HHS Public Access

Author manuscript

Lancet. Author manuscript; available in PMC 2019 August 18.

Published in final edited form as:

Lancet. 2018 August 18; 392(10147): 534–536. doi:10.1016/S0140-6736(18)31817-8.

New opportunities for malaria vector control

John E Gimnig and **Eric Ochomo**

Centers for Disease Control and Prevention, Division of Parasitic Diseases and Malaria, Atlanta, GA 30329, USA (JEG, EO); and Kenya Medical Research Institute, Center for Global Health Research, Kisumu, Kenya (EO) hzg1@cdc.gov

Owing to the scale up of malaria control interventions, malaria morbidity and mortality have declined, with much of the decline attributed to the scale up of longlasting insecticidal nets (LLINs).[1] However, the 2017 World Malaria Report[2] indicated that progress in reducing the burden of malaria has stalled and, in some countries, malaria cases and deaths are increasing. The causes of this stagnation are likely multifactorial and include stagnant donor investment, as well as the rise and spread of insecticide resistance.[2]

The spread and intensification of resistance to pyrethroid insecticides—the only class recommended for use on LLINs before 2017—has been a particular concern in sub-Saharan Africa, which shoulders the bulk of the global malaria burden. In their clusterrandomised, controlled trial in *The Lancet*, Alfred B Tiono and colleagues[3] show that a new LLIN treated with permethrin (a pyrethroid) and pyriproxyfen (an insect growth regulator) has increased efficacy compared with a standard LLIN treated with permethrin only in reducing malaria transmission and disease, even in an area with high pyrethroid resistance. In this study conducted in Burkina Faso (where *Anopheles gambiae* is more than 80% resistant to pyrethroids), children younger than 5 years sleeping under the dualtreated LLIN had a lower incidence of clinical malaria, as measured through passive surveillance, than did those sleeping under the standard LLIN treated with permethrin alone (incidence rate ratio 0·88, 95% CI 0·77–0·99; p=0·04). In a cross-sectional survey done at the midpoint of the trial, there was no difference between groups in the prevalence of *Plasmodium falciparum* infection (odds ratio 0·93, 95% CI 0·74–1·15; p=0·50), but the prevalence of moderate anaemia was significantly lower among users of the dual-treated LLIN than among users of the standard LLIN (0·48, 0·24–0·96; p=0·04). This trial provides, for the first time, evidence of added benefit from an LLIN treated with a non-pyrethroid insecticide in combination with a pyrethroid. It comes after a trial[4] of an LLIN treated with a pyrethroid plus the synergist piperonyl butoxide, which also had a significant benefit over a pyrethroidonly LLIN in an area with high pyrethroid resistance.

These trials are welcome news for the global malaria control community, which has been raising the alarm about insecticide resistance for years.[5] The question now is for how much longer can pyrethroid-only nets be an effective malaria prevention tool in sub-Saharan Africa, where pyrethroid resistance has been detected in all major vectors, is present in

We declare no competing interests. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

nearly every country, and has progressively worsened over time?[6] Arguments against switching from pyrethroid-only LLINs to dual-treated LLINs, even in areas with high levels of pyrethroid resistance, have been the lack of epidemiological data confirming their increased efficacy over pyrethroidonly LLINs, their limited availability, and their higher cost. These recent trials[3,4] have addressed the lack of evidence, and net manufacturers have answered the call for new LLINs to address pyrethroid resistance: the WHO Prequalification team now lists five LLINs treated with piperonyl butoxide and one treated with chlorfenapyr. An LLIN treated with pyriproxyfen is currently under review by WHO.[7] A shift away from pyrethroid-only nets will probably lead other manufacturers to invest in new products. The cost of dual-treated LLINs will be more than that of pyrethroid-only nets, and with investment in malaria control stagnating over the past few years, this increased cost will probably lead to reduced coverage. However, donors such as the Global Fund to Fight AIDS, Tuberculosis, and Malaria and the US President's Malaria Initiative invested in pyrethroid-only nets when they were much more expensive. Over time, competition and the economies of scale resulted in these nets decreasing in price. The same scenario could occur with dual-treated LLINs.

Dual-treated LLINs have the potential to reinvigorate malaria vector control and to contribute to further reductions in malaria burden in sub-Saharan Africa. We now have several products for use against pyrethroidresistant mosquitoes and we must be proactive to take advantage of this opportunity. The need for an accelerated pathway to implementation of these products has already been raised.[8] Additionally, the Global Plan for Insecticide Resistance Management (GPIRM)[9] will need to be revised and updated given the rapidly changing landscape of LLINs. How are these products best deployed, not only to mitigate pyrethroid resistance but also to proactively manage resistance to the new active ingredients on the new LLINs? Although dwindling, there are some regions with vectors that remain susceptible to pyrethroid insecticides. How long can we continue to distribute pyrethroid-only nets in these areas? Or should dual-treated nets be distributed pre-emptively? Addressing these questions will require increased efforts to monitor insecticide resistance, which varies spatially and changes over time, not to mention new approaches to test for resistance to active ingredients that are not easily assessed by time to knockdown or mortality in existing bioassays. Molecular markers of resistance to these new active ingredients should be identified to help predict the potential for cross-resistance, as well as contribute to our understanding of how rapidly resistance will spread and intensify in

mosquito populations. These efforts will require more support for entomological capacity in the field and for national malaria control programmes to gather the data and advocate for action based on those data.

Finally, although the GPIRM is in need of updating, its recommendation to use nets with non-pyrethroid active ingredients as soon as they become available is suddenly relevant. They are available now and it is time to use them. However, we must do so judiciously to maintain the efficacy of these new active ingredients and to avoid the crisis we have faced with pyrethroid resistance.

References

1. Bhatt S, Weiss DJ, Cameron E, et al. The effect of malaria control on *Plasmodium falciparum* in Africa between 2000 and 2015. Nature 2015; 526: 207–11. [PubMed: 26375008]
2. WHO. World malaria report 2017. Geneva: World Health Organization, 2017
3. Tiono AB, Ouédraogo A, Ouattara D, et al. Efficacy of Olyset Duo, a bednet containing pyriproxyfen and permethrin, versus a permethrin-only net against clinical malaria in an area with highly pyrethroid-resistant vectors in rural Burkina Faso: a cluster-randomised controlled trial. Lancet 2018; published online Aug 10. 10.1016/S0140-6736 (18)31711–2
4. Protopopoff N, Mosha JF, Lukole E, et al. Effectiveness of a long-lasting piperonyl butoxide-treated insecticidal net and indoor residual spray interventions, separately and together, against malaria transmitted by pyrethroid-resistant mosquitoes: a cluster, randomised controlled, two-by-two factorial design trial. Lancet 2018; 391: 1577–88. [PubMed: 29655496]
5. Hemingway J, Ranson H, Magill A, et al. Averting a malaria disaster: will insecticide resistance derail malaria control? Lancet 2016; 387: 1785–88. [PubMed: 26880124]
6. Ranson H, Lissenden N. Insecticide resistance in African *Anopheles* mosquitoes: a worsening situation that needs urgent action to maintain malaria control. Trends Parasitol 2016; 32: 187–96. [PubMed: 26826784]
7. WHO, Department of Control of Neglected Tropical Diseases. Seventh Meeting of the Vector Control Advisory Group (VCAG). Geneva, Switzerland, 24–26 10 2017 http://www.who.int/neglected_diseases/vector_ecology/resources/WHO_HTM_NTD_VEM_2017.11/en (accessed Aug 5, 2018).
8. Killeen GF, Ranson H. Insecticide-resistant malaria vectors must be tackled. Lancet 2018; 391: 1551–52. [PubMed: 29655495]
9. WHO. Global Plan for Insecticide Resistance Management. Geneva: World Health Organization, 2012.