Literature review and research protocol

Can we do it? A systematic and reproducible survey of research professionals on the perceived feasibility of and obstacles to eliminating malaria using a "wisdom of crowds" approach

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Summary

In recent years, much of the discourse regarding malaria has shifted from "control" to "eradication." The emphasis on elimination serves to 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 is high, and the expected value of these interventions is a function of their likelihood of success. In a systematic survey of experts in the field of malaria, we query beliefs regarding the likelihood and time-frame of eradication, as well as the perceived chief obstacles faced by those striving to eradicate We assess pessimism/optimism (via the proxy of years-to-eradication), broken down by academic discipline, researcher impact, and years of experience. Our results serve as a barometer of professional opinion, and identify areas of research where experts in the field expect the most resistance.

Executive summary

This document is divided into two sections:

- 1. A literature review, which provides a justification for the proposal and situates this research within the relevant literature
- 2. A proposed protocol for review by and approval of the ISGlobal scientific committee

Contents

ure Review
aground
dream of eradication is born
shift from control to eradication
ERA: The Malaria Eradication Research Agenda
need for the wisdom of crowds
ol
ground
ectives
hods and Design
uation criteria

Literature review

Background

In recent years, researchers, public health agencies and funding organizations have become increasingly interested in transitioning from an approach of malaria "control" to one of "elimination" and "eradication" [Tanner et al., 2015]. 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 [Snow, 2015, Eckhoff et al., 2014].

The economic case for striving to achieve malaria eradication is compelling [Barofsky et al., 2015]. Though the case-specific marginal cost of prevention can be expected to be high (relative to a simple control approach), successful eradication would mean massive recurring savings in the long-term. 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. Expected value of eradication, E(X) should be a function of the probability of the campaign's success, P(O:1), the average cost per case prevented, $\mu(C)$, the time-frame to eradication in years, Y, the annual discount rate optionally applied to future lives saved D (and associated cut-off for quantifying future benefits), and the associated opportunity cost (in health terms), O.

$$E(X) = P(O:1) * \mu(C)(YT)$$

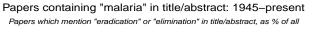
A great deal of previous research already covers the the cost per case prevented (citation needed). Likewise, a literature exists for quantifying the location-specific opportunity costs associated with funneling funds towards malaria eradication (citation needed). The correct discount rate for estimating the value of future lives saved is more of a philosphical question than an economic one. This leaves only the probability and time-frame to eradication, questions which have been addressed but never answered.

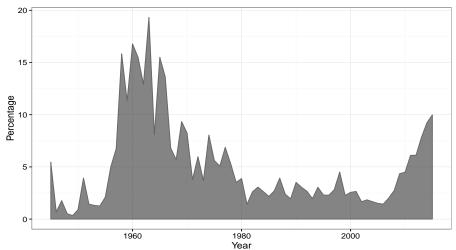
The dream of eradication is born

The scientific and public health communities have had eradication on their long-term agenda since the World Health Organization established the Global Malaria Eradication Program in the 1950s [Alonso et al., 2011]. Following the failure of the WHO's first attempt, the focus shifted away from global eradication and towards local elimination and control strategies.

The shift from control to eradication

In the last decade, interest in elimination and eradication has seen a resurgence, as evidenced by the proportion of general research on malaria which pertain to elimination and eradication (below) 1.





MalERA: The Malaria Eradication Research Agenda

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* [Tanner et al., 2015]. The participants in the Malaria Eradication Research Agenda process, in particular, have positioned themselves as thought leaders in the field of guiding research goals and identifying gaps in order for elmination to occur [Alonso et al., 2011]. 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 general ("within the lifetime of young scientists just embarking on their careers") and no mention is made of the perception of the probability of achieving eradication.

In other words, the leaders in the field of malaria have marked a clear path for moving towards eradication, but have not indicated how long walking the path will take. This omission is likely intentional, and certainly understadable, given that MalERA's goals are to guide research and technology in the direction of eradication, and not necessarily address the larger and much more subjective questions of *if* and *when*.

The need for the wisdom of crowds

Knowing whether and at what point in time humankind can achieve eradication has important ramifications for the prioritizing of more general health research and funding.

¹For the purposes of this chart, "general research on malaria" is understood as any article in the PubMed database containing the term "malaria" in either the title or the abstract. Articles which "pertain to elimination and eradication" are understood as any article containing the term malaria as well as either "elimination" or "eradication" in the title or abstract. The search was performed using RISmed package [Kovalchik, 2015] in R [R Core Team, 2015], and the chart was generated with the ggplot2 package [Wickham, 2009]

Protocol

Background

The wisdom of crowds: Patients often ask for a "second opinion", a request which implicitly recognizes two important truths: (1) that an expert can sometimes be wrong and (2) that the combined opinions of multiple experts can better approximate the truth than the opinion of only one. As Sir Francis Galton demonstrated in his famous ox-weight experiment published in Nature1, averaging the opinions of many is more accurate than taking the opinion of any single expert, since the biases of diverse viewpoints can be complementary and symbiotic.

The value of forecasting: In regards to disease eradication, proponents point to the potential ongoing returns on investment to future generations. But economically, 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, knowing the likelihood and time-frame of eradication of malaria is essential for making sound investments in health.

Why this study: Assessing likelihood and time-frame of eradication is too important of a task to be left to individuals or small panels and committees. It requires the "wisdom of crowds." 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.

Objectives

In a systematic survey of experts in the fields of malaria, we will query perceptions regarding the feasibility and time-frame of eradication, as well as the perceived gaps and chief areas that need attention in order for eradication to occur. We will report on aggregate results, and our analysis will be broken down by disease, researcher academic discipline, impact and years of experience.

Our principal objective is to measure the perceived likelihood/feasibility and time-frame of eradication of malaria among those who are professional researchers of those respective diseases, at a larger scale than any previous study. Our secondary objective is to examine the relationship between the perceived likelihood/feasibility of eradication of diseases with the respective attention allotted to them in both the popular and academic literature. Our tertiary objective is to establish which specific areas of knowledge are lacking through an examination of researcher characteristics (academic discipline, geography, etc.) insofar as those characteristics are associated with differential perceptions regarding time-to-eradication.

Methods and Design

We will "webscrape" from PubMed the authors, abstracts, and journal information of all articles related to disease X using standardized search terms. We will then send emails to all first, last, and corresponding authors (whose addresses can be located), asking 2 simple questions:

- 1. In your opinion, how many years will it be until disease X is eradicated? (0-99+)
- 2. Please rank the following ten areas in order of where attention is most needed in order to achieve eradication (10 = attention most needed; 1 = attention least needed).

These questions can also be answered via an online survey: http://goo.gl/forms/Ib80IwgwQY.

We will then compile a database which links researcher meta-information (percent and number of publications in top-decile journals, publication quantity, geography of institution, geography of research focus, gender, academic discipline) with their surveyed attitudes regarding eradication (years-to-eradication and ordered ranking of factors).

The design of this study is typical, but this study is noteworthy in two areas: (1) its scale (by using automated web-scraping, emailing, and surveying, we will reach the maximum number of experts), and (2) its democratic approach (we assume that the more experts' opinions reflected, the closer we are to approximating the "truth"). Our results will be of value not only to the scientific community, but also to policy-makers and public health practitioners. By gauging and synthesizing the "wisdom of (informed) crowds", we aim to establish a barometer of scientific opinion in a manner that is fully reproducible.

Evaluation criteria

1. What are the ethical considerations that need to be addressed and how will they be addressed?

We will not be collecting personal health information, or any biological samples. Nor will we be dealing in any way, shape or form with health outcomes or treatment data. We will only contact researchers whose information is publicly available online.

The only potential area of "sensitive" information pertains to the disclosure of researchers' opinions. However, we will state clearly in both the "invitation to participate" email as well as in the online survey form that results will be made fully public; researchers who choose not to participate are free to do so, and will not be contacted thereafter.

2. List the ethics committees (both human and/or animal) which either have reviewed or will review this proposal.

None. Given the nature of this study, no human/animal ethics committees' review is necessary.

3. Describe the expertise required for the project and which member(s) of the research team will provide each area of expertise.

Area expertise in malaria: Elisa Sicuri and Joe Brew Area expertise in economic evaluation: Elisa Sicuri

Area expertise in computer-assisted article retrieval and surveying: Joe Brew

4. How does the proposal fit in with ISGlobal's scientific agenda?

ISGlobal is a thought leader in malaria, as well as its corresponding eradication movement. By using modern, technologically-oriented means to establish a "barometer" of international researcher consensus on the perceived feasibility and time-frame of eradication, ISGlobal would cement its position at the center of the ongoing international dialogue on the subject. Furthermore, given IS-

Global's stake in eradication campaigns, the results of this study could (a) inform which disciplines and diseases have the most "research gaps" to be filled in order to achieve eradication, (b) identify areas of consensus and discord between different disciplines, (c) provide (crowd-informed) estimates of the timeline to eradication.

Budget estimation and expected source of funding for this study.

None. Given that this topic is directly relevant to the PhD-specific research of the two co-Pis (Celine Aerts and Joe Brew), no project-specific funding is required.

Other comments

Have all co-investigators read and approved this proposal? YES Do you expect to handle samples of human origin in the study? NO Do you expect to handle personal information in the study? NO.

References

- [Alonso et al., 2011] Alonso, P. L., Brown, G., Arevalo-Herrera, M., Binka, F., Chitnis, C., Collins, F., Doumbo, O. K., Greenwood, B., Hall, B. F., Levine, M. M., Mendis, K., Newman, R. D., Plowe, C. V., Rodríguez, M. H., Sinden, R., Slutsker, L., and Tanner, M. (2011). A research agenda to underpin malaria eradication. *PLoS Med*, 8(1):e1000406.
- [Barofsky et al., 2015] Barofsky, J., Anekwe, T. D., and Chase, C. (2015). Malaria eradication and economic outcomes in sub-saharan africa: Evidence from uganda. *Journal of Health Economics*, 44:118–136.
- [Eckhoff et al., 2014] Eckhoff, P. A., Bever, C. A., Gerardin, J., and Wenger, E. A. (2014). Fun with maths: exploring implications of mathematical models for malaria eradication. $Malar\ J$, 13(1):486.
- [Kovalchik, 2015] Kovalchik, S. (2015). RISmed: Download Content from NCBI Databases. R package version 2.1.5.
- [R Core Team, 2015] R Core Team (2015). R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria.
- [Snow, 2015] Snow, R. W. (2015). Global malaria eradication and the importance of plasmodium falciparum epidemiology in africa. *BMC Medicine*, 13(1):23.
- [Tanner et al., 2015] Tanner, M., Greenwood, B., Whitty, C. J. M., Ansah, E. K., Price, R. N., Dondorp, A. M., von Seidlein, L., Baird, J. K., Beeson, J. G., Fowkes, F. J., Hemingway, J., Marsh, K., and Osier, F. (2015). Malaria eradication and elimination: views on how to translate a vision into reality. *BMC Medicine*, 13(1).
- [Wickham, 2009] Wickham, H. (2009). ggplot2: Elegant Graphics for Data Analysis. Springer-Verlag New York.