OPEN ACCESS Freely available online

PLoS MEDICINE

Perspective

African Malaria Control Programs Deliver ITNs and Achieve What the Clinical Trials Predicted

Thomas P. Eisele[1]*, Richard W. Steketee[2]

1 Department of Global Health Systems and Development, Tulane University School of Public Health and Tropical Medicine, New Orleans, Louisiana, United States of America, **2** Malaria Control and Evaluation Partnership in Africa (MACEPA)-PATH, Seattle, Washington, United States of America

New Evidence for ITN Effectiveness

There is robust evidence of the efficacy of insecticide-treated mosquito nets (ITNs) in reducing malaria parasite prevalence, incidence, and all-cause child mortality from carefully conducted trials in sub-Saharan Africa across a range of transmission settings [1]. Trials have shown ITNs to both significantly reduce *Plasmodium falciparum* prevalence among children under 5 years old by 13% and post-neonatal (1–59 months) all-cause mortality by 18% in areas of stable malaria transmission in Africa [1,2]. However, there have been limited data on the effectiveness of ITNs under routine program conditions at preventing malaria morbidity and child mortality, especially at the national level. This has of course raised serious concerns abou how likely the efficacy of ITNs from trials is translating into real-world effectiveness on the ground. There are certainly examples where a proven effective intervention achieved disappointing results when programs ran into constraints with deployment at wide-scale implementation [3,4].

Stephen Lim and colleagues, in an article published in this week's *PLoS Medicine*, should be commended for their rigorous and systematic analysis of national cross-sectional survey datasets in sub-Saharan Africa assessing the association of ITNs on reducing *P. falciparum* prevalence in children under 5 and all-cause post-neonatal mortality, while controlling for contextual and potential confounding factors [5]. The results show ITN household possession to be associated with a 20% significant reduction in *P. falciparum* prevalence (from seven surveys in seven countries) and a 23% significant reduction in all-cause child mortality (from 29 surveys in 22 countries). Importantly, these results were consistent across a range of malaria transmission settings and across countries with disparate levels of ITN household coverage. They are also consistent with data from smaller-scale studies that have shown ITNs to be associated with significant reductions in malaria under program conditions [6–10].

Linked Research Article

This Perspective discusses the following new study published in *PLoS Medicine*:

Lim SS, Fullman N, Stokes A, Ravishankar N, Masiye F, et al. (2011) Net Benefits: A Multi-Country Analysis of Observational Data Examining Associations between Insecticide-Treated Mosquito Nets and Health Outcomes. PLoS Med 8(9): e1001091. doi:10.1371/journal.pmed.1001091

Stephen Lim and colleagues report findings from a multi-country analysis of household survey data on the association between possession of insecticide-treated mosquito nets and child mortality and parasitemia. Scale-up of net coverage was associated with a substantial reduction in childhood mortality and in parasitemia prevalence.

The ITN represents a brilliant intervention—it provides individual protection to the person sleeping under it from infected mosquitoes; the insecticide kills mosquitoes that seek a blood meal thereby reducing the overall propensity for transmission in the community [11,12]; and if the person under the net is already infected with the malaria parasite, the ITN prevents them from infecting mosquitoes and leading to more transmission. The ITN is tailored to the biology of the African malaria-carrying *Anopheles* mosquitoes that prefer to bite humans, bite late at night when people are sleeping (hopefully under an ITN), and rest on vertical surfaces (such as the walls of the ITN) while they digest their blood meal. National ITN mass distribution campaigns have achieved remarkably high household coverage, even among the most poor and rural areas [13–15]. Despite unsubstantiated anecdotes of misuse and non-use [16], given sufficient access to ITNs people use them for protection against malaria [17].

Still, ITNs are not the sole answer to malaria control, and they cost money and need to be continually replaced when they wear out.

Relevance to Malaria Control

Funding for malaria control has increased dramatically from ~US$100 million available in 2003 to ~U$1.5 billion available in 2010, with over three-quarters going to sub-Saharan Africa [18]. Largely based on the results of the ITN trials, there has been a considerable "leap of faith" by international donors and ministries of health across Africa in relying on ITNs as a cornerstone malaria prevention tool that will translate into real gains on the ground in reducing the malaria burden. To this end between 2004 and

Citation: Eisele TP, Steketee RW (2011) African Malaria Control Programs Deliver ITNs and Achieve What the Clinical Trials Predicted. PLoS Med 8(9): e1001088. doi:10.1371/journal.pmed.1001088

Published September 6, 2011

Funding: No specific funding was received to write this article.

Competing Interests: The authors have declared that no competing interests exist.

Abbreviation: ITN, insecticide-treated mosquito net.

* E-mail: teisele@tulane.edu

Provenance: Commissioned; not externally peer-reviewed.

2010, manufacturers delivered more than 400 million nets, with 290 million delivered since 2008, which is sufficient to cover nearly 80% of populations at risk of malaria in Africa [18].

After nearly a decade of investment in malaria control across Africa, there has been a critical need to evaluate the impact this effort has had on reducing the malaria burden, especially for child mortality. However, because nearly all national programs are scaling-up to achieve fullcoverage of populations at risk of malaria, evaluators must rely on an ecological, or plausibility, study design whe attempting to assess the impact of malaria control investments [19–21], whereby changes in intervention coverage are measured against simultaneous changes in malaria morbidity and mortality. If the malaria burden is observed to decrease concurrently with intervention coverage in the population, then one deems it plausible tha the program contributed to the improved outcomes observed. This is especially true for ITNs where there are robust empirical data from trials on their efficacy. However, the study design is strengthened immensely when there is additional evidence that the effect seen in trial translates to effectiveness on the ground.

Lim and colleagues have provided timely and vital validating evidence that national programs can decrease malaria morbidity and child mortality through program investments in ITNs. In a world of shrinking resources for global health programs, such evidence is critically important. To emphasize this point, consider what it would have meant if the analysis by Lim and colleagues had shown that despite the evidence from trials, ITNs have no demonstrable association with reducing malaria morbidity and child mortality under program conditions in Africa; this would have been devastating to the integrity of past and future investments in ITNs as a primary tool in the fight against malaria. In fact, they found the opposite and confidence, renewed attention, and investment should follow.

Next Steps

The next 5 to 10 years will be critical in the fight against malaria, especially if elimination in areas of Africa is to be achieved. As Lim and colleagues suggest, continued scale-up of long-lasting ITNs (LLINs) must be a cornerstone of this effort and there are still lives to be saved with this intervention. LLINs typically wear out after 2–3 years and thus the malaria control community must attend to finding the most efficient means of replacing worn out nets once high coverage has been achieved [22]. And, ITNs alone are insufficient to completely eliminate malaria transmission in areas of Africa suitable to perennial transmission [23]. It is therefore imperative for the malaria community to apply its program experience and success with ITNs towards a focus on testing new tools and delivery approaches to achieve the next level of malaria transmission reduction beyond what is achievable by high ITN coverage alone [24–26].

Acknowledgments

Disclaimer: The views and opinions presented in this commentary are those of the authors and do not necessarily represent an official position of Tulane University or PATH.

Author Contributions

Wrote the first draft of the manuscript: TPE. Contributed to the writing of the manuscript: RWS. ICMJE criteria for authorship read and met: TPE RWS. Agree with manuscript's results and conclusions: TPE RWS.

References

1. Lengeler C (2004) Insecticide-treated bed nets and curtains for preventing malaria. Cochrane Database Syst Rev: CD000363.
2. Eisele TP, Larsen D, Steketee RW (2010) Protective efficacy of interventions for preventing malaria mortality in children in Plasmodium falciparum endemic areas. Int J Epidemiol 39: i88–101.
3. Glasgow RE, Lichtenstein E, Marcus AC (2003) Why don't we see more translation of health promotion research to practice? Rethinking the efficacy-to-effectiveness transition. Am J Public Health 93: 1261–1267.
4. Sussman S, Valente TW, Rohrbach LA, Skara S, Pentz MA (2006) Translation in the health professions: converting science into action. Eval Health Prof 29: 7–32.
5. Lim SS, Fullman N, Stokes A, Ravishankar N, Masiye F, et al. (2011) Net benefits: associations between insecticide-treated mosquito nets and malaria morbidity and childhood mortality in sub-Saharan Africa. PLoS Med 8: e1001091. doi:10.1371/journal.pmed.1001091.
6. Noor AM, Moloney G, Borle M, Fegan GW, Shewchuk T, et al. (2008) The use of mosquito nets and the prevalence of Plasmodium falciparum infection in rural South Central Somalia. PLoS ONE 3: e2081. doi:10.1371/journal.pone.0002081.
7. Terlouw DJ, Morgah K, Wolkon A, Dare A, Dorkenoo A, et al. (2010) Impact of mass distribution of free long-lasting insecticidal nets on childhood malaria morbidity: the Togo National Integrated Child Health Campaign. Malar J 9: 199.
8. Fegan GW, Noor AM, Akhwale WS, Cousens S, Snow RW (2007) Effect of expanded insecticide-treated bednet coverage on child survival in rural Kenya: a longitudinal study. Lancet 370: 1035–1039.
9. Kleinschmidt I, Schwabe C, Benavente L, Torrez M, Ridl FC, et al. (2009) Marked increase in child survival after four years of intensive malaria control. Am J Trop Med Hyg 80: 882–888.
10. Schellenberg JR, Abdulla S, Nathan R, Mukasa O, Marchant TJ, et al. (2001) Effect of large-scale social marketing of insecticide-treated nets on child survival in rural Tanzania. Lancet 357: 1241–1247.
11. Hawley WA, Phillips-Howard PA, ter Kuile FO, Terlouw DJ, Vulule JM, et al. (2003) Community-wide effects of permethrin-treated bed nets on child mortality and malaria morbidity in western Kenya. Am J Trop Med Hyg 68: 121–127.
12. Gimnig JE, Vulule JM, Lo TQ, Kamau L, Kolczak MS, et al. (2003) Impact of permethrin-treated bed nets on entomologic indices in an area of intense year-round malaria transmission. Am J Trop Med Hyg 68: 16–22.
13. Thwing J, Hochberg N, Eng JV, Issifi S, Eliades MJ, et al. (2008) Insecticide-treated net ownership and usage in Niger after a nationwide integrated campaign. Trop Med Int Health 13: 827–834.
14. Grabowsky M, Nobiya T, Ahun M, Donna R, Lengor M, et al. (2005) Distributing insecticide-treated bednets during measles vaccination: a low-cost means of achieving high and equitable coverage. Bull World Health Organ 83: 195–201.
15. Zambia Ministry of Health (2010) Zambia national malaria indicator survey 2010. Lusaka, Zambia: Zambia Ministry of Health.
16. Eisele TP, Thwing J, Keating J (2011) Claims about the misuse of insecticide-treated mosquito nets: are these evidence-based? PLoS Med 8: e1001019. doi:10.1371/journal.pmed.1001019.
17. WHO (2010) World malaria report 2010. Geneva: WHO.
18. RBM (2010) Roll Back Malaria progress & impact series: malaria funding and resource utilization: the first decade of Roll Back Malaria. Geneva: RBM.
19. Rowe AK, Steketee RW, Arnold F, Wardlaw T, Basu S, et al. (2007) Viewpoint: evaluating the impact of malaria control efforts on mortality in sub-Saharan Africa. Trop Med Int Health 12: 1524–1539.
20. Habicht JP, Victora CG, Vaughan JP (1999) Evaluation designs for adequacy, plausibility and probability of public health programme performance and impact. Int J Epidemiol 28: 10–18.
21. Victora CG, Black RE, Boerma JT, Bryce J (2010) Measuring impact in the Millennium Development Goal era and beyond: a new approach to large-scale effectiveness evaluations. Lancet.
22. Eisele TP, Steketee RW (2009) Distribution of insecticide treated nets in rural Africa. BMJ 339: b1598.
23. Shaukat AM, Breman JG, McKenzie FE (2010) Using the entomological inoculation rate to assess the impact of vector control on malaria parasite transmission and elimination. Malar J 9: 122.
24. Alonso PL, Brown G, Arevalo-Herrera M, Binka F, Chitnis C, et al. (2011) A research agenda to underpin malaria eradication. PLoS Med 8: e1000406. doi:10.1371/journal.pmed.1000406.
25. Feachem RG, Phillips AA, Hwang J, Cotter C, Wielgosz B, et al. (2010) Shrinking the malaria map: progress and prospects. Lancet 376: 1566–1578.
26. Moonen B, Cohen JM, Snow RW, Slutsker L, Drakeley C, et al. (2010) Operational strategies to achieve and maintain malaria elimination. Lancet 376: 1592–1603.