Background and research protocol

Can we do it? A survey of research professionals on the timeline and obstacles to eliminating malaria

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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 thir lag and 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

The World Health Organisation's Global Malaria Programme has acknowledged that it "needs to take an official position on how and under what timeline malaria eradication could be achieved" [WHO, 2015]. Such a position could inform policy, and plays a crucial role in the economic analysis of the expected value of malaria control inteventions.

However, no such position has been taken. Given the inherent incentives working against a realistic assessment of the matter at the individual level (funding prerogatives, political pressure, confirmation bias), the best way to assess the likelihood of and time-frame to malaria eradication is a reliance on the anonymous "wisdom of crowds." Surveying experts, an approach already taken for assessing the time-frame to and chief innovations required for the eradication of some neglected tropical diseases [Keenan et al., 2013], can serve as a useful for barometer for filling measuring professional opinion.

This study proposes to carry out a systematic survey of malaria research professionals from a wide array of academic disciplines in order to estimate the likelihood of and time-frame to malaria eradication. Its results can serve as a barometer of professional opinion, informing policy and guiding resources.

Structure

This document is divided into three sections:

1. A background, which provides a justification for the proposal and situates this research within the relevant literature, while also outlining the history and current "état de l'art" of global discourse on malaria control and eradication
2. A proposed protocol for review by and approval of the ISGlobal scientific committee
3. Hypothetical examples of visual "knowledge products" to be generated from this research

Contents

Part 1: Background

Context

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, even if not possible in the immediate short term [Snow, 2015, Eckhoff et al., 2014].

Justification

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 applied to future lives saved D (and associated cut-off for quantifying future benefits), and the associated opportunity cost (in health terms).

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

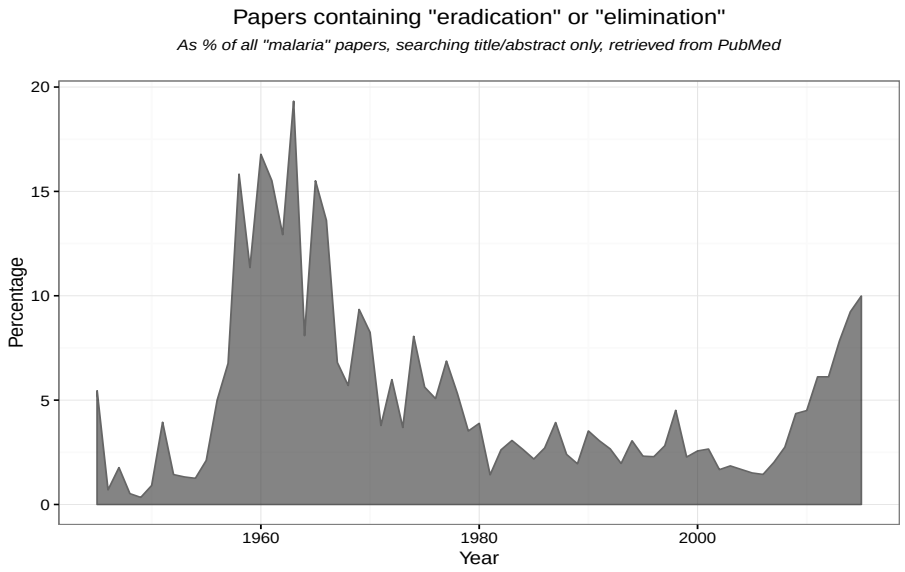
The literature

A great deal of previous research already covers the the cost per case prevented [Sicuri et al., 2011, Silumbe et al., 2015, Bôtto-Menezes et al., 2016, Ilunga-Ilunga et al., 2014, Dalaba et al., 2015]. Likewise, a literature exists which could serve as a model for quantifying the location-specific opportunity costs associated with funneling funds towards malaria eradication [Stuckey et al., 2014, White et al., 2011, Korenromp, 2012]. 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 anecdotally, but never answered quantitatively.

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, Nájera 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.

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].



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*.

[1] For 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]

Though the concept of eradication is often mentioned in both academic and policy circles [Mnzava et al., 2014, WHO, 2016], the World Health Organisation's Global Malaria Programme (GMP) acknowledges that it "needs to take an official position on how and under what timeline malaria eradication could be achieved" [WHO, 2015]. However, no official position has been taken.

The need for the wisdom of crowds

Taking an official position is not easy, as it would require the synthesis of learnings from a diversity of fields. Additionally, taking an official position faces the problem of human bias. Though it's easy to espouse intellectual honesty, leaders and well-known intellectuals in the space of global malaria control face perverse incentives. Funding prerogatives, political pressure and confirmation bias could all potentially serve to "inflate" the stated likelihood of eradication, and "deflate" the stated time-to-eradication. Furthermore, any states forecast exposes itself to the possibility of being incorrect, a reality which encourages stakeholders to embrace generalities and unquantified possibilities.

But quantifying the likelihood of and time-frame to eradication is essential, and far too important to be left o 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. Though the approach is atypical, it is feasible, having previously been undertaken for neglected tropical diseases with a surprisingly high response rate (44%) [Keenan et al., 2013].

Part 2: 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 researcher (Joe Brew), no project-specific funding is required.

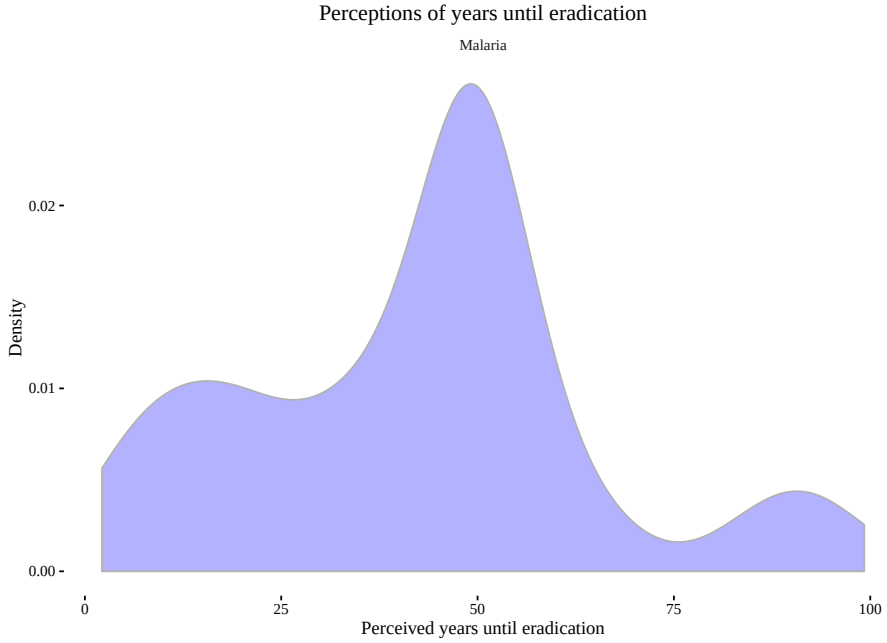
Other comments

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

Part 3: Knowledge products

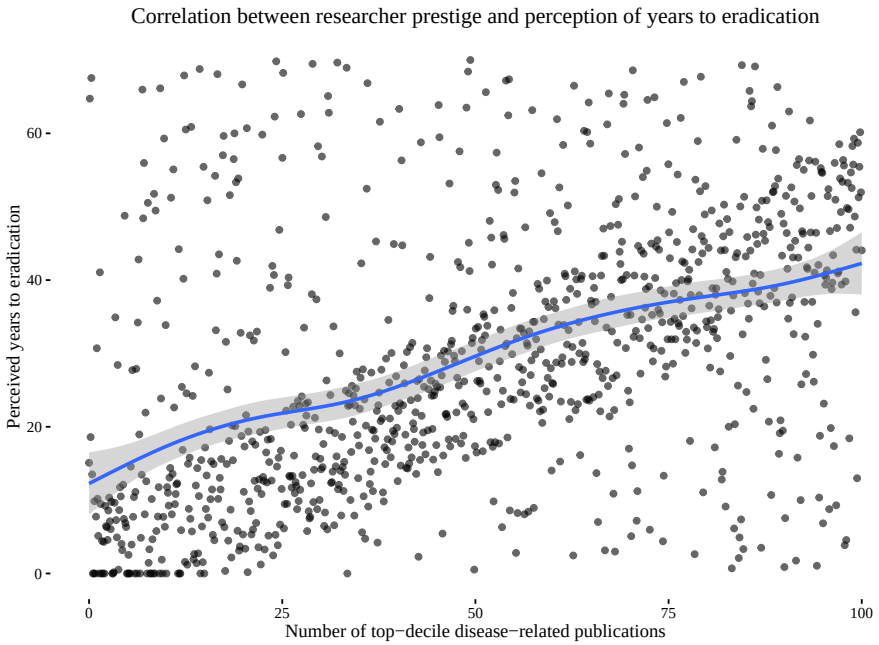
The below are examples of *hypothetical* knowledge products that could emerge from this resarch.

Example 1: Distribution of perceptions of years to eradication
This chart serves as the main "wisdom of crowds" visualization. It shows both the average amount of time experts from different disciplines believe it will take to achieve eradication, while also displaying where there is consensus (as indicated by high peaks) versus discord (as indicated by wide, low peaks).



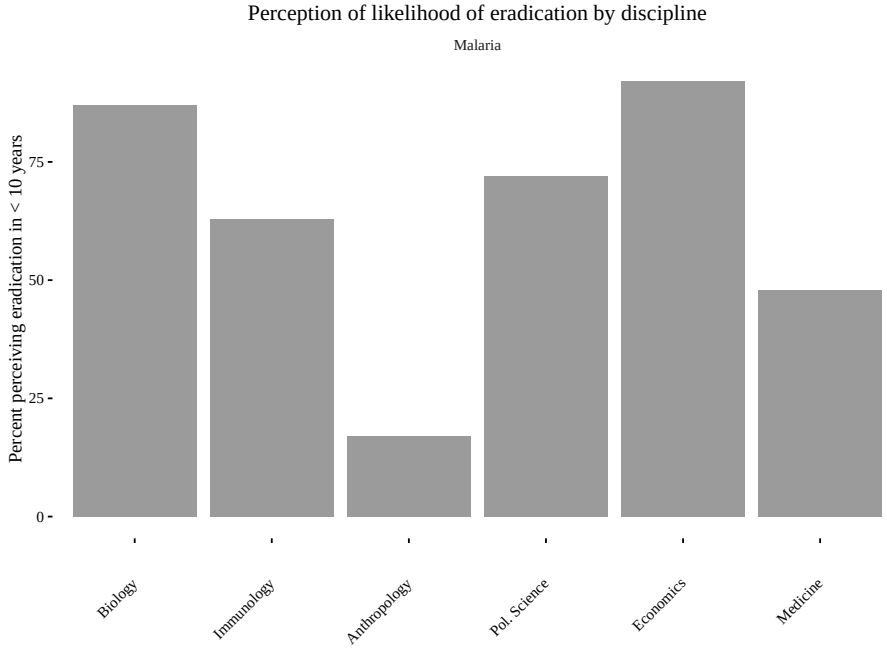
Example 2: The association between researcher "quality" and perception to eradication

The null hypothesis is that there exists no correlation between the "quality" of a researcher and his/her attitude towards eradication. The alternative hypothesis is that there does exist a correlation. In the case of the alternative hypothesis being validated, this would be evidence that expert opinion should potentially be "weighted" for researcher quality.

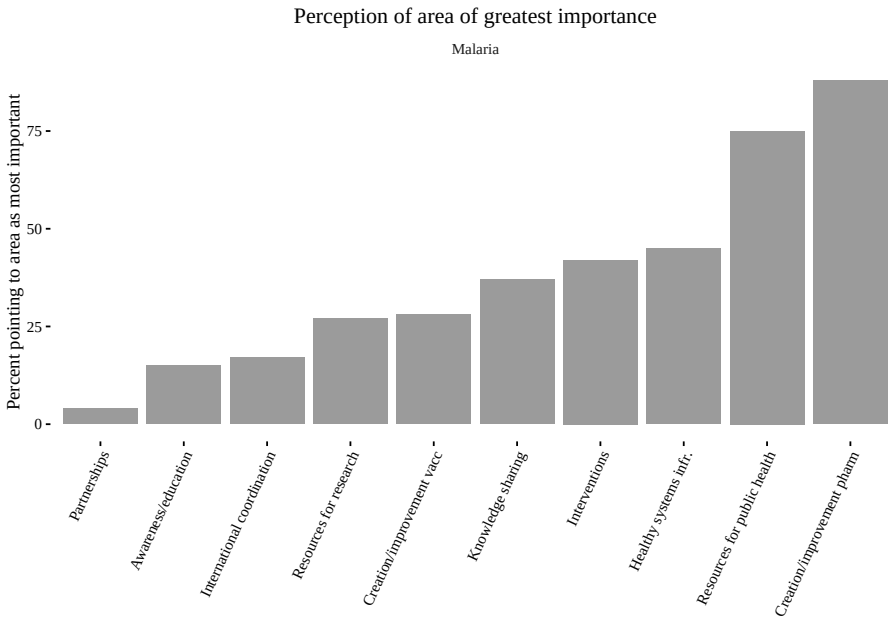


Example 3: Perception of experts of likelihood of short-term eradication by academic discipline

This chart reveals differential perceptions of the likelihood of short-term eradication by academic discipline. This chart is useful in that if differences are found, this could indicate that disciplines with lower "confidence" in short-term eradication reflect areas that require attention (ie, gaps that need to be filled). For example, if experts from biomedical fields saw high likelihood but experts from anthropology saw low likelihood, this would indicate that the challenges to eradication may be more anthropological than biomedical.

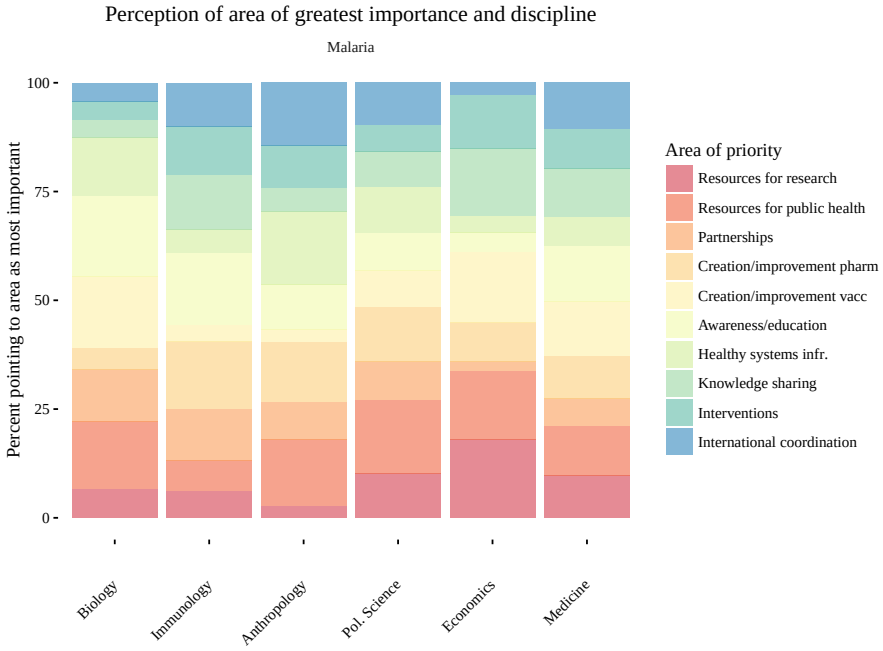


Example 4: Perception of experts regarding area of greatest importance to eradication This chart reveals differential perceptions of the area of greatest importance. This chart is useful in that if differences are found, this could indicate that certain areas should receive greatest attention. For example, in the below chart, the highest bar is for "resources for public health", indicating that (unlike with other NTDs) there is near-consensus among experts that "resources for public health" represents the most important area in order to achieve eradication of malaria



Example 5: Perception of experts regarding area of greatest importance to eradication by academic discipline

This chart is similar to example 3, but also reflects variation by academic discipline. It indicates how experts of different academic disciplines prioritize different areas of work/research. This is useful in that it indicates the primary concerns of experts from each field, highlighting areas of consensus and discord between diseases and disciplines.



References

[WHO, 2015] (2015). Malaria policy advisory committee to the WHO: conclusions and recommendations of seventh biannual meeting (march 2015). *Malar J*, 14(1).

[WHO, 2016] (2016). Malaria policy advisory committee to the WHO: conclusions and recommendations of eighth biannual meeting (september 2015). *Malar J*, 15(1).

[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.

[Bôtto-Menezes et al., 2016] Bôtto-Menezes, C., Bardají, A., dos Santos Campos, G., Fernandes, S., Hanson, K., Martínez-Espinosa, F. E., Menéndez, C., and Sicuri, E. (2016). Costs associated with malaria in pregnancy in the brazilian amazon, a low endemic area where plasmodium vivax predominates. *PLoS Negl Trop Dis*, 10(3):e0004494.

[Dalaba et al., 2015] Dalaba, M., Akweongo, P., Aborigo, R., Saronga, H., Williams, J., Aninanya, G., Sauerborn, R., and Loukanova, S. (2015). Cost to households in treating maternal complications in northern ghana: a cross sectional study. *BMC Health Services Research*, 15(1):34.

[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.

[Ilunga-Ilunga et al., 2014] Ilunga-Ilunga, F., Levêque, A., Ngongo, L. O., Kandolo, F. T., and Dramaix, M. (2014). Costs of treatment of children affected by severe malaria in reference hospitals of kinshasa, democratic republic of congo. *J Infect Dev Ctries*, 8(12).

[Keenan et al., 2013] Keenan, J. D., Hotez, P. J., Amza, A., Stoller, N. E., Gaynor, B. D., Porco, T. C., and Lietman, T. M. (2013). Elimination and eradication of neglected tropical diseases with mass drug administrations: A survey of experts. *PLoS Negl Trop Dis*, 7(12):e2562.

[Korenromp, 2012] Korenromp, E. L. (2012). Lives saved from malaria prevention in africa–evidence to sustain cost-effective gains. *Malar J*, 11(1):94.

[Kovalchik, 2015] Kovalchik, S. (2015). *RISmed: Download Content from NCBI Databases*. R package version 2.1.5.

[Mnzava et al., 2014] Mnzava, A. P., Macdonald, M. B., Knox, T. B., Temu, E. A., and Shiff, C. J. (2014). Malaria vector control at a crossroads: public health entomology and the drive to elimination. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 108(9):550–554.

[Nájera et al., 2011] Nájera, J. A., González-Silva, M., and Alonso, P. L. (2011). Some lessons for the future from the global malaria eradication programme (1955–1969). *PLoS Med*, 8(1):e1000412.

[R Core Team, 2015] R Core Team (2015). *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing, Vienna, Austria.

[Sicuri et al., 2011] Sicuri, E., Davy, C., Marinelli, M., Oa, O., Ome, M., Siba, P., Conteh, L., and Mueller, I. (2011). The economic cost to households of childhood malaria in papua new guinea: a focus on intra-country variation. *Health Policy and Planning*, 27(4):339–347.

[Silumbe et al., 2015] Silumbe, K., Yukich, J. O., Hamainza, B., Bennett, A., Earle, D., Kamuliwo, M., Steketee, R. W., Eisele, T. P., and Miller, J. M. (2015). Costs and cost-effectiveness of a large-scale mass testing and treatment intervention for malaria in southern province, zambia. *Malar J*, 14(1).

[Snow, 2015] Snow, R. W. (2015). Global malaria eradication and the importance of plasmodium falciparum epidemiology in africa. *BMC Medicine*, 13(1):23.

[Stuckey et al., 2014] Stuckey, E. M., Stevenson, J., Galactionova, K., Baidjoe, A. Y., Bousema, T., Odongo, W., Kariuki, S., Drakeley, C., Smith, T. A., Cox, J., and Chitnis, N. (2014). Modeling the cost effectiveness of malaria control interventions in the highlands of western kenya. *PLoS ONE*, 9(10):e107700.

[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).

[White et al., 2011] White, M. T., Conteh, L., Cibulskis, R., and Ghani, A. C. (2011). Costs and cost-effectiveness of malaria control interventions - a systematic review. *Malar J*, 10(1):337.

[Wickham, 2009] Wickham, H. (2009). *ggplot2: Elegant Graphics for Data Analysis*. Springer-Verlag New York.