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

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Abstract

Quantifying an event's probability and time frame is essential for calculating its expected value. In the case of global malaria eradication, uncertainty regarding feasibility makes it difficult for policymakers and public health practitioners to make fully informed decisions. The opportunity cost of investments in eradication-specific interventions can be high, particularly in contexts with other urgent health priorities. In a large survey of malaria researchers (n = 844), we query perceptions regarding the likelihood and time frame of eradication, as well as the perceived chief areas needed for improvement in order for eradication to be achieved. We assess pessimism/optimism (via the proxy of years-to-eradication), broken down by area of expertise, and adjust for selection bias. We also carry out a qualitative analysis of free-form comments provided by 61% of respondents. Our results show a disconnect between optimistic public institutional discourse and pessimistic private opinion, suggesting either (a) the necessity of a realistic accounting of eradication's low short-term likelihood in health planning and financing, or (b) the need for a more compelling case regarding eradication's feasibility to be made to the research community.

Research Highlights

- Makes novel use of a "wisdom of crowds" approach
- Assesses perceived time frame and likelihood of global malaria eradication among researchers
- Identifies challenges pertaining to eradication through qualitative analysis
- Highlights the gap between researchers' collective pessimism and institutional optimism

Keywords

Malaria, eradication, elimination, mixed methods, survey, crowdsourcing

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Introduction

Background

Malaria is a parasitic disease transmitted to humans by mosquitoes. The *Plasmodium falciparum* species, transmitted by the female *Anopheles* mosquito, accounts for a large majority of the 200 million annual cases as well as the half million annual deaths [1] [2]. Malaria "elimination", the "interruption of all local transmission of the infection in a country or region" [3] is actively being pursued by dozens of countries around the world, leading to a renewed push for "eradication" (the global elmination of malaria) [4].

This is not the first time that eradication has been in the international spotlight. The scientific and public health communities have had eradication on their policy agenda since the WHO established the Global Malaria Eradication Program in the 1950s [5]. 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 strategies. In recent years, much of the discourse regarding malaria has shifted back to global eradication [6], with funders, researchers, and public health practitioners rallying to the cause [3]. The Bill and Melinda Gates Foundation has begun actively promoting eradication as feasible "within a generation" [7], and the World Health Organization (WHO) has set ambitious goals, stating the objective of eliminating malaria in 65 new endemic countries from 2015 through 2030 (Figure 1).

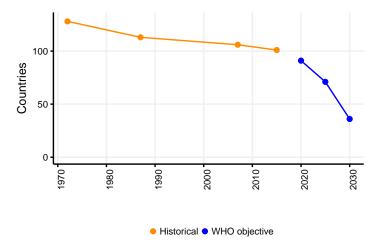


Figure 1: Countries with malaria: Observed and WHO objectives

Even in areas of high endemicity, advances in immunology, parasitology, modeling and vaccinology, along with rapid economic development, have made eradication appear a more feasible goal, though not possible in the short term [8] [9]. From both administrative [10] and scientific [11] points of view, eradication has never before received so much attention, nor appeared so within grasp.

Most of the current research on expert opinion regarding the feasibility of malaria eradication focuses on the how rather than the if and the when [3]. The participants in the Malaria Eradication Research Agenda (MalERA) process, in particular, have guided research goals and identified gaps in order for elmination to occur [11] [4]. Though the MalERA authors firmly state that eradication is not 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" [11] and "in the longer term" [4]) and no mention is made of the perception of the overall probability of achieving 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" [12]. Clarity on timeline and likelihood of eradication could inform policy, and plays a crucial role in the economic analysis of the expected value of malaria elimination initiatives. But achieving clarity is difficult, given the many complex and interacting variables

which affect malaria transmission, research funding, and technological development. The question of how is complex enough, rendering questions of if and when even more difficult to answer.

The general objective of eradication serves to inspire, rally funder support, motivate researchers, and focus the efforts of public health practitioners. Proponents of disease eradication point to the success of historical and current campaigns (smallpox and polio, respectively), and highlight the benefits in health and wealth to future generations. However, the opportunity cost of investments in eradication-specific interventions can be high. And the "expected value" of an investment in a binary scenario (eradication or not) is a function of the probability of the scenario's occurrence, and the temporal lag of that occurrence. Therefore, estimating the likelihood and time frame of eradication of malaria is essential for making sound investments in health. But how can we quantify these values given the great deal of uncertainty surrounding eradication?

Many studies have shown value in expert elicitation as a means to reduce uncertainty and inform decision making [13]. But experts can sometimes be mistaken, a fact implicitly recognized when patients request a "second opinion" from another doctor when facing uncertainty. Additionally, relying on only a small panel of experts for a problem as complex as malaria exposes one to bias, just as an overly concentrated investment portfolio exposes one to more risk. As Sir Francis Galton demonstrated in his famous study in which he showed that the crowds' aggregated estimates of cow's weight formed a quasi-normal distribution centered around the true weight [14] [15], 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 symbiotic.

Assessing the likelihood and time frame of eradication, therefore, requires the combination of multiple points of view. 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 [16]. 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.

A great deal of previous research already covers the cost per case prevented [17] [18] [19] [20] [21]. Likewise, literature exists which could serve as a model for quantifying the location-specific opportunity costs associated with funneling funds towards malaria eradication [22] [23] [24]. The correct discount rate for estimating the value of future lives saved is more of a philosophical question than an economic one. This leaves only the probability and time-frame to eradication, questions which have been addressed anecdotally, but never answered quantitatively.

The economic case for striving to achieve malaria eradication is compelling [25]. Though the case-specific marginal cost of eradication can be expected to be high (relative to a simple control approach), successful eradication would mean massive recurring savings in the long-term [26]. However, to the extent that the case-specific marginal cost of prevention in an eradication campaign is high, estimating the likelihood of success is fundamental to the correct distribution of resources, particularly in low-income environments.

In other words, the rational assignment of resources for malaria eradication campaigns hinges on the expected value of those campaigns. We can describe this relationship below:

$$I_T = P(x) \frac{B(m)}{m} (1+\delta)^{-T} - P(x) \frac{C(m)}{m} (1+\delta)^{-T}$$

- I is the return on investment
- m is the number of malaria cases
- \bullet x is whether eradication has been achievied
- T is the time-frame (to both costs and benefits)
- P is the probability (of eradication)
- B is the benefit of preventing malaria
- C is the cost of preventing malaria
- δ is the discount rate and opportunity cost

(I) is the return on investment at time (T) (the "end of malaria"). We take the present value of the benefits multiplied by the probability of success minus the value of costs times the probability of success, and multiplyboth terms by the discount rate traised to T to arrive at the return on investment.

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 systemic 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 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. 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 survey was administered and data were collected through Google Drive. The original survey is viewable at https://goo.gl/forms/IroAEooDuJ6KM5Ho2.

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.
- 4. Ranking of the WHO's "health system building blocks" [27] in regards to attention needed in order to achieve eradication (the purpose of final point was to introduce a prescriptive element to the researchers' responses, ie, identify potential areas of consensus in regards to the path towards eradication).

The survey was intentionally as short as possible, so as to appeal to time-pressed participants. However, supplementary data on researchers is of value for the assessing of selection bias and determinants of perception. Accordingly, we estimated the likelihood of a participant being of one of two genders (male or female) based on first name, and the likelihood of a participant being of one of five ethnicities (White, Black, Hispanic, Asian, Other) based on the provided last name. For gender estimations we used data from the North Atlantic Population Project, and U.S. government [28]; for ethnicity, Khanna et al's bayesian prediction algorithm for the estimation of racial categories [29] [30] was employed. The searching and retrieval of information from the PubMed database was carried out using the RISmed package [31].

Survey results were first analyzed descriptively. Following Francis Galton's example, we naively take 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 likely confidence interval of those likelihoods and time frames.

Quantitative analysis was carried out in R language [32]. Ordinary least squares regression was employed to estimate the effect of area of expertise on the eradication pessimism-optimism (through the proxy of perceived years to eradication). 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 [33]. Participants were invited to provide "any general comments on the timeline and likelihood of global eradication". Thematic content analysis [34] was employed to code responses following the 6-phase approach laid out by Braun and Clarke [35]. The approach was inductive, used open-coding to identify latent themes, and underwent several iterations in which codes were modified, discarded and created. Using the RQDA software to assist in data management and theme coding [36], four subject themes were identified. Comments were additionally coded as either descriptive (comments pertaining to the "problem" of malaria eradication) or presciptive (pertaining to potential "solutions" for eradicating malaria). Finally, free-text comments were scored for overall sentiment polarity [37].

Results

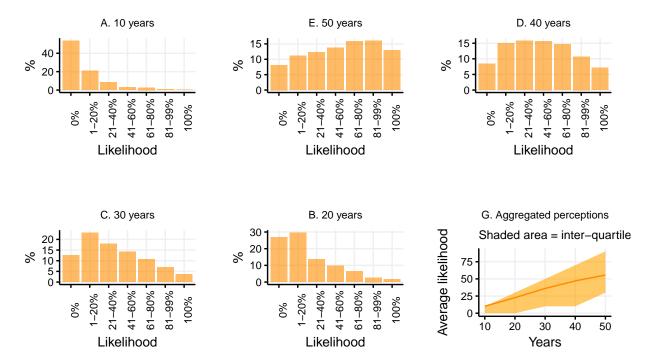


Figure 2: Perceptions of likelihood of eradication

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, with participants having the option to choose from up to 3 of 10 checkboxes, or to write in one or more "other" areas of expertise. 604 (68.3%) participants declared three or fewer areas 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).

Quantitative results

Participants were asked to quantify (as a percentage) the likelihood of eradication in the next 10, 20, 30, 40, and 50 years. Most participants saw eradication as extremely unlikely in the next 10-30 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).

Participants were asked to provide the number of years they believe it will take until eradication can be achieved. 59 (0.7%) were either blank or uninteligible, whereas 825 participants responded. Among respondants, 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 either 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

Response categories were Anthropology, Biochemistry, Bioinformatics, Biology, Chemistry, Clinical medicine, Drug discovery, Ecology, Economics, Entomology, Epidemiology, Geography, GIS, History, Immunology, Infectious disease, IT, Malaria, Medical entomology, Medicinal chemistry, Microbiology, Parasitology, Pharmacology, Pharmacy, Political science, Public health, Statistics, Vector biology, Vector control, and Virology.

among non-respondents, highlighting the greater impact of non-respondents relative to respondents. Males responded at a greater rate (12.18) than females (9.14) and those with Hispanic last names responded at a greater rate than those with last names of other ethnicities (see table).

Table 1: Response rate by author characteristics

Variable	Characteristic	Responded	Invited	Response rate
Sex	Female	209	2287	9.14 %
	Male	358	2939	12.18 %
	NA	317	2692	11.78 %
Ethnicity	Asian	86	1192	7.21~%
	Black	52	455	11.43 %
	Hispanic	56	401	13.97 %
	White	690	5870	11.75 %
Citations	0-5	621	3299	18.82 %
	6-99	179	3270	5.47~%
	> 99	84	1349	6.23~%

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 significantly greater rate than females (p < 0.001), 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 an important role: being highly-cited was associated both with eradication "pessimism" as well as likelihood of non-response. In other words, our pool of respondents was less highly-cited than our pool of invitees, and among respondents, those who were highly-cited tended to be more pessimistic (see Figure 3, Panel A).

De-biasing sample selection

In order to de-bias sample selection, we employed Heckman's two-step correction method as well a more simple binomial logistic regression model to estimate the likelihood of response as a function of sex and (binned) number of citations. To the extent that the two methods presented nearly identical value, we present here the results of latter. 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 weighted model to estimate the likelihood of eradication at 10, 20, 30, 40, and 50 years (employing a separate model for each time period). Figure 3 shows both the aggregated perceived likelihood of eradication over time by number of publications (panel A) as well as the difference in the aggregate perceived likelihood of eradication for the entire sample before and after adjusting for sample selection (panel B).

Participants were heterogenous in their perceptions, with all of the 5 pre-determined cut-offs containing the whole range of likelihoods (0-100%), and the free-form time frame responses suggesting that eradication would be achieved in a time-frame ranging from less than a decade to never. Heterogeneity can only be partly explained by area of expertise, as the differences in perception between disciplines were minor and insignificant (see Figure 4).

Qualitative analysis of comments

Of the 884 who responded to the survey, 540 (61.09%) provided a comment. Relative to non-commenters, commenters were more optimistic on average, but also more polarized in opinion. The three subject themes identified through iterative, open coding were:

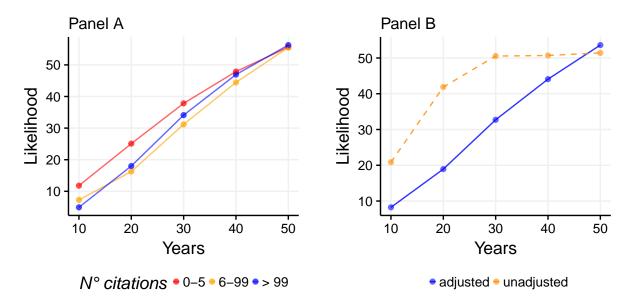


Figure 3: (A) Average perceived likelihood of eradication over time by number of author publications; (B) Aggregated perceived likelihood of eradication over time, adjusted for sample selection and unadjusted.

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

Comments were also classified as descriptive or prescriptive. A majority (59.26%) were descriptive. Descriptive commenters were more pessimistic (in regards to perceived years until eradication) than prescriptive commenters, though this difference did not reach the level of statistical significance (p=0.21). Descriptive comments also received sentiment polarity scores which were more negative than prescriptive comments, although again this difference did not reach the level of statistical significance (p=0.18).

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. Genetic engineering was mentioned by several commenters as a promising means to achieve eradication quickly. Most comments coded as "solutions" were prescriptive in nature, often suggesting the nature of the needed innovation, with a heavy 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 roughly four sub-themes: (i) lack of coordination, (ii) lack of good surveillance and health services delivery, (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

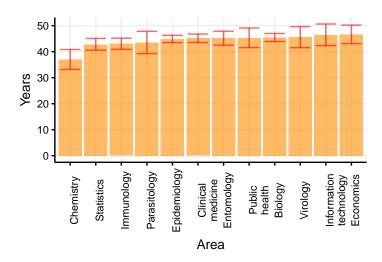


Figure 4: Average perceived years to aggregation by discipline

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. Many commenters focused on other reasons for stagnating progress, such as "weak or failing health systems...due to political unwillingness or conflict". Comments coded as "systemic" tended to be descriptive and more pessimistic than others. Many noted that malaria is a "disease of poverty", with "social injustice" as the root cause. Some made the sequential argument that "eradication of poverty" must preced disease eradication. Along the same lines, one commenter wrote:

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. As with the "systemic challenges" of eradication, comments which were coded as poverty tended to be descriptive rather than prescriptive.

Complexity was a relatively rare category (<20% of all comments), those whose comments were coded as the "complexity" category were more pessimistic than average in regards to the timeline and likelihood of eradication. Many commenters 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. Many comments addressed the fact that the conversation on eradication is largely taking place within the public health community, whereas the causes of malaria endemicity are largely orthogonal to public health interventions, "going beyond the health sector". Several commenters pointed out the multitude of prerequisite conditions for eradication to even be considered feasible:

To my mind, 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 the them all together, so as to not repeat the mistakes of the WHO GMP in the 1950s. For example, some highlighted that talking about "malaria" as one disease misses the mark, since the different species of parasite and contexts in which they live make elimination in each area

very distinct from other areas. 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." Many stated that global malaria eradication was simply not possible, and two argued that it may not be desirable or ethical. One stated that the concept was "absurd" and that "I'm not even sure why people talk about it". Another questioned the utility of discussing "eradiction" as a concept:

Eradication is a different objective than elimination. Elimination means that the disease is not endemic but could reappear even in a country like Norway if infrastructure breaks down. Elimination may be possible in poor endemic countries, following socioeconomic development. Eradication means that the parasite disapears from the planet, which is not realistic...

Comments questioning the utility of eradication as a concept or goal tended to be skeptical of the 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

Our survey reveals a notable gap between the public discourse on malaria eradication, and those views held (largely privately) by malaria researchers. Approximately three-quarters of respondents believe that malaria will not be eradicated in the next 50 years; in other words, assuming our pool of respondents is of typical post-PhD age, most believe they will not live to see eradication. When adjusted for selection bias, the perceived likelihood of eradication 50 years from now remains similarly low, but estimates for shorter-term eradication are even lower.

If we take the pooled opinions of researchers, as revealed through this survey, as the best approximation of truth available, then the disconnect between public discourse on malaria eradication and private opinion is troubling. This has important implications for spending in public health, since the attention and resources of funders, researchers and government agencies are directed to those areas where a result is expected.

In regards to differences by academic discipline, it is important to note that diversity within disciplines was greater than diversity between them. That said, one might surmise as to why disciplines at the extremes differed. Chemists, on average, reported that eradication will be achieved in less than 40 years, whereas economists thought it would take a full ten years more. The collective optimism in the field of chemistry may be attributable to recent advances in drug development and insecticides, whereas economists may be more pessimistic due to concerns such as free-riding when it comes to global public goods [38] [39]. This study was not designed to generate inference regarding reasons why disciplines might differ in perception, but it does suggest further lines of research.

Limitations

There are several reasons to be skeptical that the combined "wisdom of crowds" of malaria researchers is a reliable indicator of truth. First, academic researchers are specialists - their narrow, field-specific view of eradication's feasibility is arguably less reliable than the more "global" views of large institutions. Though crowds have been found to be more "wise" than individuals in many cases, the application of a wisdom of crowds approach is not suitable to all classes of problems [40]. Crowds can be susceptible to social biases [41] (although this survey's anonimity 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.

Among these biases, four 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 subconciously realize that they actually stand to lose out profesionally in the case of eradication.

We made no distinction between quality of research, years of experience, academic achievements, geographical area, etc. Our inclusion criteria were simple and rudimentary, allowing us to access many diverse viewpoints, but (perhaps inappropriately) weighting all viewpoints as equal.

This study included the first authors of indexed journals. Though certainly a group with important knowledge related to malaria, this misses malaria control program employees, health agency workers, and other stakeholders. Their experiences and viewpoints may be different from those of academics, and arguably more relevant. Additionally, in public health journals, first authors are often more junior than their collaborators. By focusing solely on first authors, we may have unintentionally created a sample which is qualitatively different than the true universe of malaria researchers; to the extent that in our result pool researchers with less experience (as represented through publications) tended to be more "optimistic" regarding eradication, it is reasonable to assume that the restriction of first authors may have lead to an overly optimistic sample, making the results of the survey even more striking.

Conclusion

Our survey attempted to quantify the likelihood of and time frame to malaria eradication by gauging the collective opinion of malaria researchers. Our survey shows that the opinions of malaria researchers appear to diverge from those of malaria programme financiers in regards to the feasibility and timeframe of eradication, with researchers expressing more pessism than the institutions and individuals which finance and oversee global eradication efforts. The causes for pessimism are diverse, but common themes were the need for innovation, systemic challenges, and the complexity of the disease and its transmissio.

The implication of these results are three-fold: (1) that those working or investing in eradication-specific campaigns should factor in researchers' perceived low likelihood and 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; and (3) that discord between malaria researchers and institutions regarding eradication suggests a need for open discussion and concensus-making, so that efforts and focus are directed appropriately.

We have strived to present the results of our study without insinuation regarding the "true" feasibility and timeframe of eradication, and only time will tell whether the collective "wisdom" of researchers was worth adhering to or not. If the research community is unduly pessimistic, efforts should be made to convince them that eradication is more feasible than they realize (so that resources are directed accordingly). If, on the other hand, collective wisdom is a better forecasting agent than the stated objectives of global health leaders and institutions, then it is important to recognize the sad truth that we are likely further from eradication than we would like to be. In this case, though the discourse on eradication can be motivating and inspiring, resources should be directed in a manner that reflects an intended outcome's likelihood of occurrence.

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