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Researchers' perceptions of malaria eradication: findings from a mixed-methods analysis of a large online survey --Manuscript Draft--

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Abstract:	<p>The expected value of an investment hinges on the probability of, and time until, its realization. Though the long-term benefits of global malaria eradication promise to be large, the upfront costs and uncertainty regarding feasibility and timeframe make it difficult for policymakers and researchers to forecast the return on investment. Since a notion of the future of global malaria eradication is required in order to make fully informed health spending decisions in the present, we set out to quantify the probability and time frame of eradication through a large online survey of 844 peer-reviewed malaria researchers of different scientific backgrounds. Adjusting for selection bias, we found that the average perceived likelihood of global eradication among malaria researchers approximates the number of years into the future: approximately 10% of researchers believe that eradication will occur in the next 10 years, 30% believe it will occur in the next 30 years, and half believe eradication will require 50 years or more. The 61% of researchers who gave free form comments highlighted systemic challenges and the need for innovation as chief among obstacles to achieving global malaria eradication. Our findings highlight the difficulty and complexity of malaria eradication, and can be used in prospective cost-benefit analyses to inform stakeholders regarding the likely return on eradication-specific investments. Though researchers are generally sceptical regarding the possibility of eradication in the short-term, even failed eradication campaigns may offer substantial return on investment given the associated reductions in morbidity and mortality.</p>
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Researchers' perceptions of malaria eradication: findings from a mixed-methods analysis of a large online survey

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Abbreviated running title:

Survey on malaria eradication

Key messages:

- We estimate probability of and time frame of eradication given researchers' perceptions.
- Our results suggest that most malaria researchers believe short-term global malaria eradication to be unlikely.
- We identify challenges pertaining to eradication through qualitative analysis.
- We highlight implications for health spending and policy, given the perceived low probability of eradication.

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Abstract

The expected value of an investment hinges on the probability of, and time until, its realization. Though the long-term benefits of global malaria eradication promise to be large, the upfront costs and uncertainty regarding feasibility and timeframe make it difficult for policymakers and researchers to forecast the return on investment. Since a notion of the future of global malaria eradication is required in order to make fully informed health spending decisions in the present, we set out to quantify the probability and time frame of eradication through a large online survey of 844 peer-reviewed malaria researchers of different scientific backgrounds. Adjusting for selection bias, we found that the average perceived likelihood of global eradication among malaria researchers approximates the number of years into the future: approximately 10% of researchers believe that eradication will occur in the next 10 years, 30% believe it will occur in the next 30 years, and half believe eradication will require 50 years or more. The 61% of researchers who gave free form comments highlighted systemic challenges and the need for innovation as chief among obstacles to achieving global malaria eradication. Our findings highlight the difficulty and complexity of malaria eradication, and can be used in prospective cost-benefit analyses to inform stakeholders regarding the likely return on eradication-specific investments. Though researchers are generally sceptical regarding the possibility of eradication in the short-term, even failed eradication campaigns may offer substantial return on investment given the associated reductions in morbidity and mortality.

Introduction

Background

Malaria is a parasitic disease transmitted among humans by mosquitoes. The *Plasmodium falciparum* species accounts for a large majority of the 200 million annual cases as well as the half million annual deaths worldwide (White et al., 2014) (WHO, 2016) (Ashley et al., 2018). Malaria “elimination”, the “interruption of all local transmission of the infection in a country or region” (Tanner et al., 2015) is actively being pursued by dozens of countries around the world, leading to a renewed push for “eradication” (Hopkins, 2013) (Rabinovich et al., 2017) (Lancet, 2011).

This is not the first time that eradication has been in the spotlight. The public health community have had it on their policy agenda since the World Health Organisation (WHO) established the Global Malaria Eradication Program in the 1950s (Nájera et al., 2011). In 1957, U.S. President Dwight Eisenhower told Congress that malaria could be expected to be eradicated in five years. Following the failure of the WHO’s first attempt, the focus shifted away from global eradication towards local elimination and control. In recent years, much of the discourse regarding malaria has shifted back to global eradication (Roberts and Enserink, 2007), with funders, researchers, and public health practitioners rallying to the cause (Tanner et al., 2015). The Bill and Melinda Gates Foundation has begun actively promoting eradication as feasible “within a generation” (Gates, 2014), and the WHO has set the ambitious goal of eliminating malaria in 65 new endemic countries from 2015 through 2030 (Figure 1).

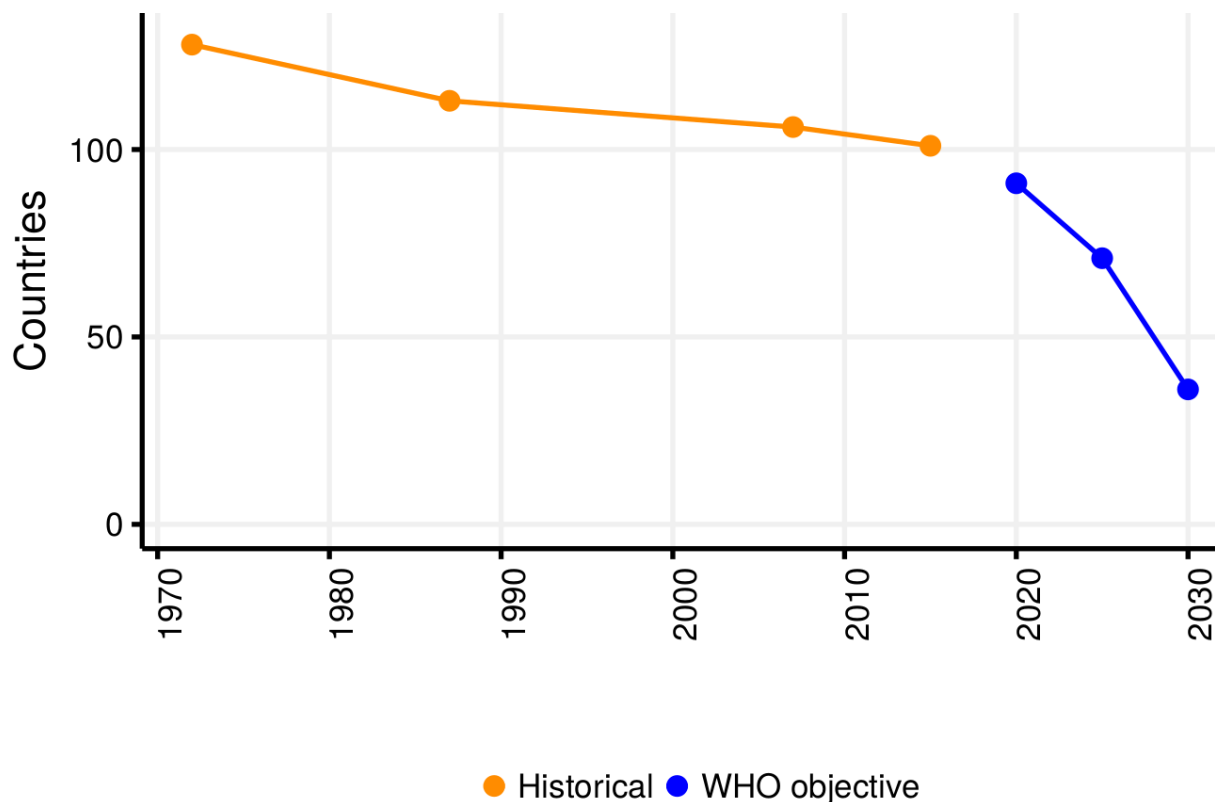


Figure 1: Countries with malaria: Observed and WHO objectives

Even in areas of high endemicity, advances in immunology, parasitology, and modeling, along with economic development, have made eradication appear a more feasible goal, though not in the short term (Snow, 2015) (Eckhoff et al., 2014). From both policy (Yamey, 2004) and scientific (Alonso et al., 2011) points of view, eradication has never before received so much attention.

Most of the current research on expert opinion regarding the feasibility of malaria eradication focuses on the *how* rather than the *if* and *when* (Tanner et al., 2015). The participants in the Malaria Eradication Research Agenda (MalERA) process, in particular, have guided research goals and identified gaps in order for eradication to occur (Alonso et al., 2011) (Rabinovich et al., 2017). Though the MalERA authors state that eradication is feasible given the “current tools and state of knowledge”, mentions to the time frame are vague (“within the lifetime of young scientists just embarking on

their careers” (Alonso et al., 2011) and “in the longer term” (Rabinovich et al., 2017)) and no mention is made of the perception of the overall probability of eradication. International programmes, such as the WHO Global Malaria Programme (GMP), have acknowledged the need “to take an official position on how and under what timeline malaria eradication could be achieved” (“Malaria policy advisory committee to the WHO,” 2015). Clarity on timeline and likelihood of eradication plays a crucial role in the economic analysis of the expected value of malaria eradication initiatives, ultimately informing health policy decisions. But achieving clarity is difficult, given the many complex factors which affect malaria transmission, research funding, and technological development.

Proponents of eradication point to the success of historical and current campaigns (smallpox and polio, respectively), and highlight the long term benefits in health and wealth to future generations (Barrett, 2013). One often cited figure is for smallpox eradication, in which the investment of each dollar led to a return of greater than 400 (Barrett, 2006). Unlike smallpox (for which analysis was able to be retrospectively constructed based on observed costs and benefits), forecasting models have to be used in order to estimate the value of a prospective investment. Malaria’s eradication is even more difficult to predict than many other infectious diseases, given the lack of a highly effective vaccine (Coelho et al. 2017).

The general objective of eradication serves to inspire, rally funder support, motivate researchers, and focus the efforts of programmes. The recently established Lancet Commission on malaria eradication, while acknowledging that there exists “scepticism about [its] technical feasibility”, states that “eradication is the only acceptable end goal” (Chen et al., 2018). To the extent that malaria eradication (by definition) has never

occurred, the parameters needed for an ex post cost-benefit analysis are unknown.

Nonetheless, prospectively estimating eradication's return on investment is crucial to deciding when and how to pursue the goal, especially in light of the high direct and opportunity costs of eradication-specific interventions.

One approach to economic evaluation is the use of infectious disease transmission models. These have been applied to diseases which are closer to eradication than malaria, since the uncertainty around model input parameters is less, requiring fewer cascading assumptions in order to present possible comparative scenarios. For example, Kastner et al. were able to describe 4 relatively realistic pathways to Lymphatic Filariasis eradication, as well as the pre-requisite role and magnitude of certain interventions (Kastner et al., 2015). A similar modeling framework was then used to estimate the cost of eradication (Kastner et al., 2017). A recent modeling analysis on onchocerciasis eradication, based on a disease transmission model, showed that the costs of elimination (relative to staying in "control mode") in Africa would be far lower even in the short term, thanks to the improvements it would lead to in both treatment times and prevented surveillance costs. Given the relative proximity of eradication, and the narrow geographic scope, the authors were also able to estimate the timeline to eradication (Kim et al., 2017).

This level of detail and specificity in the economic evaluation landscape of malaria eradication, unfortunately, is not possible, given its high prevalence and epidemiological complexity. In fact, there are no transmission models estimating the likelihood and time frame of eradication, or its derivative cost-benefit ratio. Globally, where transmission modeling has been used for the purposes of forecasting the future epidemiology of malaria, the methods have generally been aimed at optimizing elimination methods

(Slater et al., 2015), determining whether a strategy is scalable (Brady et al., 2017), guiding funding and drug development (Patouillard et al., 2017) (Slater et al., 2017), or comparing a range of hypothetical morbidity scenarios (Winskill et al., 2017), rather than assessing the likelihood of or time until the occurrence of eradication.

To the extent that estimating eradication's likelihood and timeframe is essential to forecasting the cost-benefit ratio of eradication interventions, alternative methods are needed to forecast such parameters. Just as the stock market aggregates perceptions to provide an assessment of something as complex as a company's value, aggregating perceptions may be a useful tool for tackling the complexity of malaria eradication. Many studies have shown value in expert elicitation as a means to reduce uncertainty and inform decision making (Morgan, 2014), and various techniques exist to generate consensus from multiple points of view (Li 2005). As Francis Galton famously demonstrated by showing that crowds' aggregated estimates of cow's weight formed a quasi-normal distribution centered around the true weight (Wallis, 2014) (Galton, 1907), averaging the perceptions of many can be more accurate than taking the opinion of any single expert, since the biases of diverse viewpoints can be complementary and corrective. Measuring consensus and discord among disease-specific researchers from a variety of disciplines can serve as a barometer of (informed) opinion, both guiding resources and identifying areas of concern (Keenan et al., 2013).

The optimal assignment of resources for malaria eradication campaigns hinges on the expected value of those campaigns, the latter being a direct function of the discounting applied to future benefits multiplied by the time to and probability of eradication. Holding constant factors such as the cost and benefits of eradication, the return on investment of malaria eradication initiatives is a function of eradication's timeframe.

Given this, estimating these parameters is crucial to evaluating if and when attempts at eradication should be undertaken.

We propose that the aggregation of malaria researchers' perceptions regarding the time frame and likelihood of eradication forms a probability distribution which can be used to estimate the expected value of eradication-specific investments. The objective of this study is to gauge (expert) opinion about, estimate the likelihood of, and quantify the potential time frame to malaria eradication through a systematic online survey of malaria research professionals from a wide array of academic disciplines. In doing so, we aim to help guide the optimal distribution of health resources by informing subsequent estimations of the expected value of malaria eradication efforts.

Methods

Our study population included all first authors (with available email addresses) returned in a PubMed search for the term "malaria" from January 1, 2010 through December 20, 2016. We used PubMed because it was the most comprehensive publication database for malaria-related research, and also exposed enough metadata about articles and authors so as to allow for relevant bias control. Personalized emails addressing the author by name and mentioning the relevant paper were sent to each of the 7680 authors during the period from December 20, 2016 through January 2, 2017. Researchers were invited to participate by clicking a link to the survey form. The survey was simple, consisting of only name, email, and four content-related fields along with a "general comments" section. The original survey is viewable at <http://economicsofmalaria.com/survey>.

Content-related survey fields consisted of:

1. Area of expertise.
2. Perceived probability (%) of malaria eradication in 10, 20, 30, 40, and 50 years.
3. Free choice perceived number of years until malaria eradication.

Supplementary data on researchers is useful for the assessment of selection bias and determinants of perception, we estimated participant gender, total number of citations, and total number of peer-reviewed articles published. In order to estimate whether a user was male or female, we used data from the North Atlantic Population Project, and U.S. government (Mullen, 2015). We binned total citations and total publications into three categories: 0-5 (junior-level researchers, PhD students, etc.); 6-99 (most professional academics); and >99 (the most prolific researchers). The searching and retrieval of information pertaining to articles and citations from the PubMed database was carried out using tools from the RISmed package (Kovalchik, 2015). Information retrieved about authors was used to de-bias parameters in an ordinary least squares regression, analyzing the association between number of publications and perceived years to eradication.

Following Francis Galton's example, we took the average of all responses as the likely point estimate for event probabilities, and the totality of the responses to each numeric question as the distribution around which the likely confidence interval of those likelihoods and time frames could be formed.

Quantitative analysis was carried out in R language (R Core Team, 2015). All analysis code, as well as the code used for the identification and contacting of participants, is publicly available at (https://github.com/joebrew/malaria_survey).

Qualitative analysis of free text comments was carried out using thematic content analysis, with inductive open coding (Markey et al., 2014). Thematic content analysis (Vaismoradi et al., 2016) was employed to code responses following the 6-phase approach laid out by Braun and Clarke (Braun and Clarke, 2006). The approach underwent several iterations in which codes were modified, discarded and created. Themes were identified and comments were coded as either descriptive (comments pertaining to the “problem” of malaria eradication) or prescriptive (pertaining to potential “solutions” for eradicating malaria).

Results

A total of 884 researchers participated in the survey from the 7918 invitations sent (participation rate of 11.16%). Areas of expertise were non-exclusive and self-described. 604 (68.3%) participants declared at least one area of expertise.

Participants had a total of 219 unique (self-described) areas of expertise. The five most popular were Epidemiology (357), Information Technology (344), Parasitology (319), Biology (277), Clinical medicine (207).

Most participants saw eradication as extremely unlikely in the next 30 years, but increasingly likely thereafter. Figure 2 shows the distribution of year-specific likelihood perceptions (panels A-E), as well as an illustration of how both likelihood and uncertainty grow over time (panel F). At the 40 year mark, the distribution of perceived likelihood of eradication appears “normal”, and by 50 years it is slightly shifted to the right (ie, consensus is towards eradication more probable than not).

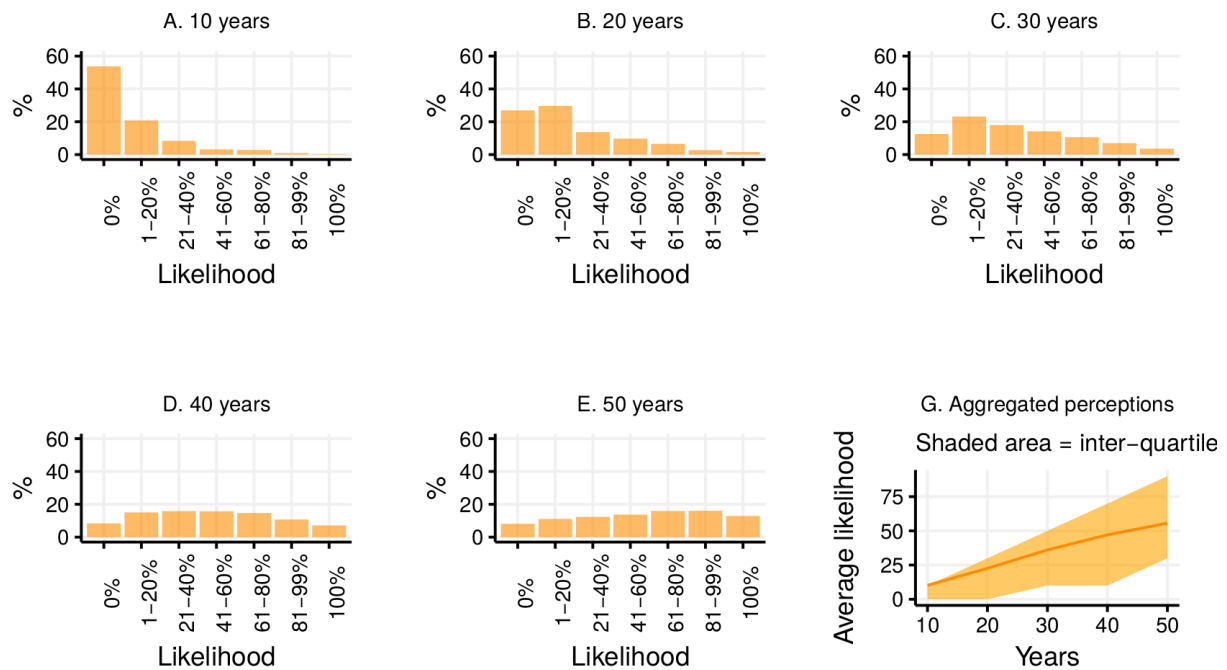


Figure 2 - Perceptions of likelihood of eradication

In regards to responses to perceived years until eradication, 59 (0.7%) were either blank or unintelligible, whereas 825 participants responded. Among respondents, 616 (74.7 %) estimated that it would be 50 or more years until eradication.

Respondents were qualitatively different from non-respondents. Importantly, the average number of total author-specific citations was 40.91 among respondents, but 92.92 among non-respondents. This suggests a tendency for more senior or impactful researchers not to respond. When examining the number of average citations per article, the difference between respondents remained: 4.75 among respondents, and 8.95 among non-respondents, highlighting the greater impact of non-respondents relative to respondents. Males responded at a significantly greater rate (12.18) than females (9.14) ($p < 0.001$, Pearson's Chi-squared).

Variable	Characteristic	Responded	Invited	Response rate
Sex	Female	209	2287	9.14 %
	Male	358	2939	12.18 %
	NA	317	2692	11.78 %
Citations	0-5	621	3299	18.82 %
	6-99	179	3270	5.47 %
	> 99	84	1349	6.23 %

Table 1: Response rate by participant characteristics

Selection bias is not of concern in the case of differential response if the groups for whom there are differences are not different in terms of the outcome variable. This was the case for sex: males responded at a greater rate than females, but were not statistically significantly different in regards to pessimism/optimism (ie, time frame or likelihood of eradication). In the case of researcher impact (as measured by the total number of citations), selection bias plays a role: being highly-cited was associated both with eradication “pessimism” as well as likelihood of non-response.

In order to de-bias sample selection, we estimated a binomial logistic regression model to assess the likelihood of response as a function of sex and (binned) number of citations. Having estimated the odds of survey participation, we then used the inverse of the selection model’s predictions as weights in a simple linear model to adjust our estimates. We run a separate weighted model to estimate the likelihood of eradication at 10, 20, 30, 40, and 50 years. Figure 3 shows both the aggregated perceived likelihood of eradication over time before and after adjusting for sample selection based on binned number of publications. Our adjusted and unadjusted estimates coincide in the long-term, but diverge sharply in the near-term; adjustment suggests that had our pool of respondents been less biased, the average perceived likelihood of near-term eradication would have been lower.

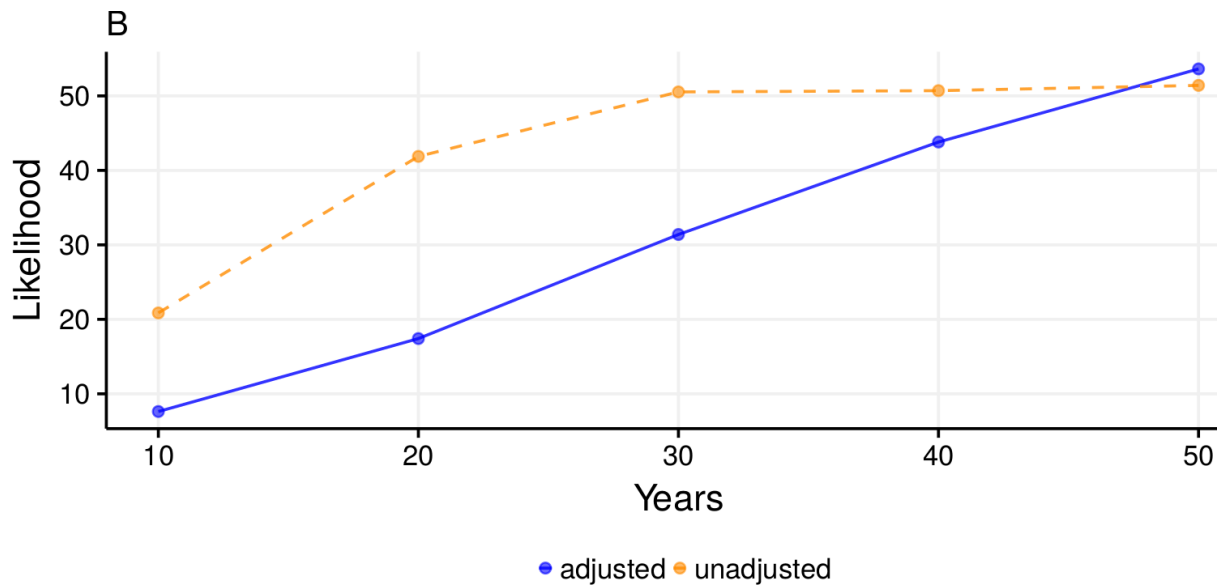


Figure 3: Aggregated perceived likelihood of eradication over time.

Qualitative analysis of comments

Of the 884 who responded to the survey, 540 (61.09%) provided a comment. The three subject themes identified through iterative, open coding were:

1. *Solutions*: Comments pertaining to the innovations required to achieve eradication, priorities, and the desirability of certain approaches.
2. *Systemic challenges*: comments pertaining to political, social, environmental or logistical issues related to eradication.
3. *Complexity*: comments which focus on the multi-dimensional components of eradication.

Comments were also classified as descriptive or prescriptive. A majority (59.26%) were descriptive. Descriptive comments were more pessimistic (in regards to perceived

years until eradication) than prescriptive comments, though this difference did not reach the level of statistical significance ($p = 0.21$, Pearson's Chi-square).

In regards to **solutions**, comments largely pertained to the necessity of further technological advances and innovations. One participant wrote that “currently available technology can't achieve [eradication], even if delivered optimally”; another argued that eradication could not be achieved without a “game-changing innovation”, whereas multiple others referred to the need for “transformative” technologies:

We can't achieve eradication with our current tools. We'd need new medicines, a better vaccine, and maybe other vector control tools.

Many noted the need to “overcome the challenge of drug resistance”. More than 10% of commenters noted the need for an effective vaccine. Most “solutions”-coded comments were prescriptive in nature, often suggesting the nature of the needed innovation, with a slant towards pharmaceutical options and vaccination.

Systemic challenges to malaria eradication were noted by the majority of commenters. Comments in this category can be divided into four sub-themes: (i) lack of coordination, (ii) lack of good surveillance and health services, (iii) lack of political will and (iv) poverty. In direct contrast to the previous comments, many emphasized that “we already have the tools to achieve eradication” and that the only piece lacking was “robust health systems”. Many commenters noted problems of coordination, as illustrated in the below quote.

It will be very difficult to eradicate malaria... not because we don't have the technologies, which we already have... the problem is politics. Malaria doesn't stop in (sic) borders of a country and it would take a joint effort of a lot of political

leaders to get programs in place to fight malaria. Unfortunately I don't see this happening anytime soon.

Others echoed the sentiment, with many comments focusing on the need of strong surveillance and treatment delivery systems. Some made the sequential argument that “eradication of poverty” must precede disease eradication:

Eradication requires a full systems-wide approach, not a disease-specific approach.
The eradication of smallpox was a triumph of management, not medicine or technology.

Another noted that the survey “left off the list the most important factor - economic development”. Many echoed the sentiment, stating that “with no economic development, you cannot have eradication” and that poverty is the “cause” of malaria. Comments coded as “systemic” tended to be descriptive and more pessimistic than others.

“Complexity”-coded comments were rare (18% of all comments) and more pessimistic than average in regards to the timeline and likelihood of eradication. These comments highlighted the inherent challenges in the epidemiology of malaria, such as the changing dynamics of malaria transmission, the resilience of the parasite and vector, climate change, and the inability to aim interventions accurately with an “ever-moving target”. The potential for adaptation was highlighted in reference both to the mosquito as well as the parasite itself. Several commenters pointed out the multitude of prerequisite conditions for eradication to even be considered feasible:

This question is highly dependent on background context, e.g. global political and economic dynamics, as well as international conflict. Complete global eradication is

an extremely singular goal that requires a vast array of necessary conditions - if any of these fail, eradication will not be achieved.

Many commenters thought that the terms “eradication” and “malaria” were so complex and nebulous that the public health practitioners should avoid them all together, so as to not repeat the mistakes of the WHO GMP in the 1950s. One commenter wrote that eradication is a “postwar” idea that developed from the “abandonment of a broad sociopolitical understanding of the causes of disease, and the emphasis on technological solutions.” “Complexity”-coded comments tended to question the utility of eradication as a concept or goal tended to be skeptical of its feasibility. Largely, they were prescriptive, advocating for a re-framing of the conversation so that the focus was not on an “arbitrary” goal like eradication, but rather on scaling up control and making region-specific progress.

Discussion

This study has elicited researchers’ view, through an online survey, on likelihood and time to malaria eradication. Approximately three-quarters of respondents believe that malaria will not be eradicated in the next 50 years. When adjusted for selection bias, the perceived likelihood of eradication in 50 years remains similarly low, but estimates for shorter-term eradication are even lower.

Areas of high malaria endemicity are often also those with high competing health costs. When estimating the return on investment of malaria elimination initiatives, not only must one take into account the potential benefits (even in the case of failure), but also the opportunity costs (even in the case of success). After all, eradication and elimination are not binary success/failure propositions - an initiative should be judged both on its

epidemiological circumstances (Churcher et al., 2014) as well as the counterfactual improvements in health which could have been achieved via other paths. Even “failed” eradication may still bring about significant improvements in health.

Limitations

This paper has several limitations. Conceptually, academic researchers are specialists - their narrow, field-specific view of eradication’s feasibility is of arguable reliability, given that they may be unfamiliar with the operational, cultural and “real-world” challenges of malaria eradication. Though crowds have been found to be more “wise” than individuals in many cases, the application of an approach similar to the “wisdom of crowds” is not suitable to all classes of problems (Mannes et al., 2014). Crowds can be susceptible to social biases (Lorenz et al., 2011) (although this survey’s anonymity largely protects against this issue), and other biases may come in to play, especially given that our study was of a crowd of “specialists”, rather than the population as a whole.

Four potential biases are worth mentioning specifically. (1) “Conjunction fallacy” suggests that the general goal of eradication may seem less likely than the sum of the goals of country-specific elimination. (2) A (reverse) variant of the “hot hand fallacy”, in which researchers may mistakenly base their assessment of current chances of eradication on previous failures. (3) Parkinson’s law of triviality suggests that researchers may disproportionately see the challenges of their own research (antimalarial drug resistance, etc.) as larger or more relevant to the global eradication campaign than they really are. (4) Finally, and ironically, “optimism bias” may play a perverse role in researchers’ responses; though eradication is certainly a goal desired

by all, one could argue that malaria research specialists subconsciously realize that they actually stand to lose out professionally in the case of eradication.

As with Keenan et al's survey of experts regarding the feasibility of eradication of neglected tropical diseases, our survey detected relatively high levels of eradication skepticism and did not delve into whether researchers had clinical or operational experience, nor did it assess opinions of program workers, nor did it explore complexities pertaining to different types of or forms of existence of malaria (Keenan et al., 2013).

Conclusion

The findings of our survey show researchers expressing doubt about the likelihood of eradication and suggesting a long time frame until it is achieved. The causes for scepticism are diverse, but common themes were the need for innovation, systemic challenges, and the complexity of the disease and its transmission.

The implication of these results are two-fold: (1) that those working or investing in eradication-specific campaigns, as well as those modeling these campaigns' hypothetical cost-benefit, should factor in researchers' perceived long time frame when calculating those campaigns' expected value; (2) that champions of near-term eradication may need to make a more compelling case to malaria researchers of eradication's feasibility, in order to better focus and inspire the latter.

We have strived to present the results of our study without insinuation regarding the "true" feasibility and timeframe of eradication, as only time will tell whether the collective "wisdom" of researchers was worth adhering to or not. The actual cost-benefit of eradication interventions is not only a function of eradication's success, but also of a

number of other factors. This study's primary contribution is the provision of a snapshot of perceptions of malaria researchers, whose opinions may be of value not only to other researchers, but also to the malaria and public health communities at large.

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Author statement

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A handwritten signature in black ink that reads "JOE BREW". The letters are slightly slanted and connected in a casual, cursive-like style.

Author signature

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