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Malaria control under unstable dynamics: Reactive vs. climate-based strategies

Andres Baeza[a], Menno J. Bouma[b], Ramesh Dhiman[c], Mercedes Pascual[a,d,*]

[a] Department of Ecology and Evolutionary Biology University of Michigan, Ann Arbor, MI, USA
[b] London School of Hygiene and Tropical Medicine. University of London, London, UK
[c] National Institute of Malaria Research (ICMR), Delhi, India
[d] Howard Hughes Medical Institute, Chevy Chase, MD, USA

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ABSTRACT

In areas of the world where malaria prevails under unstable conditions, attacking the adult vector population through insecticide-based Indoor Residual Spraying (IRS) is the most common method for controlling epidemics. Defined in policy guidance, the use of Annual Parasitic Incidence (API) is an important tool for assessing the effectiveness of control and for planning new interventions. To investigate the consequences that a policy based on API in previous seasons might have on the population dynamics of the disease and on control itself in regions of low and seasonal transmission, we formulate a mathematical malaria model that couples epidemiologic and vector dynamics with IRS intervention. This model is parameterized for a low transmission and semi-arid region in northwest India, where epidemics are driven by high rainfall variability. We show that this type of feedback mechanism in control strategies can generate transient cycles in malaria even in the absence of environmental variability, and that this tendency to cycle can in turn limit the effectiveness of control in the presence of such variability. Specifically, for realistic rainfall conditions and over a range of control intensities, the effectiveness of such 'reactive' intervention is compared to that of an alternative strategy based on rainfall and therefore vector variability. Results show that the efficacy of intervention is strongly influenced by rainfall variability and the type of policy implemented. In particular, under an API 'reactive' policy, high vector populations can coincide more frequently with low control coverage, and in so doing generate large unexpected epidemics and decrease the likelihood of elimination. These results highlight the importance of incorporating information on climate variability, rather than previous incidence, in planning IRS interventions in regions of unstable malaria. These findings are discussed in the more general context of elimination and other low transmission regions such as highlands.

1. Introduction

Malaria transmission is low and highly seasonal at the edge of the distribution of the disease where climate variables, either temperature or rainfall, limit vector abundance and parasite development. Thus, in these regions, control efforts unavoidably operate in highly variable environments where malaria dynamics are known as 'unstable' or 'epidemic'. It is the interplay of control and climate variability in one such environment, desert fringes, that interests us here, especially for the kind of dynamic intervention policy that would prove most effective.

Historically, the discovery of effective and long lasting residual insecticides, such as DDT, contributed to a significant extent to WHO's global initiative to eradicate malaria initiated in 1955. These campaigns dramatically reduced India's estimated annual malaria deaths from an estimated million (Russell, 1936) to only a few hundred. When malaria eradication was no longer considered feasible at a global scale, policy shifted to treatment of the disease to limit clinical burden, and the use of Indoor Residual Spray (IRS here on) was mostly abandoned and viewed as an expensive short term eradication tool. However, with the dramatic resurgence of malaria in South Asia in the mid 1970s, IRS made a comeback as a proven method to reduce morbidity, but without a careful appraisal of spraying methods previously used as a long-term control. The legacy of the eradication efforts in India are still visible in the form of an impressive network of diagnostic services (microscopy) and the continued dependence on indoor spraying, that proved so effective in large parts of the country

* Corresponding author at: 2039/2041 Kraus Natural Science Building, 830 North University, Ann Arbor, MI 48109-1048, USA. Tel.: +1 734 615 9808.
E-mail address: pascual@umich.edu (M. Pascual).

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where vectors are rather inefficient because they are short-lived and exhibit zoophilic behavior.

Another legacy from the eradication era is the use of the Annual Parasite Incidence rate (API), usually expressed as cases per 1000 per year, to evaluate the effectiveness of interventions and plan the subsequent phases of the campaign (Najera et al., 2011). In India, areas with API > 2.0 cases per 1000 population in the preceding 2 years qualified for intervention (NMEP, 1983). Although the absolute number justifying IRS intervention has been modified over the years, the reactive nature of insecticide use has remained unchanged until the present. In addition to the inherent delays in the purchasing and delivery of commodities and supplies, reasons for a response that applies in the following transmission season include the practical requirements of a national scale and of a rigorous implementation that considers for example the timing of the transmission season after the monsoon and the duration of insecticidal activity. The uniform approach that characterized the eradication design did not take into account however the dynamic differences of malaria within the country such as those between endemic and epidemic regions, and the potential implications of a delayed response if elimination were not to be achieved in the short term.

Thus, an important but often unrecognized consequence of relying on these indices for the planning of subsequent interventions is the potentially reactive nature of the public health response. We specifically refer here to this kind of response as 'reactive' to describe a delayed response whose level depends on the disease burden in the past over some temporal window of time, for example cases in the last season. This effectively establishes a dynamic feedback between past incidence levels and current control efforts. Such feedback can arise either from explicit control policies or from the myriad processes underlying the allocation of intervention efforts and the perception of risk in public health systems operating under limited resources. Regardless of the actual mechanisms, case-detection would trigger control intervention in affected areas leading to the subsequent decrease in incidence. This reduction in the number of cases would in turn result in a decreased perception of risk leading to the relaxation of control before actual elimination is achieved. Because malaria incidence in the absence of intervention would then return to previous levels defined by environmental and socioeconomic conditions, a reactive intervention has the potential to generate recurrent disease cycles and unexpected epidemics.

These dynamics are of particular relevance where transmission is 'unstable' or 'epidemic' and under the influence of highly variable environmental drivers such as rainfall. In these regions, climate variability is known to generate strong interannual variation in the number of cases (e.g. Laneri et al., 2010) but its interaction with vector control is poorly understood. Although a vast body of work has addressed and compared the effects of particular interventions (Goodman et al., 2001; Guyatt et al., 2002; Smith et al., 2008; Pedercini et al., 2011; White et al., 2011; Kigozi et al., 2012; Hamusse et al., 2012), there has not been much work exploring the effectiveness of different strategies under high environmental variability (but see Worrall et al., 2007). Here we hypothesize that in these areas reactive control policies can generate long cycles between IRS interventions and epidemics, and also influence the efficiency of the allocation of resources and the risk of malaria in the long run.

The long-term malaria control program in the arid northwestern states of India provides a unique opportunity to simultaneously follow malaria epidemiology and IRS intervention in a seasonal and low-transmission region under strong rainfall forcing, where control policy explicitly defines target areas based on the number of recorded cases in previous years. To investigate the dynamical consequences of this policy, a coupled human-mosquito transmission model is parameterized for this semi-desert region. With this model, the effectiveness of reactive control is also compared against that of an alternative strategy based on rainfall variability. Results show that transient multiannual cycles can emerge in the absence of climate variability. When driven by observed daily precipitation, the model exhibits intermittent unexpected epidemics corresponding to large rainfall events and situations of unpreparedness and inefficient control. These patterns are consistent with observations in time series of cases and IRS coverage in the region. Our findings further suggest that control efforts whose level is determined based on rainfall itself provide a more effective and efficient strategy.

2. Background and motivation

2.1. Malaria situation and large scale control strategy in the states of Gujarat and Rajasthan, India

Gujarat and Rajasthan are the western states of India and their combined population exceeds 120 million people in an area of 196.000 km^2. In most northern and western districts, total rainfall does not exceed 200 mm per year, while in the southernmost districts more than 1000 mm can be recorded. High interannual variation in rainfall intensity is observed over the region. As a consequence, large fluctuations in the abundance of the mosquito population from year to year can be generated, and these fluctuations in vector abundance are reflected in the pronounced interannual variability of the seasonal malaria outbreaks (Laneri et al., 2010). The principal species of malaria are *Plasmodium falciparum* and *Plasmodium vivax*, and the principal malaria vector is *Anopheles culicifacies* (Barik et al., 2009).

Since the resurgence of malaria in the 1970s, several malaria control intervention strategies have been implemented to decrease the burden of malaria in the region (Sharma and Sharma, 1989; Sharma et al., 1991). The malaria endemicity of an area (village, talukas or districts) is estimated based on the number of cases detected by the surveillance system, consisting of clinical malaria cases diagnosed in health centers (passive case detection) and cases brought to light by outreach workers (active case detection). Based on these estimations, the modified plan of operation (MPO) since 1977 consisted of the use of IRS in rural areas recording an API > 2 from the previous 2 malaria seasons (NMEP, 1983). In the last 15 years, this threshold has been calculated based on the previous 3 years (NMEP, 1995). This policy is reflected in the delayed increase in control levels that follows large epidemic years (Fig. 1).

3. Methods

3.1. The malaria-mosquito model

We developed a mathematical model to investigate the temporal dynamics generated under this mechanistic feedback between intervention and incidence, and their consequences for the interannual variability of seasonal outbreaks and control itself. The model is a coupled mosquito-malaria model that explicitly considers a control intervention that increases the mortality of the adult mosquito population. It is written as a system of differential equations and organized into three modules: The first one is the epidemiological module which divides the total human population, N, into 4 classes for susceptible (S), exposed (E), infected (I) and recovered (R) individuals respectively. The transitions between classes and the structure of the model are represented in the diagram of Fig. 2, and a more detailed explanation of the model is given in section 8 (Appendix A).

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