ALTERNATIVES TO THE HUMAN LANDING CATCH

SUMMARY REPORT

UNIVERSITY OF WASHINGTON STRATEGIC ANALYSIS, RESEARCH & TRAINING (START) CENTER

REPORT TO THE BILL & MELINDA GATES FOUNDATION

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STRATEGIC ANALYSIS, RESEARCH & TRAINING CENTER

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1. Introduction

1.1 PROJECT OVERVIEW

In June of 2021, the Bill & Melinda Gates Foundation (BMGF) contracted the Strategic Analysis, Research, and Training Center (START) to aid future funding decisions on alternatives to the human landing catch (HLC). The START team was asked to provide the following: (1) build a framework for change to introduce alternatives to the HLC; (2) conduct a synthesis of two recent literature reviews about alternatives to HLC; and (3) conduct key informant interviews (KII) on their perspectives on whether there is a need for alternatives to HLC.

For the KIIs, the START team interviewed experts identified by the BMGF, to understand their perspectives on the need for alternatives to HLC, their perceived desirable qualities in a replacement method, current advances in alternatives to the HLC, and any barriers to implementing these alternatives. The themes arising in these interviews, along with the key themes from the literature review, were documented and are summarized in the "Synthesis of Results" section. The team applied a Framework for Change Model (FOC) to highlight themes brought out by the interviews and key literature related to root causes, needs, strategies, expected outcomes, and impacts of implementing an alternative method to the HLC. This report summarizes the START team's methods, findings, and recommendations.

1.2 BACKGROUND

The Human Landing Catch (HLC) has been considered the gold standard for monitoring vector populations and estimating malaria transmission rates (1-3). In malaria-endemic locations, vector control measures such as insecticide treated nets (ITNs) and indoor residual spraying (IRS) are critical for malaria prevention and control (4). These vector control measures largely depend on mosquito behavior and insecticide resistance patterns. Given this, the WHO recommends conducting entomological surveys of mosquito populations, and observing mosquito biting behavior, in order to determine the effectiveness of malaria control programs (5).

HLC has been the traditional method to monitor vector populations for this entomological data. The method involves having a human sitting down on a chair or stool with their lower legs exposed. They will collect any mosquitoes that land on their body for a specified period of time, but the practice is directed at *Anopheles* (3). Since the *Anopheles* mosquitoes that transmit malaria tend to bite at night, HLCs are typically conducted overnight - usually between 18:00 and 06:00 hours (6). The HLC provides data on several important entomological endpoints (e.g. mosquito abundance, infection rates, inoculation rates, parity rate as proxy for longevity, etc.) which are essential to understanding human disease outcomes and making decisions concerning mosquito control (7). However, to obtain

reliable data through the HLC, there must be intensive supervision of personnel to ensure that they must remain awake throughout the night to perform the tedious, and repetitive task of collecting every mosquito that lands on them.

2. Human Landing Catch

2.1 HLC BIASES

2.1.1. DATA QUALITY BIASES

Several factors can inhibit the generalizability of the data collected by HLCs, such as collector bias (e.g., human attractiveness to mosquitoes, human odor unicity, collector skill at catching the mosquitoes, etc.), variation in mosquito biting behavior, and the lack of standardization in how HLCs are carried out.

One example of collector bias is that there are natural variations in human attractiveness to the mosquito. Dr. Lobo explained “Mosquitoes are differentially attracted to different individuals. This is further complicated by if a person just bathed, the type of soap they used, etc. All these things come into play as far as attractiveness. None of these factors have been characterized or quantified wrt HLCs.” Dr. Burkot added, “The variation in transmission intensity between people is still a knowledge gap: why some people get most of the bites while others get less bites, that is part of the nature of the transmission.” In addition to collector attractiveness, the variation in the collector’s skill, dexterity, level of experience, and degree of alertness can influence the number of mosquitoes caught during HLC (8-10).

Mosquito behavior is highly variable even within the same species of mosquito. “Exactly the same trap setup in exactly the same way, for the same mosquito species, but placed in different sites will function differently. This is because the same mosquito species at those two different sites might have different behaviors.” Published literature also found that collector variations lead to biases in the mosquitos collected. Lindsay et al. ran five trials over the span of 2.5 years to measure the relative attractiveness of individual sleepers to mosquitoes. The study concluded that the number of bites an individual receives in the field depends upon location, number of hosts in the room, and host defensive behavior, as well as innate attractiveness (11).

It should be noted that the variability of human-to-mosquito attractiveness, and the variability of mosquito behavior impacts other surveillance methods in ways that can bias results. According to Dr. Russell, “the labor intensiveness of the HLC tool does bias the dataset because sampling efforts are often underpowered because of the high labor (and associated costs) required.” Dr. Stevenson noted that “every trapping methodology is biased in some way, it may be, one is more attractive to a

particular species or a particular fraction of the population… for example, some traps suck [flying] mosquitoes into it, so you don't know whether the mosquito would have necessarily landed on this host they were seeking -- they were just sucked in once they're within a certain radius...so it's targeting slightly different behaviors." The heterogeneity in how surveillance methods are used also makes it challenging to compare levels of effectiveness. Dr. Lobo noted that "There are lots of different traps and each trap captures a different set of mosquitoes based on the species-specific behavior the trap takes advantage of - a really good and fascinating thing. Also, people can use the same trap, at the same site with different implemented methodologies (e.g. an hour difference in PSC collections, or a different attractant/bait with CDC-LTs) and we may catch a completely different set of mosquitoes.

Despite its perceived limitations, HLC is still being used as "this is a direct measure (with caveats) of the number/species/etc. of *Anopheles* that approach a human to feed - the most direct measure of transmission or exposure. An alternative would ideally replicate this (based on the question being asked)." To fill the knowledge gap, Dr. Lobo suggested that "we can look at how [HLC] impacts data quality," also noting that this type of study is more likely to receive funding than a large-scale study assessing the health consequences of HLC.

2.1.2. User experience

2.1.2.1. Cost

HLC is a labor-intensive and costly procedure (13) requiring trained collectors and extensive supervision. This also makes it unsustainable for large-scale operational sampling of malaria vectors (14). During our Panel Discussion, Dr. Burkot also emphasized that "the biggest disadvantage of the human landing catch is cost: both labor and supervision costs." Dr. Farlow added that "you'll always have the cost issue because you have to compensate participants." Dr. Lobo pointed out that "ideally, an alternative method would be cheap, easy to use, [and produce] good data. If we had this, the entire NGO/Research/MoH body would take it up - especially with data demonstrating this and WHO support."

To mitigate the cost ineffectiveness of HLC, *Kenea et al* investigated light traps as HLC replacements for vector surveillance in Ethiopia. Over a five-month study period, they compared HLC to CDC light traps and carbon dioxide-baited light traps, both indoors and outdoors. They concluded that light traps are affordable, easy to use and can be deployed in large-scale, longitudinal, community-based trapping schemes using solar-powered battery chargers (9). Another study by *Sikaala et al* conducted in rural Zambia did a cost comparison between HLC, CDC light traps, and Ifakara Tent Traps (15). Their study presented CDC light traps as a more affordable option for routine vector population dynamics monitoring at programmatic level that yields more

spatial and, especially, temporal resolution than is otherwise possible (15). The only previous study to have validated the affordability, accuracy and epidemiological relevance of a community-based trapping system relates to a municipal-scale platform for monitoring and evaluating the impact of an urban larvicidal program where *An. gambiae s.s.* is the predominant vector present (19). However, even with these strengths, the alternatives did not quite produce data equivalent to the HLC. Therefore, as aforementioned, HLC remains the best method to directly measure the *Anopheles* that land on humans to feed upon them.

2.1.2.2. ACCEPTABILITY AND CULTURE

The individuals or families who live near research centers often volunteer their households for researchers to catch vectors inside of them. Sometimes researchers will sleep in a bedroom all night to catch mosquitoes, and those volunteering their households end up bearing the burden of inconvenience of hosting a stranger in their home as they sleep. In addition to this practice being an invasion of privacy to households and creating a noise disturbance, collectors themselves can also be fearful of engaging in this research. Dr. Hawkes highlighted that it is “insensitive...and embarrassing to households to have strangers set up and come into households multiple times in the night or even just stand outside...it can be socially compromising and damaging to the [family’s] reputation [due to a lack of privacy in the home]. Collectors have also reported...being worried that they're going to be accused of being a thief or [being] vulnerable to attack by bandits. [Collectors] even [had] supernatural fears around HLC, especially because they think that owls or dogs barking in the night are actually people who are coming to attack them in the forms of animals. Dr. Stevenson described the discomfort that communities had with this surveillance method as they were “providing their homes for those captures to take place.” On the other hand, Dr. Hawkes emphasized that it was important to connect with community gatekeepers prior to the data collection, to ensure that they are comfortable and accepting of the people entering their communities and homes for the research.

Beyond anecdotal experiences, we do not really know the acceptability and cultural impacts of HLCs, as it is missing from the literature. Thus, it is important to note that all collection activities should be carried out in collaboration with local communities. Field collection is a labor-intensive process, requiring field entomology teams to be on site at the point of collection for several days each month. Large portions of this time should be used to engage with local stakeholders to ensure that they understand how and why the collections are being carried out, to share information and feedback between local residents and the collection teams, and to ensure residents have the opportunity to meaningfully give or revoke consent to the collections being undertaken (whether it is individual consent for activities happening in the household of an individual or community-wide acceptance for activities taking place at village level). Efforts should be made to involve the

community in the research, and this might entail taking community gatekeepers to mosquito research centers and labs, where entomologists collect data on the mosquitoes, and higher-level programmatic individuals map out mosquito prevalence for that specific community.

2.1.2.3. INVOLVEMENT OF WOMEN

WHO recommends that for field trials in areas endemic for vector-borne disease, HLC data collection should only engage "healthy male recruits aged between 18 and 45 years. Males from outside the trial area and pregnant women should be excluded." While WHO's guidelines exclude pregnant women and recommend recruiting men, studies often exclude all women regardless of pregnancy status. Dr. Stevenson mentioned that her team was "advised by a number of people not to use women because of the risk that they may be pregnant and contract malaria, but also because of [concerns for] their safety at night." She also mentioned that it could be costly or inconvenient to make a pregnancy test available to women who want to take part in a HLC study. Excluding women from HLCs means that researchers are not fully capturing accurate transmission events--especially considering that, under an untreated bed net, pregnant women are more attractive to *An. gambiae* mosquitoes than non-pregnant women (16).

Restricting women from even being offered an opportunity to participate in HLCs, means women are completely blocked from the economic opportunities associated with being a catcher, and are even less likely to be involved in knowledge sharing from any data generated. As Dr. Hawkes believed, any alternative method or "tool that…[is] implement[ed] is not going to…exacerbate that problem." Instead, an alternative should be one "that the community can be engaged with on an equal footing." Thus, the HLC "raises a lot of wider questions about reinforcing gender stereotypes and disengaging women from any stake in this kind of research." Also, women overall may play a large part in transmission events based on site specific exposure (such as women in outdoor cooking spaces or vending in outdoor markets) and may differentially attract mosquitoes (17).

2.2. STANDARDIZATION OF HLC AND OUTCOMES

HLC is used for: (i) estimating human exposure to mosquitoes; and (ii) catching mosquitoes and understanding their behaviors - monitoring programs. Dr. Stevenson elaborated and said, "if you want to know how long they survive for, whether they are resistant to insecticides, or looking for eggs, you would need freshly caught samples." The CDC Light Traps catch damaged mosquitoes (i.e., mosquitoes that have been electrified), and these mosquitoes would not be able to answer those questions.

However, as indicated earlier under the “HLC Biases” subheading, results obtained via HLC can be biased due to natural human variations in attractiveness to mosquitoes. In addition to that, people are almost as variable as mosquitoes in terms of reliability and compliance. Dr. Burkot pointed out that “typically, there is a dip in the number of mosquitoes captured at midnight oftentimes and that is because the people who are working from 6 PM to midnight quit a little bit early, and the people that are starting that midnight to 6 AM [shift] are starting a little bit late! So, reliability is a critical issue.” With regards to standardizing data obtained about mosquitoes, Dr. Burkot reported that “mosquitoes' densities are variable over time as well as over locations – that is an important inherent property of the biological population being sampled. There are a lot of questions and decisions that need to be made, based on good, solid standardized data. This data should come from multiple studies with enough power (with sufficient temporal and geographical scale of mosquito collections). However, power is still lacking because HLC is too expensive and too labor intensive to roll out and obtain the numbers of mosquitoes that meet the desired power calculation. This is particularly the case in low-transmission areas where the densities are quite low.” He added that “another downside to HLC is the lack of an epidemiological relevant standard. The fact that findings from all techniques need to be correlated back to biting rates as estimated by HLC is problematic because people do take steps to avoid being bitten by mosquitoes and that makes interpretation difficult.” Dr. Russell also highlighted that “mosquitoes have a lot of different behaviors, and HLC only targets mosquitoes when they are seeking hosts (humans), but there are other behaviors and other things that mosquitoes do, e.g., they seek animals, they rest, they sugar feed, they have larval aquatic habitats... and those are not captured by HLC. These different behaviors play into the different tools that could be rolling out and there are a lot of different tools in development, and there is a need to understand those behaviors to help develop those tools.” While these issues may sometimes be counterbalanced with the experimental design, there are questions about mosquitoes’ behavior that HLC simply cannot answer.

2.3. SAFETY CONCERNS

Though HLCs are the sampling method most indicative of mosquitoes biting humans, they have come under scrutiny due to ethical concerns of exposing collectors to infectious bites. Although there is no analysis that scientifically evaluates data related to risk to collectors in the published literature, many studies highlight that there is a risk in having participants expose their arms or legs to mosquito biting. In 2012, Ndebele and Musesengwa published a qualitative study on the ethical dilemmas around malaria vector research in Africa (20). They conducted focus groups with participants and concluded that many people serving as human bait were repeatedly infected by malaria and received treatment. They raised the question of the role of malaria studies influencing long-term outcomes such as malaria drug resistance among participants who take part in HLC

surveillance. Moreover, they listed that the bites from participating in HLC may lead to short- and long-term “pain, damage to skin, swelling and other problems.”

Dr. Stevenson agreed, noting that “risks to participants are now being recognized more by the NMCPs because of more vector-borne diseases, but that is not the driving factor [for switching to an alternative method] right now. But I think it should be considered because the alternative traps are safer, and we are seeing the spread of more vector-borne diseases around the world. There are no preventative drugs for all possible mosquito-borne diseases, yes there is prophylaxis for malaria but not all the others. The stakeholders who are concerned about the risk of disease to the collector, are coming from researchers and implementers.” Abong’o et al.’s comparison of four potential replacements to the HLC were driven by ethical considerations as well (21). While provision of malaria chemoprophylaxis has been demonstrated to be protective to HLC collectors, there is still potential for transmission of arboviruses and other mosquito-transmitted pathogens (21).

Tangena et al (3) concluded that HLC can expose participants to diseases, such as dengue, for which no chemoprophylaxis or sterilizing vaccine exists. Furthermore, whilst collectors can be protected from malaria using chemoprophylaxis (3), chemoprophylaxis is less effective on *Plasmodium* strains that are less sensitive to antimalarials (3). These considerations support the need for alternative mosquito collection methods. Dr. Lobo confirmed that while HLC may place participants at risk, further studies must be done to collected quantitative data on HLC safety: “we tried to do a literature review on risk associated with HLCs, and we did not find any literature on that, and though there is real risk associated with HLC, we can’t quantify it, so there is *no data* to support these decisions.” However, Dr. Lobo also noted that these studies would need to be large: “we can’t actually collect the data on that—it's really hard to collect data on risk because you'd have to [do] large scale studies. [Hypothetically] if one out of every 10,000 people [in the study] get a virus infection with HLCs, you’d have to have a statistically significant sample size.”

Our panel discussion with Drs. Burkot, Russell, and Farlow highlighted a different perspective; one that did not view the HLC as an ethical issue. Dr. Burkot stated that “it's not a human ethics issue, because the person doing the collection is not the subject of the research. It's an occupational health issue, it may seem like a small point, but people keep talking [about] ethics and everyone gets all scared when they hear the word ‘ethics.’ It's actually ‘occupational health’ is what it is.”

3. Alternative Methods

3.1 Qualities needed in an alternative method

Incorporates an Attractant: The alternative method needs to incorporate the use of a mosquito attractant. Carbon dioxide is considered a universal attractant that would add value to any trap, but it is often difficult to source and standardize. According to Dr. Burkot, there are currently no good alternatives to carbon dioxide. Dr. Hawkes shared that researchers are continuing to try to manufacture "human odors in a bottle" to attract mosquitoes. However, the caveat to this is that there is no universal odor that could replace the wide variations in individual human scent.

Operates in Spite of Preventive Measures: According to the Drs Burkot, Russell, and Farlow, the method needs to allow tracking trends in the risk of being bitten by mosquitoes regardless of preventive measures people may apply. For example, Dr. Lobo suggested that "Different sampling devices may function differently in the face of different interventions. This is because each sampling device takes advantage of specific bionomic traits...and if there is an intervention that impacts a specific behavioral trait, the sampling device efficacy would be consequently impacted - e.g. a long-lasting insecticidal net (LLIN) versus a spatial repellent (SR). How do we have an HLC alternative that similarly reflects how these are impacted? Can we?" Ensuring that the alternative method can still sample/collect mosquitoes while also operating with a preventative method, is especially important.

Consistent across Time: Dr. Lobo shared that "it would be really good if the HLC alternative had consistent trapping efficacies across space and time relative to the HLC. This way we could have a simple conversion factor between HLCs and the alternative device."

Logistically Feasible and Scalable: The panel agreed that the logistics of an alternative should not be a barrier to implementation. The alternative method should be something that a team of technicians can set up in a village and be able to set up for collections that night, so as not to lose time that could be used for collection. Specifically, Dr. Russell mentioned that it should remove "the need for one or two humans to be involved, usually as a bait, throughout the entire trapping period." Dr. Lobo also explained that a "successful HLC alternative would be one that people can easily learn, train, adapt and implement in the field with limited resources giving people the ability to conduct studies sustainably (in a possibly resource poor environment)."

Safe: The panel highlighted that the method needs to reduce human feeding of mosquitoes, because that is when the transmission happens. Although there isn't published data describing the risks of the collectors, Dr. Stevenson agreed that most alternative methods do not put humans at risk of vector-borne disease transmission.

Reduces Human Error: the panel recommended an automated technique that replaces the human factor and reduces the attributable error. According to Dr. Hawkes, “[host decoy traps] are catching similar numbers of mosquitoes and when that number of mosquitoes starts getting really high, the number that you have in a human landing catch really plateaus.” This may be because “humans just cannot keep up with that number of insects landing on [them] if there are five mosquitoes landing on their leg, your chances are they're not going to collect all of them. This also links to reducing the need for supervision, as collectors’ fatigue, take longer breaks than planned, etc.”

Affordable: An alternative should provide valuable entomological data of the impact of vector control interventions, while also being affordable, easy to use, and scalable. For example, CDC light traps are portable, can be solar-powered, and require fewer human resources in comparison with HLC. Dr. Stevenson modified the light traps to include artificial baits and compared those to animal and human landing catches (22); although there were minor species-composition differences, they are becoming more accurate (in terms of catching the same species as HLC) and were pretty efficient even without the presence of CO_2. They are also scalable and affordable (22).

3.2. SUMMARY OF PROBLEMS AND BARRIERS TO IMPLEMENTING ALTERNATIVE METHODS

Currently used alternatives to HLC have a number of problems and barriers to implementation, including:

Logistic problems with carbon dioxide: Even though CO_2 is an excellent attractant for mosquitoes and experts recommended incorporating it in HLC alternatives, there is a need for a better source or means to transport CO_2. The lack of availability of refrigerated gas, the need for cylinders for transportation to study locations, and the primarily the high importation and purchase costs are all logistical constraints that might limit the availability of alternative methods. Dr. Stevenson pointed out that “you will have to have a carbon dioxide source and the issue with carbon dioxide is how you generate that. We worked in the past using CO_2 tanks, but they're extremely heavy. You have to have a regulator valve on it to know exactly how much CO_2 has been produced that is standardized through the night, and then you have the logistics of trying to fill them--which in field settings is extremely difficult and again, of course, if you're wanting to do this on scale and have this deployed by a program in multiple places that then becomes a limiting factor.”

HLC is currently required to collect the minimum entomological information needed: Programs need to undertake vector surveillance at a large scale and collect specific entomological indicators (e.g., biting rates, receptivity of the environment, number of mosquito types, and most importantly, mosquito densities). In particular, mosquito density is an essential parameter needed for measuring other indicators such as indoor/outdoor biting rates, peak biting time, seasonality,

receptivity, and insecticide resistance testing. In turn, biting rates are a key parameter that underpin most of the interim entomological indicators for both research and/or programmatic purposes. The bare minimum information needed is the adult mosquito species in their area. According to Dr. Russell, “The bare minimum information [entomologists] need to know is the occurrence of adult mosquitoes, specifically which species occur in their area...this is a hugely complex question as there are something like 52 species of mosquitoes that transmit malaria. So just to answer that question, what mosquitoes do you have that are adult mosquitoes--not larvae--adults in the area that you're working in, you need human landing catch.” Since no alternative currently exists, HLC is still needed for the purpose of answering this question. Furthermore, Dr. Burkot elaborated that “the problem is the lack of an epidemiologically relevant standard and a lot of these other traps like a light trap... is going to have to be correlated back to biting rates and potential, and I mean again, you need the human landing catch to determine that.”

More research is needed to identify a practical alternative: The panelists reported that “the field of vector control has not been prioritized enough, that is why the value of vector biologists has been low even though the need is high, but funders do not perceive that! There is a lack of respect for entomological indicators.” In addition, when new HLC replacement methods are introduced, more data is needed to prove that these are viable alternatives. Dr. Russell emphasized that “an entomological tool is not just about estimating human exposure to the mosquitoes--this is one part--but it's also to capture mosquitoes, and to understand bionomics and behavior. This is a really big component of monitoring programs in terms of ensuring that the vector control tools are best matched to the situation.” There is also a need to understand the effects of the various modifications made to the different alternatives. Dr. Hawkes pointed out that “in the last five years, there has been a kind of huge expansion in the different types of traps that people are coming up with and testing as a potential.” There simply isn’t enough information about these different traps to confirm that they are equivalent to or better than HLC. Dr. Lobo wanted to understand how a replacement would impact the dynamics of mosquito surveillance: “you might have this really good conversion between HLCs and the replacement, but with an intervention, it might also throw things off completely so we don't understand that as well and that's part of something I would like to understand.”

Other limitations that relate to specific alternatives include:

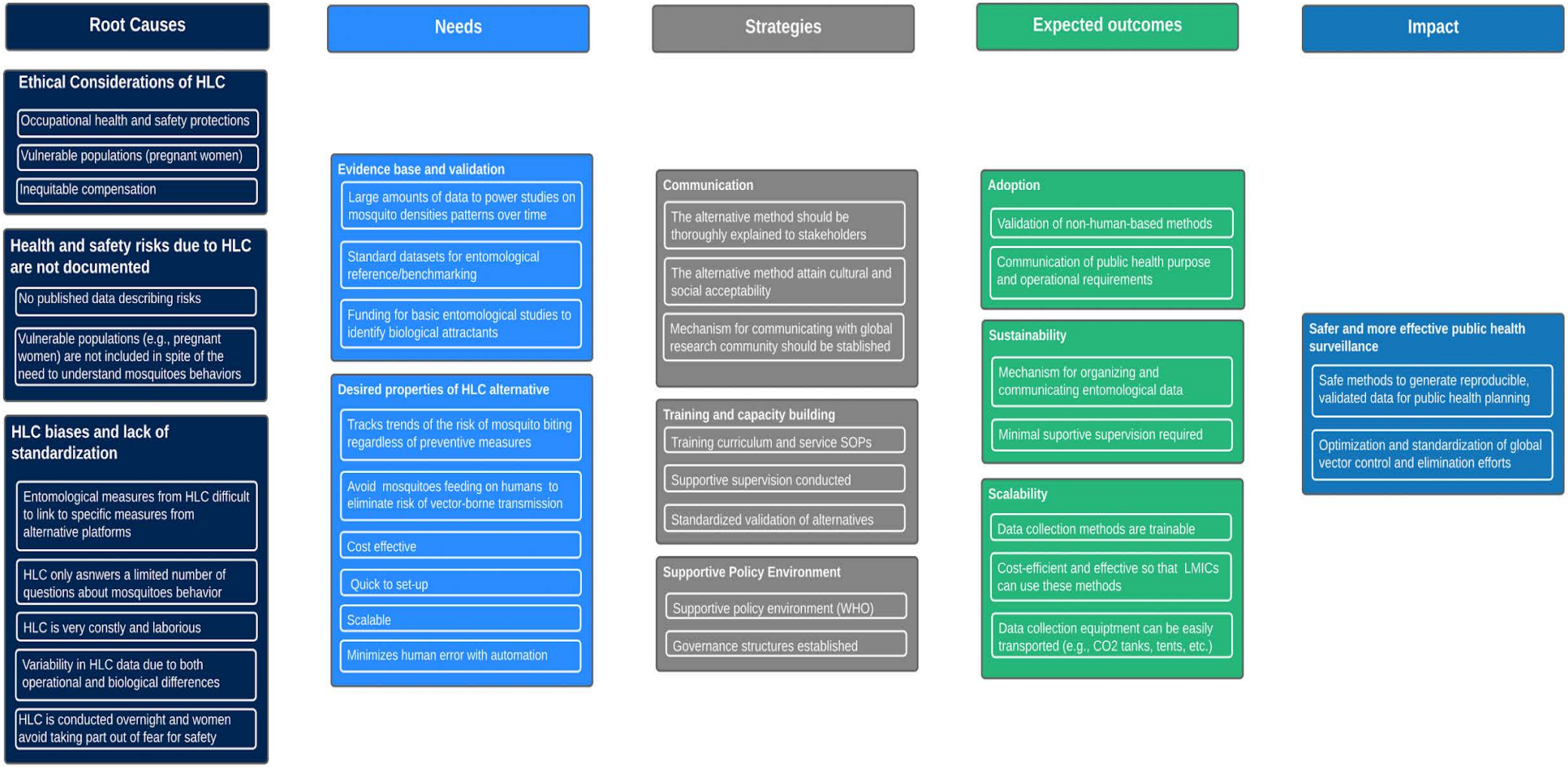
Human-baited traps/Double net traps: This method was not successful in gaining the support of community stakeholders. Dr. Burkot reported that “people absolutely hated that technique, because they believe in ghosts, and they're inside a tent and they hear noises in the night and they're by themselves, they can't see where noises came from. They freaked out and did not want to do it the following night because it was too scary!” The panel also agreed that human-baited traps are logistically difficult to undertake in multiple locations concurrently. Dr. Russell said that “The main

problem with human-baited tents (of any variety) is that they do not remove the need for a human to act as a bait, and thus the logistical requirements remain very high. In fact, higher, because you know how to organize the equipment, as well as the human volunteers." This method is also difficult to set up and would not be feasible to scale. According to Dr. Burkot, it is time-consuming to "tie and untie a Gordian knot, it takes a long time to set up these things...and you have to have a tool that is amenable to a team going into a village." Concerns have also been raised about double-net traps underestimating the true mosquito abundance as mosquitoes would escape the double net trap when they cannot feed (23).

Yeast brew (as an alternative source for the attractant, carbon dioxide): The panel reported that it is not scalable, and results are highly variable. Smallegange et al. reported that the yeast brew was also not as efficient in catching *An gambiae s.s.* during the field trials, compared to the HLC (24).

Light Traps: Dr. Russell mentioned that "generally, CDC light traps are thought to catch about 70% of the gambiae that would be caught with HLC. You can readily deploy CDC light traps but can really only sample indoors without a good source of CO_2. You then use a calibration factor when analyzing the data." Dr. Burkot reported that the light traps do not mimic the variability of human attractiveness; he said that "that's the nature of this work; mosquito numbers are highly variable and it doesn't matter...if you use a human or if you use the CDC light trap--you're just going to get this high variation and that's the mosquitoes. You have a light trap out there and it's not the same thing. It's a tech where [with] the landing catch, you've got someone sitting outdoors or someone sitting indoors and they're catching the mosquitoes that are attracted to them, so you get the same attractiveness going on there [with HLCs]. Some of those indicators are not easily adapted to collection methods that aren't [HLC]."

3.3. Framework for Change Model



4. Conclusion

4.1. Discussion

There are significant logistical challenges associated with the HLC, such as with implementation, generalizability, gender equity, ethics, and safety risks. The experts we spoke with underscored that there are some positive approaches to alternatives. Dr. Stevenson emphasized that CDC light traps are portable and require fewer human resources in comparison with HLC. She worked with modified light traps to include artificial baits and compared those to animal and human landing catches (21); although there were minor species-composition differences, CDC light traps are becoming more accurate (in terms of catching the same species as HLC) and were fairly efficient even without the presence of CO_2. They can also be scaled and are affordable (21). While strengths in alternative methods do exist, a major challenge to implementing alternatives is reconciling data due to a lack of comparability across the studies. There is a need for further research to make these methods linkable to HLC data. Dr. Lobo is currently part of an in-progress meta- analysis of 17 published studies comparing HLCs and alternative methods for collecting outdoor *Anopheles* spp.. The study makes 59 quantitative comparisons between varying trap types and sub-trap classifications (e.g., biological, chemical, physical, etc.). Preliminary results from the study suggest that there are no significant differences between the tested alternative trapping methods and outdoor HLCs for *Anopheles* collections and that these methods can be considered comparable (10).

Further studies are required to explore additional indicators of HLC risk. One example mentioned by Dr. Burkot is to explore the antigens associated with mosquito bites in different regions, to get a better understanding of biting risks associated with different populations. “We’ve got to do a lot more work, we can't take one antigen from one mosquito in Africa and say we can use that to predict biting rates of people in Asia and the Americas and the Pacific--it's too simplistic of an approach to a complex problem.” Another area of research is to optimize the efficacy of existing alternative methods in a standardized way so that surveillance methods can be compared to find the most effective alternative. Dr. Farlow mentioned that we need more research to be able to “automate these techniques [to remove] the human variability from [data collection], and it also reduces the cost significantly--so the ultimate goal is replace the human, automate it so you have reproducibility over time, and it can be implemented at scale.”

4.2. APPENDIX

TABLE 1. LIST OF KEY INFORMANTS

NAME	ROLE	LOCATION	DATE INTERVIEWED
Dr. Neil Lobo	Research Professor, Eck Institute for Global Health, University of Notre Dame	Notre Dame, USA	July 7, 2021
Dr. Tanya Russell**	Medical entomologist working as a senior research fellow co-leading the Mosquito-Borne Diseases Group at James Cook University	Cairns, Australia	July 14, 2021
Dr. Robert Farlow**	Owner at R. Farlow Consulting LLC	Burkeville, USA	July 14, 2021
Dr. Thomas Burkot**	Vector biologist at James Cook University and Research leader at the Australian Institute of Tropical Health and Medicine (AITHM). Previously a research entomologist with the United States Centers for Disease Control for 20 years	Townsville, Australia	July 14, 2021
Dr. Jennifer Stevenson	WHO Technical Officer, former research scientist overseeing the entomological activities of the International Center of Excellence for Malaria Research (ICEMR) of southern Africa, in two sites in Zambia and one in Zimbabwe	Geneva, Switzerland	July 15, 2021
Dr. Frances Hawkes	Senior Research Fellow at the Natural Resources Institute of the University of Greenwich	London, UK	July 16, 2021

***Participated in a Panel Discussion rather than individual interviews due to their collaborations on multiple projects analyzing alternative methods to HLC, including the development of a Target Product Profile*

SUMMARY OF BARRIERS TO IMPLEMENTING HLC ALTERNATIVES

The ethics of HLC need to be clearly documented

- The ethics surrounding HLC are controversial
  - Some researchers consider use of HLC as intentional harm while others classify it as involving occupational safety hazards
  - The lack of involvement of women in HLC leaves a gap in surveillance.
- The risks associated with HLC are not, to date, documented in the literature

A better understanding is needed of the science of vector attraction and feeding behavior

- CO_2 is a major attractant for mosquitoes, but there is poor understanding of other modifiers of insect behavior
- Little is documented about the reproducibility of HLC data
- A better understanding of mosquito attraction would improve our understanding of what each alternative to HLC is measuring.

The acceptability of HLC and alternatives to the community need to be documented

- There are often challenges to community acceptability for HLC
- The alternative method should be thoroughly explained to stakeholders, so that they may engage in, and support the surveillance work
- The alternative method should not create or sustain existing inequities in community settings
- Research teams should always communicate with community gatekeepers to ensure cultural and social acceptability

The costs of HLC and alternatives need to be documented

- The alternativesxs should minimize the costs of human resources
- The supplies needed for the alternative method should be cost-effective so LMICs can use them

Adoption of a HLC Alternative

The Variations in Alternative Methods

- There is much variability in how alternative methods are used— which make them difficult to compare with other HLC replacement methods
- These variations include trap orientation and distance from the human collector, time of day and season of data collection, number of collectors, etc.

Health and Safety Risks to Collectors and Communities

- Much of our risk assessments on HLC come from assumptions, as no data or studies exist on defining what the risks are to communities/community members
- Women are excluded from studies as they may be at a higher risk of malaria (and could be pregnant), but data on mosquito attraction to women is also essential.

SOPs need to be developed for any platform to address and minimize bias

- Further research needs to be done to understand why there is variation in transmission intensity between people
- All vector surveillance methods have bias; HLC has its own set of challenges
- Developing a standardized protocol will help minimize biases in data collection

Alternative is Trainable & Scalable

- Local entomologists need to be trained on using an alternative method
- The alternative methods need to be implemented at a wide scale
- The alternative method should be easy to transport and automated

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EVIDENCE FROM INTERVIEWS FOR BARRIERS TO IMPLEMENTING HLC ALTERNATIVES

Identifying the Components of an Effective Trap

"The problem with the traps is the lure – very much dependent on having CO2, and there is currently no good alternative to it." – Tanya Russell

"So you got the CO2 to bring [mosquitoes] close and then you need these other attractions to take over and bring them to that final destination…and a lot of mosquitoes are near the trap, but only a small fraction actually come close enough for actually enter the trap." —Tom Burkot

"There is a better need or an alternative better source of CO2 or something that will take the place of CO2 in as an attractant to mosquitoes." –Tom Burkot

"The alternative would need to be an automated technique that replaces the human factor and reduces the attributable error." – Tanya Russell

The Ethics of HLC

"If you have something that smells like human, looks like, even feels like a human, but you're not exposing a collector to this very ethically problematic issue of being exposed to mosquitoes but other vectors as well". –Frances Hawkes

"t's not a human ethics issue, because the person doing the collection is not the subject of the research. It's an occupational health issue, it makes it seem like a small point but people keep talking ethics and everyone gets all scared when they hear the word ethics it's actually occupational health is what it is." –Tom Burkot

"There is risk associated with HLCs, but we need to quantify it because there's currently no data to support these decisions. Even though we know there is a risk associated with it, I mean there must be risk associated with it." –Neil Lobo

Acceptability to the Community

"It's another reason to come away from [HLC] that any tool that we implement is not going to be exacerbating that problem it's going to be something that the community can be engaged with on an equal footing, so this is what I mean about kind of it raises a lot of wider questions about reinforcing gender stereotypes and disengaging women from any stake in this kind of research". –Frances Hawkes

"It was something that that was voiced a lot… the acceptability of the people who are conducting the human landing catches, but also the people who are providing their homes for those captures to take place." – Jenny Stevenson

"People absolutely hated [tent traps], because they believe in ghosts, and they're inside a tent and they hear noises in the night and they're by themselves and they can't see where noises came from. They freaked out and did not want to do it the following night because it was too scary!" – Tom Burkot

Alternative is Affordable & Sustainable

"The biggest disadvantage of the human landing catch is cost: the labor costs and supervision costs." –Tom Burkot

"You still have the cost issue because you have you have to compensate participants." –Bob Farlow

"[An alternative] would have to be cheap easy to use, [and produce] good data; those are the first three things, because if you have that the entire research NGO body would take it up anyway." – Neil Lobo

Adoption of a HLC Alternative

Health and Safety Risks to Collectors and Communities

"Why aren't people conducting studies on this parallel to ongoing studies, without any extra money to ensure that there is no risk? We don't have data on it--everything's in assumption." –Neil Lobo

"What's really interesting to me is that countries will say 'no, you can't do this with the assumption of risk,' but there's no data [on the risks]" –Neil Lobo

"And one of the other things, is that we were advised by number of people not to use women. Because of the risk that they may be pregnant and contract malaria, but also because of their safety at night." –Jenny Stevenson

The Variations in Alternative Methods

"There are a lot of different traps and each trap will have its own variation and actually, this is a good point and a really fascinating thing is that two studies can use the exact same treatment, the same trap and use different methodologies and that compare the two and then not comparable. For example, CDC light trap kept by a person under a bed net will catch different mosquitoes than CDC light traps next to a person not under a bed net--and if it's kept a foot away from their feet versus a foot away from their head: completely different mosquitoes because the mosquitoes have their own behaviors and you're basically trying to intercept those behaviors." –Neil Lobo

"There is no tool presently available that is going to be comparable to HLC. It's a matter of priorities and vector control has not been prioritized enough, that is why the value of vector biologists has been low even though the need is high, but funders do not perceive that!" —Tom Burkot

SOPs need to be Developed to Address and Minimize Bias

"The variation in transmission intensity between people is still a knowledge gap: why some people get most of the bites while others get less bites, that is part of the nature of the transmission." –Tom Burkot

"Every trapping methodology is biased in some way, it may be, one is more attractive to a particular species or a particular fraction of the population… for example, some suck mosquitoes in so actually the mosquito isn't necessarily showing that they would have necessarily landed on this host if they were seeking, they were just sucked in once they're within a certain radius so it's supporting slightly different behaviors." –Frances Hawkes

"The human landing catch just has so many difficulties associated with it, although it's being used as the gold standard it again is far from perfect." –Jenny Stevenson

Alternative is Trainable & Scalable

"There's been real efforts recently to develop capacity of local scientists and entomological techniques and trainings provided. Through centers in South Africa, Tanzania Kenya, to train African scientists." –Jenny Stevenson

"Programs need to undertake vector surveillance at a large scale to better data (with power), to be able to target interventions to the different vectors, stratified by variables e.g., receptivity of the environment, number of mosquito types, and most importantly, mosquito densities." –Tom Burkot

"We worked in the past with using CO2 tanks, but they're extremely heavy you have to have a regulator valve on it certainly know exactly how much CO2 has been produced through the night, and then you have the logistics of trying to fill the tanks." –Jenny Stevenson

"It's really hard to collect data on risk because you'd have to large scale studies. And if one out of 10,000 people get a virus infection with agencies, you have to have a statistically significant sample size." –Neil Lobo

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4.3 POSITIONALITY STATEMENT

The START Center recognizes that there are power asymmetries that exist in global health and acknowledge that there is a need to address this and recognize the limitations that come with these imbalances. We acknowledge that the KIIs we conducted were limited to the perspectives of researchers whose current academic institutional affiliations are from the Global North, and that we did not conduct any interviews with researchers from the Global South. In order to fully understand all the perspectives on advantages and disadvantages to the HLC, as well as barriers to implementing alternatives to the HLC, START recommends engagement with local and regional experts, community stakeholders, and Ministries of Health in the countries where HLCs take place.

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