controlled trials of vector control interventions. A study in *The Lancet Infectious Diseases* by Vincent Suydts and colleagues showed that community-scale distribution of free topical mosquito repellents in Cambodia did not reduce malaria transmission because of human behaviour. In the study area, a high proportion of malaria vectors bite outdoors in the evenings when people are active; therefore, theoretically a mosquito repellent could prevent malaria in this setting. However, even though the repellent was freely available and highly effective, the authors also did a mixed-methods study and discovered that only 8% of participants regularly used it, despite 70% reporting daily use. User compliance is difficult to measure in trials and the study team used parallel observational studies to show disparity between reported and actual compliance with the intervention. Low compliance resulted in a non-significant association between repellent allocation and malaria risk. This study is the largest and most comprehensive controlled study done to measure the effect of mosquito repellents for additional malaria control when used in conjunction with long-lasting insecticidal nets.

This cluster randomised trial included roughly 25,000 participants in each study group (picaridin mosquito repellent vs identical placebo), and regularly screened around 2500 participants per group for malaria with sensitive molecular diagnostics. This robust design gives strong evidence that distribution of effective personal protection tools do not necessarily translate into protective efficacy against clinical malaria at an individual or community level. If compliance with repellents is suboptimum and requires substantial behavioural change by users, repellents are unlikely to be selected by donors for inclusion in programmatic malaria control.

Topical insect repellents are excellent tools for personal mosquito bite prevention with a long history of use and excellent safety profiles. Although several controlled trials have shown that repellents do prevent malaria, a systematic review and meta-analysis showed no overall trend in protective efficacy. Topical repellents are an imperfect vector control tool simply because they must be used frequently, inevitably resulting in inconsistent compliance and incorrect application. Even soldiers who are well educated about repellents did not apply them daily if they did not perceive a biting nuisance or risk of disease.

Massive scaling up of malaria vector control has averted an estimated 663 million clinical cases of malaria in Africa through widespread free or subsidised distribution of long-lasting insecticidal nets that kill mosquitoes attempting to feed on people sleeping under them and spraying of dwellings with residual insecticides that kill mosquitoes resting inside houses (68% and 11% of cases averted, respectively). However, in many malaria endemic regions including South America and southeast Asia, malaria vectors have a high preference for outdoor and early evening feeding which means that they do not often come into contact with either long-lasting insecticidal nets or residual insecticides used indoors. Worryingly, in some areas of Africa, the proportion of control achievable through residual insecticides and long-lasting insecticidal nets might decline as vectors evolve resistance to insecticides or adapt to bite during the evenings or mornings when people are not under their long-lasting insecticidal nets because this is the only time they can find their preferred blood host unprotected.

Therefore, a method to prevent malaria transmission outside of sleeping hours is urgently needed for malaria elimination: ideally one that will kill mosquitoes. However, there remains an absence of existing tools with this capacity. Fortunately, several tools are in development with good potential for future implementation, including toxic sugar baits and killing stations baited with synthetic human odours. There is also renewed interest in the use of larval source management to kill immature mosquitoes.

Although the large-scale distribution of topical repellents might not fill the requirement for community malaria protection outside of sleeping hours, repellents are still useful. Providing repellents to specific risk groups that potentially contribute disproportionately to malaria transmission and development of longer-lasting personal protection measures needing minimum
compliance (eg, insecticidal clothing that protects for 3–6 months\textsuperscript{17}) should be pursued. Additionally, travellers to malaria endemic areas are strongly advised to use repellents because they are highly effective bite prevention tools when used correctly and consistently.

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