Malaria risk mapping in Africa

The historical context to the Information for Malaria (INFORM) project

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Background

The use of malaria cartography is not a new discipline. It was regarded as paramount to the design of pre-elimination strategies during the Global Malaria Eradication (GMEP) efforts in Africa from the mid-1950s. This has been resurrected as a key component to the future design of malaria control and elimination across the continent, to sustain recent gains made possible by massive increases in donor assistance and a recognition that a more cost-effective approach is required to accelerate impact. Here we review the long history of malaria risk mapping in Africa to provide a context for the current Africa-based scientific support to national malaria control programmes under the Information for Malaria (INFORM) project.

Malaria risk mapping 1900-1960s

The science and application of malaria risk mapping has a long legacy in Africa. Only a few years following the discovery by Sir Ronald Ross of the role played by the mosquito vector, detailed maps of mosquito breeding sites in relation to human habitation were developed for Freetown, Sierra Leone [1] (Figure 1). Assembling a cartographic knowledge of human hosts in relation to mosquito breeding localities, topography, climate and agriculture was critical to the early malaria control efforts in Algeria [2], Morocco [3] and early European settled centres of commerce and administration, including Guinea [4], Burkina Faso [5], Malawi [6] and Tanzania [7,8]. These maps provided control agencies a plan for larval control, environmental management, target mass-drug administration and unproven and unsavory interventions including racial segregation.



Figure 1: Malaria risk map developed for Freetown, Sierra Leone [1]

Plan of portion of high ground above Freetown showing area to be avoided in choosing site for European houses.

Understanding the global extents and risks posed by malaria were mapped during the 1930s [9,10], however, the information used to construct these maps were never documented and were largely, one assumes, qualitative, expert opinion of gradations from malaria free, to low and high "endemicity".

At the onset of the Second World War, the US military began to develop new global maps of disease risk, including malaria, in preparation for military engagements overseas. This resulted in an atlas - *Global epidemiology: a geography of disease and sanitation,* published in 1944 [11,12]. From the 1950s several cartographic representations of the global distribution of malaria were developed by malariologists, and the newly formed World Health Organization [13,14]. After the Second World War, George Macdonald provided the most biologically explicit mapped classification of risks of malaria worldwide, based on the distributions of vectors forming 12 zoographical eco-zones loosely connected to his concepts of stability [15].

In one of the earliest textbooks on malaria, Boyd states that "It is inexcusable to initiate control activities in any community without a prior survey to determine (a) the endemic level at which malaria is prevailing, and the extent of its localization, (b) the transmitting anophelines and their production areas, (c) the control procedure or procedures best adapted to the local elimination, from the standpoints of efficiency and economy, of the transmitting anopheline mosquito" [16]. For several decades this formed an important basis for malariology and control in Africa.

During the 1950s and 1960s, colonial governments across Africa began to develop national maps of malaria risk as part of pre-elimination planning under the GMEP. Examples of these maps include those developed in Angola [17,18], Botswana [19], Burundi [20], Cameroon [21], Democratic Republic of Congo [22], Ethiopia [23], Kenya [24], Madagascar [25], Mauritania [26,27], Mozambique [28], Namibia [29], Senegal [30], Somalia [31,32], Sudan [33], Swaziland [34], Tanzania [35] and Uganda [36-38]

The quantities used to describe malaria risk varied considerably between national maps. Maps were based on ecological zonation (e.g. Saharan, Sahelian and Riverine in Mauritania or highveld and lowveld in Swaziland), duration of transmission seasons (Kenya, Tanzania and Uganda), or more empirically defined based on measures of host infection (parasite rates and/or spleen rates, for example Angola, Mozambique, Sudan and Uganda). Several of these original maps, or adaptations of these maps, continue to be used national malaria control programmes up to the present day.

These early attempts at national malaria cartography were hand-drawn, crude representations of risk (Figures 2a-f), however they highlight one important concept behind malaria control and elimination 60 years ago - understanding the diversity of malaria within national borders was a fundamental guiding epidemiological pre-requisite to the design of the attack phases of intervention.

Figure 2: Examples of national malaria risk maps developed between 1930 and 1968 in a) Angola [17]; b) Mauritania [27]; c) South Africa [39]; d) Senegal [30]; e) Tanzania [35]; f) Uganda [37]



In 1968, two Russian malariologists published a global malaria risk map that represented, at the time, the largest ever assembly of existing information [40]. The final map was based on a synthesis of historical records, documents and maps of a variety of indices, including records of disease and vector presence, spleen and parasite rates, prevalence of sickle cell trait, sporozoite rates, biting rates and other malariometric parameters. These data were then interpolated globally at the peak of malaria's assumed historical distribution in 1900, using a combination of expert opinion, global elevation, temperature, rainfall isohyets and ecological "nosoforms" or zoographical eco-zones. The information presented included the expert opinion natural range of transmission, areas subject to epidemic transmission and a mapped range of endemicity based on criteria for *P. falciparum* transmission intensity related to parasite or spleen rates in childhood: hypoendemic, mesoendemic, hyperendemic and holoendemic, terms formalized at the WHO conference on malaria in Africa held in Kampala, Uganda in 1950 [41].

Lysenko and Semashko used the global map in a qualitative sense to consider the status and future of malaria eradication and the threats posed by the hyper-, holoendemic regions of the world, however they conclude that "[The map] *should reflect the dynamics during the implementation of malaria eradication programmes, or the successful results of campaigns to combat malaria in the countries where they were implemented. This map therefore has to be updated regularly"* [40]. The WHO did produce a sequence of about 19 maps between 1956 and 1999 that portrayed the distribution of malaria limits worldwide and areas that were under elimination attack, consolidation or maintenance phases [e.g. 42-46]. There were inconsistencies between these iterations and none were supported by much empirical data [47] and as might be expected these varied little between years across Africa south of the Sahara. For almost four decades the "Lysenko" map formed the basis of our understanding of the range of malaria

transmission intensity in Africa despite other attempts to develop global distributions based on less on empirical data but related to temperature, elevation and rainfall conditions [48].

From the 1960s the mapped extents of clinical cases, parasite transmission and control efforts were used to monitor the shrinking extents of malaria in all North African countries, Madagascar, Reunion, Mauritius, Cape Verde, Ethiopia and South Africa as part of their eradication efforts. However, when the GMEP ground to a halt across much of sub-Saharan Africa, this was accompanied by a changing emphasis from defining and interrupting transmission to the less specialized primary care of fevers for control. At this point the art and skills of malaria risk mapping were lost. During the 1970s and 1980s there is very little evidence of a sustained synthesis of malaria risk information within national borders in any sub-Saharan African country.

The renaissance in malaria risk mapping during the 1990s

In 1996, a Pan-African collaboration was started to resurrect the importance of malaria cartography [49-51]. The Mapping Malaria Risk in Africa/Atlas du Risqué de la Malaria en Afrique (MARA/ARMA) was initiated as a collaboration between African research institutes to assemble a repository of available published and unpublished data on the prevalence of malaria infection, dominant malaria vector species of the *An. gambiae* and *An. funestus* complexes, entomological inoculation rates and case-incidence. Searches were made at national research libraries and from published materials using five regional nodes. By 1998, the collaboration had assembled information of parasite prevalence at 2529 survey locations undertaken between 1926 and 1997 [52]. By 2001, the funding for the first phase of this African project came to an end. In 2006, the Swiss Tropical and Public Health Institute, Basel, continued to assemble data which presently contains *circa* 13,000 parasite prevalence survey data points [53].

There were several important outcomes from the initial first phase of the MARA/ARMA collaboration that began to shape the value attached to malaria risk mapping after several decades of neglect in Africa. First, the collaboration assembled information on parasite prevalence from a wide variety of national archive sources, this had not been attempted for over 30 years and highlighted the wealth of information available in national libraries and ministry of health archives across Africa. 64% of all available information was sourced from Ministry of health or unpublished reports [52].

Second, while not based on empirical survey data, several climate based models of the distribution of malaria [54] and seasonality of malaria transmission [55] were developed. These maps can still be found in the offices of National Malaria Control Programmes (Figure 3 example from Tanzania) and are often used to illustrate malaria risks in national strategies, applications for donor assistance and programme reviews [56]. However, despite the fuzzy climate-suitability map for stable *P. falciparum* malaria transmission being a milestone in the mapping of malaria in Africa, it remains widely misinterpreted, as it represents a measure of the likelihood that stable transmission can occur, rather than ranges of transmission intensity, as often inferred by national programmes.

Figure 3: Fuzzy suitability for stable *Plasmodium falciparum* transmission in Tanzania produced by MARA/ARMA collaboration in 1999



Finally, the MARA/ARMA collaboration brought together a cohort of African scientists interested in new geographical information system tools, spatial epidemiology and climate. The first phase of the MARA/ARMA project led to new malaria risk map products at sub-regional [57-59] and national scales [60-64]. The approaches taken to develop these maps included new spatial modelling approaches based on empirical data, an entire science not available to malaria cartographers during the GMEP era.

Advances in computing, geographic information systems [65], remotely sensed satellite data on climate and ecology [66], and the development of model-based geostatistical (MBG) methods [67] have all revolutionized the mapping of infectious disease [68], especially malaria. A unique advantage of MBG in disease mapping is in the handling of uncertainty. Interpolating sparse, often imperfectly sampled, survey data to predict disease prevalence across wide regions results risk maps of inherently variable precision, with the level of uncertainty varying spatially as a function of the density, quality, and sample size of available survey data, and moderated by the underlying spatial variability of the disease in question. These model forms are complex and described in detail elsewhere [67,69,70], but all operate on a simple geographers principle that the properties of things closer in space and/or time are more similar than if they are further apart [71].

At the same time as MARA/ARMA was established, French malariologists based at the Institute for Research and Development, Montpellier, assembled a rich set of contextual data on malaria distributions, parasite species, vectors, historical control and available maps from across the world [72]. The Afrotropical region was classified according to ecological and vegetation classes, linked to distribution niches of vector species [73]. The narrative descriptions of risks versus

control over time, while not configured in a single database, modeled or mapped, were an important basis to understand the biodiversity of malaria within and between countries in Africa. One further notable global map developed during this period used assemblies of dominant vector species linked to vector bionomics to produce a malaria 'stability index' that was loosely based upon a simplification of the vectorial capacity [74].

In 2005, the Malaria Atlas Project (MAP) was founded as a collaboration between scientists in Kenya and the University of Oxford [75,76]. This initiative continued the principles established by MARA/ARMA to identify and geo-code published and unpublished data on malaria prevalence and dominant vector species [77]. Several important products emerged from the MAP collaboration, which represented the first of their kind for forty years at a global scale. Using MBG methods, MAP produced the first global *P. falciparum* endemicity map based on empirical survey data since the Lysenko map of the 1960s [78]. The information used to constrict this map included information from 4,873 time-space malaria prevalence surveys undertaken in Africa between 1985 and 2009 to interpolate a prediction of *P. falciparum* endemicity across the continent for the year 2007 [78]. This exercise was repeated with increasingly complex models and environmental covariates to provide predictions for the year 2010, including 13,840 empirical *P. falciparum* estimates assembled from surveys undertaken between 1985 and 2010 from Africa [79]. These global products have been used by the WHO to define the global extents of *P. falciparum* malaria risks [80], used by international donor partners for appropriateness of funding based on risk [81-83] and in analyzes of the biological readiness for elimination [84].

The important difference between MARA/ARMA and MAP, was that MAP had a global perspective and its ambitions were to provide an international community with new modeled estimates of malaria risk, rather than support national government malaria risk mapping needs. As such far fewer MAP products have been used by national governments and their partners in Africa than those produced under MARA/ARMA [56].

To tailor the cartography of malaria for use as part of decision-making by national malaria control programmes, an independent project was started by scientists based in Africa from 2012. This initiative led to a revised map of *P. falciparum* intensity for Africa with predictions for the years 2000 and 2010 [85]. This product differed from those of Gething and colleagues (2011) in several important respects: first predictions were based on almost twice as much empirical data across a much wider geographical range (26,746 space-time survey data points between 1980 and 2012); second, interpolation was only allowed within countries and not between countries, avoiding "contaminated" predictions across national borders; and finally, a more conservative use of environmental covariates was used to avoid model over-fitting, allowing the data themselves to drive the model predictions. In line with the recommendations made by Lysenko and Semashko, this was the first ever attempt to map the *changing* malaria risks in Africa, from the largest repository of data assembled up to this date. The results showed that some countries had reduced transmission since 2000, others had not and that within countries some areas seemed resilient to changing parasite transmission while others had substantially declined despite equivalent levels of intervention coverage [85].

Malaria risk mapping to support national malaria control programmes

By 2010, following a decade of increased malaria support, it was recognized that an epidemiologically driven, evidence-based platform should from the framework to design control and elimination. While universal coverage of all malaria interventions, pursued since the launch of Roll Back Malaria (RBM) initiative in 2000, might have been an appropriate response to the malaria epidemic, a more nuanced, targeted approach to control is now required. Paradoxically, at the launch of the GMEP in Africa, during the late 1950s, significant efforts were made to build an epidemiological basis for elimination, but no funding for these ambitions followed. Since 2000, under the RBM initiative, massive funding has been dedicated to malaria control without any improved epidemiological analysis of the diversity of malaria that might direct improved, targeted responses of malaria endemic countries in Africa. The concern now is that the success attributed to recent investment in malaria control in Africa will be lost unless a more rational basis for financing is established.

The Global Fund, the largest provider malaria financing to Africa, began to insist upon detailed epidemiological profiles from individual country submissions for funding [86]. It was recommended that these profiles, and maps, be tied to justifications for sustained targeted insecticide-treated net (ITN) distributions, novel approaches to seasonal malaria chemoprevention, legitimacy of intermittent presumptive treatment in pregnant women and whether combined or single approaches to vector control might be suitable. Re-defining packages of interventions across a spectrum of malaria risk should therefore provide a more intelligent basis to reach different measurable milestones with time. These may seem obvious, but to-date, despite the efforts of MARA/ARMA and MAP, the effective assembly of data from multiple sources and integrating these in novel ways to define risk, intervention, financial needs and priorities for future monitoring has been poor at country levels [56].

The WHO Regional Office for Africa started developing more elaborate national malaria programme reviews (MPRs) from 2010 that included a better articulation of malaria risk and epidemiology for each country [87]. Many of the MPRs have identified the lack of any contemporary malaria risk stratification as a weakness for future country level control planning, with countries relying on outdated maps or poor use of available data to generate new malaria epidemiological maps.

The growth in national malaria survey data since 2005, that have included the collection of geocoded infection prevalence has enabled the application of MBG methods to provide high resolution malaria endemicity maps for individual countries. These have included new modelled malaria risk maps developed by scientists based at the Swiss Tropical Institute, Basel for Angola [88], Côte d'Ivoire [89], Nigeria [90], Senegal [91], Tanzania [92] and Zambia [93]; and modelled map predictions based on national survey data undertaken as sub-regional collaborations between the KEMRI-Wellcome Trust Programme in Nairobi and national malaria control programmes in Kenya [94,95], Somalia [96], Sudan [97], Djibouti [98], Malawi [99] and Namibia [100-102].

The Information for Malaria Project (INFORM)

In 2013, the UK's Department for International Development (DFID) began to develop a strategy to support the Africa Region for a sustained approach to accelerate malaria impact though a more effective use of information. DFID's business case recognised the value of information to design control: "A platform of evidence in Africa can help countries by mapping the malaria epidemic and defining "what works where". This platform will include up to date temporal spatial malaria transmission patterns, entomological data, drug and insecticide resistance patterns, health system and social science research. The platform will draw upon latest modelling of the benefits associated with different combinations of malaria control interventions and remain dynamic so that it can respond to the evolving epidemic, emerging risks (such as artemisinin and insecticide resistance) and the opportunities of new technology and malaria specific tools." [103].

DFID supported pilot projects were started in 2013 in partnership with the Roll Back Malaria (RBM) initiative and the KEMRI-Wellcome Trust Programme based in Nairobi to initiate more detailed assemblies of malariometric and intervention coverage data across eight high burden African countries. These were undertaken in Nigeria [104], Tanzania [105], Uganda [106], Ghana [107], Malawi [108], Ethiopia [109], Democratic Republic of Congo [110] and Mali [111]. As part of these epidemiological profiling exercises countries were provided with summary dashboards of mapped information (for example, Figure 4).



Figure 4: Uganda epidemiological profile summary "dashboard" 2013

As a result of the 2013-2014 epidemiological profiling experiences the Information for Malaria (INFORM) Project was founded as an African initiative to harness the combined efforts of national malaria control programmes, researchers and other regional partners to assemble and package malaria information for efficient national decision making [112]. The ambitions of INFORM are similar to those of its predecessors, MARA and MAP, building multiple layers of spatially defined epidemiological data from all available sources, but differs in three important respects.

First, one key theme is to ensure that data are owned, managed, used and brokered for more effective malaria control at national levels. Ensuring country ownership of epidemiological data, risk maps and research outputs will enhance their long-term value and application beyond the current poor use of global or regional products generated by scientific groups based in the North. The modern day equivalents of national malaria risk maps share some practical parallels with those developed during the GMEP: when developed by, or in partnership, with those responsible for control and elimination at the country level they are more likely to be used as tools for strategic approaches to control.

Second, defining the current (2015) extents and intensity of malaria risk, is only valuable if these have not changed with time under sustained malaria control. Countries therefore require additional information on the counterfactual risks likely to be experienced if intervention coverage or efficacy declined. These pre-post maps becoming increasingly important as national malaria programmes fight to articulate a business case for continued national and/or international investment. The INFORM project therefore aims to provide a sequence of maps based on empirical data to examine short-term and long-term cycles in malaria risk.

Finally, while assembling the full range of malaria data available within each African country is non-trivial [113], national malaria control programmes need additional information on population distributions, urbanization, locations of refugees, private sector mining or agricultural sectors and increasingly ways to integrate improved health information system data. These additional requirements of epidemiological planning demand country specific engagement to ensure that new malaria map products reflect the needs of each country and information is of a granular enough nature to support an understanding of progress, targeted requirements and future projections within a decentralized health system. This marks a significant departure from a previous strategy of a single blueprint for malaria control, an increasing awareness of the complexities of sub-national planning and the importance of data relevant to administrative and demographic decision-making units used by national governments for planning.

Re-establishing a data-driven approach to investing in malaria requires a long-term commitment, anchored in a regional support framework such as that provided by the World Health Organization's Regional Offices. Short-term pilot approaches to building evidence-platforms, as undertaken between 2013 and 2014, will not establish a long-term legacy or paradigm shift in designing, tailoring and monitoring the impact of malaria investment [114,115].

As a first step, it is important to harness the collective effort of national malaria control programmes and partners to ensure the use of carefully assembled layers of data to help malaria control in endemic countries. Building a more legitimate sense of data ownership is an important step in a long process of building the epidemiological and public health skills to use spatial data. This data must then be used to develop an evidence platform to make sub-national decisions on the effective, efficient and equitable distribution of interventions to control malaria. This requires a regional effort built on a credible connection between the science of spatial epidemiology and the practicalities of policy decision-making and a regional presence to effectively respond to the need of countries. These are the reasons that have motivated the establishment of INFORM.

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