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EDITORIAL

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Attractive targeted sugar baits series in *Malaria Journal*

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As part of a three-country evaluation [1] and the first site with full data available, this series of articles provides a detailed look at the Western Province, Zambia site and deployment experience (November 2021 through June 2023) during a phase III cluster-randomized controlled trial (cRCT) of attractive targeted sugar baits (ATSBs). The intervention consisted of deploying two ATSB bait stations per eligible structure in households in 35 intervention clusters during two consecutive transmission seasons (November to June) and was compared to a contemporaneous group of 35 clusters receiving no ATSBs. All 70 clusters received the standard vector control [insecticide-treated mosquito nets (ITNs) or indoor residual spraying (IRS)] and care and treatment for malaria cases per national programme services [2].

This three country cRCT evaluation was deemed appropriate by the World Health Organization (WHO) Vector Control Advisory Group (VCAG [3]) and experts in the field that followed earlier studies of the remaining burden of outdoor and daytime malaria transmission [4, 5], of mosquito biting and sugar feeding behaviour [6–8], of earlier smaller studies showing promising effects on entomologic outcomes [9–12], and on modelled estimates suggesting that ATSBs might be able to achieve a 30% or greater reduction in malaria transmission—infection and prevalence rates and clinical illness rates [13–17]. The studies were then powered to observe that 30% reduction.

The summary epidemiology results focused on clinical malaria incidence in children aged 1–14 years and parasite prevalence in participants over the age of 6 months followed over the two consecutive transmission seasons in 2022 and 2023 [18]. Entomologic outcomes were evaluated in a subset of 20 clusters to facilitate interpretation of epidemiologic findings and assessed vector abundance, parity, biting rates, sporozoite prevalence and entomologic inoculation rates [19].

The additional articles collected here addressed a variety of scientific and programmatic evaluations including: site characteristics [20], ATSB deployment procedures [21], community acceptance of ATSBs [22], involvement of community health workers during the research trial [23], a preliminary study on vector feeding rates on ATSBs [24], an evaluation of the persistence of the bioefficacy of ATSBs over time [25], assessment of ATSB damage [26], and time to loss of physical durability of ATSBs [27]. Taken together, these articles provide critical information on ATSB efficacy for human and mosquito outcomes and the key programme actions required if ATSBs are to be deployed more widely. If the efficacy is deemed insufficient to merit further deployment, these studies can help understand the determinants of the limited efficacy.

The important good news is that the manuscripts describe a well-done study, where care and attention to designing, planning, and conducting the study [1, 13] led to highly comparable intervention and control groups and a high likelihood that the outcome estimates were unbiased, accurate, and valid.

Unfortunately, the study showed limited and non-significant efficacy of the ATSBs in reducing clinical illness in the highest risk population of children 1–14 years of

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age and in altering parasite prevalence in participants over the age of 6 months. The per-protocol assessment of the population covered with ATSBs showed only a non-statistically significant 9% reduction in clinical malaria illness and less than 3% difference in RDT-positive infection prevalence in the intervention versus control groups [18, 19]. Clinical malaria incidence in the ATSB arm and the control arm were similar at 2.56 and 2.75 episodes per child-year, respectively. Parasite prevalence in survey participants over the age of 6 months was high and similar in the ATSB arm and the control arm at 50.7% and 53.5%, respectively. Entomological outcomes were similarly modest and statistically non-significant and consistent with the human infection and disease outcomes.

Additional post-hoc analyses were done to explore ATSB efficacy. Analytic adjustments for baseline cluster prevalence, trial year, age group, ITN use, and IRS coverage remained statistically non-significant and did not change the magnitude of the ATSB effect. Efficacy estimates for populations with one or more structures per hectare (more densely populated) and for intervals and areas with higher rainfall did show slightly higher efficacy estimates, but again, none of these were statistically significant.

Previous and preparatory studies and modelling estimates suggested better results would be expected—what happened?

- For openers, Western Province has very high malaria transmission with an estimated entomologic inoculation rate (EIR) of approximately 70 infectious bites per person per year. As most of this is experienced in the 6–7 months of the high transmission season, that translates to everyone experiencing approximately 10 infectious bites per month or one every 3 days. Approximately two-thirds of these infections were likely to have occurred indoors, thus an outdoor intervention may have had limited opportunity to reduce overall malaria transmission and disease burden.
- *Anopheles funestus* mosquitoes were responsible for nearly 95% of the local transmission and were still infecting people via their dominant indoor biting habits. Occasionally, these mosquitoes were biting, resting, seeking sites for their egg laying, and feeding on sugar sources outside of houses; but this investigation deployed ATSBs only outdoors and thus addressed only outdoor sugar feeding. Indoor vector control with ITNs and IRS was similar for intervention and control groups and was not specifically enhanced in these clusters for the study interval. Consequently, the saturated transmission intensity, which was still dominated by indoor biting and resting, was not altered sufficiently to change the human malaria experience—the 50% population parasite prevalence and clinical malaria case incidence of 2.5–3 episodes per child per year.
- Many of the previous evaluations of ATSBs have been done with other vector species; thus, there is a need to better understand the *An. funestus* bionomics and ecology. For example, the laboratory studies done to evaluate the efficacy of the ATSB stations were conducted with starved adult male and female *Anopheles gambiae* sensu stricto mosquitoes from a laboratory colony; and among these, the feeding (and thus kill rate) of females was 24% lower than for males. What would be found in the natural setting among females who are not starved and likely to prioritize a blood meal? Might they forgo sugar feeds and remain unexposed to the ATSB toxicant? Similarly, as ATSBs were only deployed outside of the house but many of the females (especially blood fed females) may have rested indoors, were they likely to bypass the ATSBs as they exited houses in search of sites for egg laying?
- Could the ATSBs and their deployment and durability be part of the problem? The concept of ATSBs has led to many development iterations to maximize mosquito feeding attractiveness and efficacy while also maximizing safety [28]—especially to limit any adverse effects on pollinating insects and any potential exposure for children. Of note, the ATSB bait stations deployed in this study used a neonicotinoid pesticide and a previous study suggested that this potentially attracts bees [29]. To avoid child interest in tampering with the ATSB station, the manufacturers included Bitrex (denatonium benzoate), an extremely bitter substance. Bitrex was used in some of the ATSB feeding studies [24] and there may be unpublished studies showing its effect on *Anopheline* mosquito feeding on ATSBs; however, Bitrex is documented to have repellent and antifeeding effects in insects including mosquitoes [30–33]. This merits further evaluation as ATSB manufacturing and components may need to change over time.
- The deployment of two ATSB stations per structure was a choice based on observing similar efficacy when using two versus three bait stations [10]. The optimal density of bait stations may vary with mosquito, human, housing, climate and ecologic factors contributing to that variation. However, if ATSBs are to be deployed in programnes, this bait station density requirement will merit further attention.
- The ATSB bait stations have a durability problem with essentially one-half of all bait stations requiring replacement during the transmission season. While this requires fifty-percent extra product cost and a

system of predictable procurement for the additional bait stations, the important challenge is the requirement of intense and continuous monitoring of bait stations for the required replacement. While most national malaria programmes deploy ITNs, there is no existing continuous monitoring system that leads to immediate ITN replacement when the net is no longer effective (e.g., lost to fire, stolen, develops large holes or loses its effective insecticidal properties). Would an ATSB deployment programme require continuous monitoring and thus be responsible for both the introduction of this new tool and the establishment of a sophisticated monitoring system reaching all villages, communities and households for the required near-immediate replacements. As an aside, given the much higher proven efficacy and effectiveness of ITNs, should emphasis be first placed on the existing ITN programmes to establish a continuous quality monitoring system in each community with immediate replacement when needed?

- The choice of outside deployment reflects the emphasis on the specificity of evaluating mosquito outdoor sugar feeding as a target and not adding to the existing indoor use of ITNs or IRS for indoor vector control. Given the demonstrated modest impact on vector and human outcomes and the understanding that indoor transmission remains a dominant force for transmission, combined indoor and outdoor use of ATSBs with high coverage and use of ITNs and/or IRS likely merits additional study [34, 35]. Of note, bait stations deployed indoors versus outdoors may have different requirements; the safety concern for indoor ATSBs is still about children but not so much about impact on outdoor-dwelling pollinators. The efficacy of ATSBs deployed both indoors and outdoors would require additional evaluation.

The study results reported in this series of papers are only the first ones. Findings from the study sites in Kenya and Mali were recently presented in a symposium sponsored by the Integrated Vector Control Consortium (IVCC) held in conjunction with the American Society of Tropical Medicine and Hygiene (ASTMH, [36]) and demonstrated similar results to the Zambia study—limited non-significant evidence of efficacy in reducing childhood malaria illness episodes or population parasite prevalence; peer-reviewed publication of final results are awaited.

Based on this first well-documented experience in Zambia, the past studies and more recent models appear to have overestimated the expected benefit of ATSBs. The models are only as good as the parameter choices and estimates going into the models. Have the redundancy of the force of infection indoors, outdoors, and combined that maintain high rates of parasite prevalence and case incidence in populations been underestimated? Have the ATSB feeding rates of female *An. funestus* in nature been overestimated? Did the Bitrex repel or deter female *Anopheline* feeding? Are there substantial subsets of the Anopheline mosquito population that are just not encountering the ATSBs? Has the impact of bait station damage and its dependance on protective housing construction been underestimated? Is there a need for reconsideration of the outcome measures, as population parasite prevalence and childhood clinical illness rates reflect combinations of effects and are quite blunt and perhaps relatively immovable across a wide spectrum of infection transmission intensity?

There is much to untangle here. The good news is that it appears that the Zambia study was well done and the investigators should be complimented for their contribution to our knowledge base that goes well beyond the specific primary efficacy outcomes. While a much better impact from this new tool was expected, we should appreciate that it remains based on a biologic need for some or even many malaria-carrying mosquitoes to feed on liquid and sugar as well as the required blood meal for the females. The peer-reviewed results from Kenya and Mali will be important—for findings that are similar as well as those that are different.

The findings from these studies are unlikely to lead to near-term recommendations for wider-scale deployment of ATSBs in malaria endemic populations. However, endemic countries certainly need expanded and additional transmission reducing interventions against malaria that can take the EIR from 70 to 7, down to 0.7, and ultimately to zero. In the absence of future substantial reductions in malaria transmission, national health systems will be relegated to the unfortunate position of having to find infections and illness after the transmission has happened and hoping that the clinical management can do better than just keeping up with the devastating burden that we already witness.

Author contribution

As the sole author, RWS reviewed all of the submitted manuscripts for this ATSB series of articles, reviewed the relevant cited literature, conceived, wrote, and approved the manuscript.

References

1. Attractive Targeted Sugar Bait Phase III Trial Group. Attractive targeted sugar bait phase III trials in Kenya, Mali, and Zambia. Trials. 2022;23:640.

2. National Malaria Elimination Center, Zambia. National malaria elimination strategic plan 2022–2026. Ministry of Health, Republic of Zambia; 2022. https://static1.squarespace.com/static/58d002f017bffcf99fe21889/t/632a4cb0fcd87c13d0165372/1663716530614/ZNMESP+2022+to+2026_SIGNED+120722.pdf. Accessed 25 Oct 2024.
3. WHO Vector Control Advisory Group. Chemosensory interference: bait station. Geneva: World Health Organization; 2020. https://www.who.int/groups/vector-control-advisory-group/summary-of-new-interventions-for-vector-control/bait-station. Accessed 25 Oct 2024.
4. Sougoufara S, Diédhiou SM, Doucouré S, Diagne N, Sembène PM, Harry M, et al. Biting by *Anopheles funestus* in broad daylight after use of long-lasting insecticidal nets: a new challenge to malaria elimination. Malar J. 2014;13:125.
5. Thomsen EK, Koimbu G, Pulford J, Jamea-Maiasa S, Ura Y, Keven JB, et al. Mosquito behavior change after distribution of bednets results in decreased protection against malaria exposure. J Infect Dis. 2017;215:790–7.
6. Sougoufara S, Ottih EC, Tripet F. The need for new vector control approaches targeting outdoor biting Anopheline malaria vector communities. Parasit Vectors. 2020;13:295.
7. Omondi S, Kosgei J, Agumba S, Polo B, Yalla N, Moshi V, et al. Natural sugar feeding rates of *Anopheles* mosquitoes collected by different methods in western Kenya. Sci Rep. 2022;12:20596.
8. Gu W, Müller G, Schlein Y, Novak RJ, Beier JC. Natural plant sugar sources of *Anopheles* mosquitoes strongly impact malaria transmission potential. PLoS ONE. 2011;6: e15996.
9. Traore MM, Junnila A, Traore SF, Doumbia S, Revay EE, Schlein Y, et al. The efficacy of attractive targeted sugar baits in reducing malaria vector abundance in low-endemicity settings of northwest Mali. Malar J. 2024;23:319.
10. Diarra RA, Traore MM, Junnila A, Traore SF, Doumbia S, Revay EE, et al. Testing configurations of attractive toxic sugar bait (ATSB) stations in Mali, West Africa, for improving the control of malaria parasite transmission by vector mosquitoes and minimizing their effect on non-target insects. Malar J. 2021;20:184.
11. Müller GC, Beier JC, Traore SF, Toure MB, Traore MM, Bah S, et al. Field experiments of *Anopheles gambiae* attraction to local fruits/seedpods and flowering plants in Mali to optimize strategies for malaria vector control in Africa using attractive toxic sugar bait methods. Malar J. 2010;9:262.
12. Qualls WA, Müller GC, Revay EE, Allan SA, Arheart KL, Beier JC, et al. Evaluation of attractive toxic sugar bait (ATSB) - Barrier for control of vector and nuisance mosquitoes and its effect on non-target organisms in sub-tropical environments in Florida. Acta Trop. 2014;131:104–10.
13. Yukich J, Eisele TP, ter Kuile F, Ashton R, Staedke S, Harris AF, et al. Master statistical analysis plan: attractive targeted sugar bait phase III trials in Kenya, Mali, and Zambia. Trials. 2023;24:771.
14. Fraser KJ, Mwandigha L, Traore SF, Traore MM, Doumbia S, Junnila A, et al. Estimating the potential impact of Attractive Targeted Sugar Baits (ATSBs) as a new vector control tool for *Plasmodium falciparum* malaria. Malar J. 2021;20:151.
15. Marshall JM, White MT, Ghani AC, Schlein Y, Muller GC, Beier JC. Quantifying the mosquito's sweet tooth: modelling the effectiveness of attractive toxic sugar baits (ATSB) for malaria vector control. Malar J. 2013;2:291.
16. Zhu L, Marshall JM, Qualls WA, Schlein Y, McManus JW, Arheart KL, et al. Modelling optimum use of attractive toxic sugar bait stations for effective malaria vector control in Africa. Malar J. 2015;14:492.
17. Kiware SS, Chitnis N, Tatarsky A, Wu S, Castellanos HMS, Gosling R, et al. Attacking the mosquito on multiple fronts: insights from the Vector Control Optimization Model (VCOM) for malaria elimination. PLoS ONE. 2017;12: e0187680.
18. Ashton RA, Saili K, Chishya C, Banda H, Arnzen A, Orange E, et al. Efficacy of attractive targeted sugar bait stations against malaria in western Province Zambia: epidemiological findings from a two-arm cluster randomized Phase III trial. Malar J. 2024;23:343.
19. Wagman J, Chanda B, Chanda J, Saili K, Orange E, Mambo P, et al. Entomological effects of attractive targeted sugar bait station deployment in Western Zambia: vector surveillance findings from a two-arm cluster randomized phase III trial. Malar J. 2024;23:214.
20. Arnzen A, Wagman J, Chishya C, Orange E, Eisele TP, Yukich J, et al. Characteristics of the Western Province, Zambia, trial site for evaluation of attractive targeted sugar baits for malaria vector control. Malar J. 2024;23:153.
21. Orange E, Kyomuhangi I, Masuzyo M, Mwenya M, Mambo P, Saili K, et al. Deployment of attractive targeted sugar baits in western Zambia: installation, monitoring, removal, and disposal procedures during a Phase III cluster randomized controlled trial. Malar J. 2024;23:204.
22. Orange E, Arnzen A, Muluma C, Akalalambili S, Tobolo T, Ndalama F, et al. Community acceptance of a novel malaria intervention, attractive targeted sugar baits, in the Zambia phase III trial. Malar J. 2024;23:240.
23. Ndalama F, Mulenga D, Arnzen A, Akalalambili S, Tobolo T, Maluma C, et al. Comparative analysis of the engagement of Community Health Workers (CHWs) while deploying the Attractive Targeted Sugar Bait (ATSB) for malaria control in Western Province, Zambia. Malar J. 2025 (in press).
24. Chanda J, Wagman J, Chanda B, Kaniki T, Ng'andu M, Muyabe R, et al. Feeding rates of malaria vectors from a prototype attractive sugar bait station in Western Province, Zambia: results of an entomological validation study. Malar J. 2023;22:70.
25. Mwaanga G, Ford J, Yukich J, Chanda B, Ashton RA, Chanda J, et al. Residual bioefficacy of attractive targeted sugar bait stations targeting malaria vectors during seasonal deployment in Western Province of Zambia. Malar J. 2024;23:169.
26. Kyomuhangi I, Yukich J, Saili K, Orange E, Masuzyo MH, Mwenya M, et al. Evaluating trends in damage to attractive targeted sugar baits (ATSBs) deployed during the second year of a two-year Phase III trial in Western Zambia. Malar J. 2024;23:263.
27. Karabo RY, Mundia MH, Mwenya M, Saili K, Miller J, Silumbe K, et al. Time to loss of physical integrity of Attractive Targeted Sugar Bait (ATSB) stations in Western province, Zambia: a survival analysis. Malar J. 2025; (in press).
28. Fiorenzano JM, Koehler PG, Xue RD. attractive toxic sugar bait (atsb) for control of mosquitoes and its impact on non-target organisms: a review. Int J Environ Res Public Health. 2017;14:398.
29. Kessler S, Tiedeken EJ, Simcock KL, Derveau S, Mitchell J, Softley S, et al. Bees prefer foods containing neonicotinoid pesticides. Nature. 2015;521:74–6.
30. Perera MTMDR, Armstrong G, Naylor REL. Antifeedant effects of denatonium benzoate and a neem derivative on *Myzus Persicae* (Sulzer). Trop Agric Res. 1995;7:39–47.
31. Weiss LA, Dahanukar A, Kwon JY, Manerjee D, Carlson JR. The molecular and cellular basis of bitter taste in Drosophila. Neuron. 2011;69:258–72.
32. Kessler S, Vlimant M, Guerin PM. The sugar meal of the African malaria mosquito *Anopheles gambiae* and how deterrent compounds interfere with it: a behavioural and neurophysiological study. J Exp Biol. 2013;216:1292–306.
33. Kessler S, Vlimant M, Guerin PM. Sugar-sensitive neurone responses and sugar feeding preferences influence lifespan and biting behaviours of the Afrotropical malaria mosquito, *Anopheles gambiae*. J Comp Physiol A Neuroethol Sens Neural Behav Physiol. 2015;201:317–29.
34. Qualls WA, Müller GC, Traore SF, Traore MM, Arheart KL, Doumbia S, et al. Indoor use of attractive toxic sugar bait (ATSB) to effectively control malaria vectors in Mali, West Africa. Malar J. 2015;14:301.
35. Furnival-Adams JEC, Camara S, Rowland M, Koffi AA, Ahoua Alou LP, Oumbouke WA, et al. Indoor use of attractive toxic sugar bait in combination with long-lasting insecticidal net against pyrethroid-resistant *Anopheles gambiae*: an experimental hut trial in Mbe, Central Côte d'Ivoire. Malar J. 2020;19:11.
36. Results from large-scale trials of the Sarabi Attractive Targeted Sugar Bait to reduce malaria burden in Kenya, Mali, and Zambia. Sponsored Symposium, Integrated Vector Control Consortium. Nov 15, 2024, Annual Meeting of the American Society of Tropical Medicine and Hygiene, New Orleans, LA. https://www.astmh.org/getmedia/1477e250-3f6d-4005-9ebc-8bb046300311/ASTMH-2024-Annual-Meeting-Session-Schedule.pdf

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