The application of geographical information systems to important public health problems in Africa
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Abstract
Africa is generally held to be in crisis, and the quality of life for the majority of the continent’s inhabitants has been declining in both relative and absolute terms. In addition, the majority of the world’s disease burden is realised in Africa. Geographical information systems (GIS) technology, therefore, is a tool of great inherent potential for health research and management in Africa. The spatial modelling capacity offered by GIS is directly applicable to understanding the spatial variation of disease, and its relationship to environmental factors and the health care system. Whilst there have been numerous critiques of the application of GIS technology to developed world health problems it has been less clear whether the technology is both applicable and sustainable in an African setting. If the potential for GIS to contribute to health research and planning in Africa is to be properly evaluated then the technology must be applicable to the most pressing health problems in the continent. We briefly outline the work undertaken in HIV, malaria and tuberculosis (diseases of significant public health impact and contrasting modes of transmission), outline GIS trends relevant to Africa and describe some of the obstacles to the sustainable implementation of GIS. We discuss types of viable GIS applications and conclude with a discussion of the types of African health problems of particular relevance to the application of GIS.

Background
The physical and ecological structure of Africa is as varied as its social, political and demographic characteristics [1]. Major biomes in the continent include tropical rainforest, montane forest, moist and dry savanna, semi-desert and desert and temperate grasslands [2]. The political environment, poverty and generally low levels of well-being for the majority of the people in the continent combine with the varied climatic conditions, vegetation and biogeography to explain the prevalence of disease-causing organisms, or pathogens such as bacteria, viruses and worms [3].
factors and the health care system [14]. Public health practice needs timely information on the course of disease and other health events to implement appropriate actions and GIS are an innovative technology for generating this type of information. Unfortunately, the importance of the spatial distribution of disease has been too often overlooked [8].

Africa is generally held to be in crisis and the quality of life for the majority of the continent’s inhabitants has been declining in both relative and absolute terms[15]. The health problems are different to those in the developed world and if GIS is to be used for the health challenges facing Africa, then it must respond to these realities and priorities. Due to infrastructural and cost constraints, there is a lack of reliable statistics and disease reporting in Africa. Where data do exist, they tend to be clinically (as opposed to diagnostically) based. Disease estimates in Africa can therefore range between ‘educated guesses and wild speculation’ [16]. GIS can help significantly in this area by filling the gaps through empirical disease modelling techniques.

If the potential for GIS to contribute to health research and planning in Africa is to be properly evaluated then the technology must be applicable to the most pressing health problems in the continent. In this article we focus on the human immunodeficiency virus (HIV), malaria and tuberculosis as some of the most important public health threats in Africa [17,18] as well as having diverse modes of transmission. Furthermore we review work done in the spatial analysis of health systems (that must assist in the attenuation and control of these diseases).

Review

Africa’s health priorities

HIV/AIDS is the leading cause of mortality and morbidity in Africa [18]. Since its appearance more than two decades ago the virus has spread to almost every country in the world affecting an estimated 34 million people [19]. Nearly 24 million people in Africa currently live with HIV/AIDS and the epidemic continues to ravage the development prospects for millions of Africans throughout the continent. In 1999, about 3.8 million Africans were infected with HIV during that year, and a total of 10.7 million children were estimated to be orphaned by it[15]. The 21 countries with the highest HIV prevalence are in Africa. In South Africa, Botswana and Zimbabwe, one in four adults is infected. A child born in Zambia or Zimbabwe today is more likely than not to die of AIDS. In many other African countries, the lifetime risk of dying of AIDS is greater than one in three [15]. While prevalence in many west and central African countries has remained relatively low and stable, eastern and southern Africa have experienced explosive epidemics with HIV prevalence exceeding 40% among pregnant women in some regions. Around 5 million new infections are currently occurring annually worldwide, over 90% in developing countries[19].

One of the reasons for the severity of Africa’s HIV/AIDS epidemic is the high prevalence of other sexually transmitted infections (STIs) and the inadequacy of STI services. Another reason for the recent rise in HIV in Africa is the gradual adaptation to new environments, for example, as people migrate from rural to urban areas in search of work. However, the spread of sexually transmitted diseases can also be sharply intensified by crises such as natural disasters, social disintegration, armed conflict and mass population movements[20]. HIV is especially burdensome as the infection and resultant disease primarily affects young and mature adults in their most productive years (15–25) when older and younger family members are dependent on them. The global HIV pandemic is composed of a series of several smaller epidemics. Even within Africa, where levels of infection are the highest in the world, there is substantial heterogeneity of levels of infection.

Tuberculosis is the leading infectious cause of death worldwide, killing more people aged over 5 years of age than AIDS, malaria, diarrhoea and all other tropical diseases combined. The World Bank estimate that the disease accounts for 26% of all avoidable adult deaths in less-developed countries[21]. So serious is the threat of tuberculosis that in 1993, the World Health Organisation took the unprecedented step of declaring this disease a global emergency[22]. HIV infection renders a person infected by Mycobacterium tuberculosis much more likely to develop overt tuberculosis, and the evolution of the disease is considerably accelerated. About 20% of tuberculosis cases in Africa are believed to be related to HIV infection[23]. WHO has calculated that, unless urgent action is taken the annual global number of deaths could rise from 3 million to 4 million by the year 2004. The need for effective intervention is compelling because tuberculosis treatment is one of the most cost-effective of all health interventions. In response to this re-emerging epidemic, the World Health Organisation is promoting the DOTS control strategy (directly observed therapy, short course) with community based treatment at its core[24].

In the last decade, in Africa, the incidence of malaria has been escalating at an alarming rate. Cases in Africa account for 90% of malaria cases in the world [25]. Until recently, malaria was ranked as the leading disease in terms of disease burden[21]. It is now estimated that only HIV has a larger impact on the health of the African population than that of malaria[18]. Malaria is estimated to cause disease in 400 million individuals in Africa and is responsible for 20–50% of all hospital admissions.
tality associated with cerebral malaria has not improved in the past 30 years [26] and severe malaria anaemia is on the increase[27]. One study has estimated (using empirical methods) that during 1995, 0.75 to 1.3 million deaths resulted from malaria in Africa and that approximately 80% of these occurred in children < 5 years of age[16].

The development of drug-resistant strains of the malaria parasite *Plasmodium falciparum* has been one of the greatest obstacles to controlling the disease [28]. Drugs such as chloroquine, which were once highly effective, are now almost useless for treating malaria in many parts of the world [29]. Frequent armed conflicts, migration of non-immune populations, changing climatic patterns, adverse socioeconomic patterns (e.g. gross inadequacies of funds for drugs), high birth rates and changes in the behaviour of the vectors are also responsible for the upsurge[30]. The upsurge has also been attributed in part to the declining nutritional status of individuals in both urban and rural areas[2]. Malaria and underdevelopment are closely intertwined. The disease causes widespread premature death and suffering, imposes financial hardship on poor households, and holds back economic growth and improvements in living standards. Malaria flourishes in situations of social and environmental crisis, weak health systems and disadvantaged communities[18].

Health systems in Africa face increasingly diverse and complex health problems, rapidly growing populations, and severe resource constraints. Improving the performance of health systems has been identified as a major global health priority[18]. Health systems’ performance makes a profound difference to the quality, as well as the length of the lives of the billions of people they serve. If health systems are poorly constituted and managed, life-enhancing interventions cannot be delivered effectively to those in need. Malaria and tuberculosis are examples of diseases that thrive in the absence of well constituted, effective health systems. This is particularly pertinent for Africa where health systems often perform poorly and are unreliable.

**GIS research in health in Africa**

Much remains to be understood about the relationship between space and disease. The spatial dynamics of tuberculosis, HIV and malaria are different because of the different modes of transmission and differing relationships to the environment. For example, tuberculosis (transmitted by respiratory droplets) and HIV (transmitted largely through sexual contact) rely on close human contact for transmission. Malaria however is transmitted by mosquitoes and is constrained only by the flight distance of mosquitoes. This has been measured in one vector species at a maximum distance of 1.8 km [31]. Climatic factors play a large part in determining the distribution of malaria, whereas HIV and tuberculosis are affected more by the social environment. These differences will necessarily affect the types of GIS methodologies used to understand the various spatial components of these diseases.

GIS has been widely applied to the understanding and management of malaria in Africa. For example GIS has been used to generate models of malaria occurrence [32,33], seasonality [34,35] and transmission intensity [36–41] using climatic and remotely sensed data. The outputs of such models have been combined with population data [16,42] to estimate population exposure, mortality and morbidity [16,42] and to analyse [43] and project [44,34] the effects of climate change on malaria. GIS has been used to map malaria vectors [45–47], vector habitats [48] and infection [49]. It has also been used in the management and control of malaria [50–52], to measure the effects of access to malaria treatment [53] and to evaluate the effects of intervention strategies [39]. The above studies were undertaken at scales ranging from micro to continental.

We were only able to locate a handful of published studies using GIS to study tuberculosis in Africa, all of which were undertaken in South Africa. GIS has been used to map tuberculosis cases in an Urban area in the Western Cape of South Africa [54] and analyse childhood tuberculosis in two urban communities of Cape Town [55]. In a rural area of KwaZulu-Natal, GIS has been used to analyse the distribution of treatment points and the effect of community-based (as opposed to facility-based) treatment on increased access to nearest treatment supervision point [56,57].

GIS could have an important role to play in tuberculosis control programme management, service development, and research. In terms of planning and managing the service, GIS can assist in the planning of the number and distribution of the supervision points as proximity of treatment is one important factor in promoting adherence to treatment. Much remains to be understood about tuberculosis transmission dynamics in developing countries[58] and GIS will be a useful addition to molecular techniques and conventional epidemiology, in elucidating transmission pathways, and clusters of multi-drug resistant cases for example.

Although several studies analysing geographic variations in HIV in Africa have been conducted [59–63], and the importance of place in targeting areas for priority intervention[64] has been emphasised, only one published study could be located that applied GIS to the analysis of HIV [65]. The study provided some evidence for an ecological relationship between transport accessibility (distance to roads) and HIV prevalence. This was believed to
be related to the amount of sex work taking place along the major routes as well as the higher mobility of persons living near transport routes. However, this relationship needs to be tested at an individual as well as at an ecological level. Though studies have documented heterogeneity in the geographical distribution of the HI virus [66–68], much remains to be learnt about the causes and nature of this heterogeneity. Most research has focussed on temporal analysis ignoring the spatial dimensions of the HIV/AIDS epidemic. Yet, spatial analysis may be an important tool to monitor the epidemic, predict future treatment demands and to target areas for public health interventions. Work in Europe and North America [e.g. [69,70]] has focused largely on the distribution and diffusion of the disease [71]. In addition, the delimitation of high-risk areas (based on the distribution of co-factors) using standard risk analysis techniques could prove invaluable in Africa. Furthermore, the technology could also assist in the optimal spatial organisation of health care delivery including home-based care. The difficulty of obtaining HIV data and the stigma associated with disclosure however, is a major obstacle to the use of GIS in HIV research in Africa.

Surprisingly, there were few published examples of the use of GIS in health systems research in Africa but there is an encouraging amount of work in progress. One group used GIS to study inequalities in population per bed ratios and the implications of open access to the private and the formerly white hospital services in the province of KwaZulu-Natal, South Africa [72]. One study used GIS to equitably distribute fieldworker workload in a large health survey. The methodology predicted average inter-homestead walking time and divided the heterogeneous study area into units of equal workload [73]. The author suggests that an extension of the same methodology can be used to optimally distribute community health workers and tuberculosis DOT supervisors, for example. Another study analysed modal patterns of fixed and mobile clinic attendance across an integrated rural health district [74] and developed indices to analyse the relative attraction and repulsion by the various clinics in the district. The most important outcome of the research was the development of a composite measure of clinic usage and inter-clinic interaction based on the ratio of total actual versus predicted distance travelled to attend clinic. The same data set has been used to validate a model of travel time to the various clinics based on a network analysis of a road network. Relative clinic attraction and inter-clinic interaction were again studied using travel time as the denominator in the index (F.C. Tanser & K. Herbst, In prep., 2002). A study using a similar methodology is underway in the Ruzizi district of Tanzania to investigate the relationship of wealth quintiles and health outcomes to travel time to nearest health facility (D. de Savigny et al., In prep., 2002). Researchers are using GIS to investigate the relationship between clinic access and maternal and child health indicators in rural Kwa-Zulu Natal South Africa (J. Tsoka et al., In prep., 2002) In four districts of Kenya, GIS is being used to capture and model both population’s access and utilisation of health services with a view to increasing the effectiveness of malaria treatment coverage (A. Noor et al., In prep., 2002).

Limited physical access to primary health care is a major factor contributing to the poor health of populations in developing countries[75]. The world health report of 2000 [18] was dedicated to improving the performance of health systems. Health systems performance make a profound difference to the quality, as well as the length of the lives of the billions of people they serve. However, an important omission from the report was the spatial aspect of health systems research. GIS can be used to effectively spatially analyse health systems coverage and identify deficiencies. The potential exists for GIS to play a key role in rational and more cost-effective health service planning and resource allocation in Africa.

GIS trends relevant to Africa

GIS is largely technologically (as opposed to research) driven. Some of these global technological trends are irrelevant to health research in Africa at the present time. However, some global trends (both technological and non-technological) are of significant relevance to Africa’s health crisis.

It is becoming clear that although GIS started out as a technological tool, it is rapidly evolving into a science in its own right[76], albeit in embryonic form. At present it lies somewhere along the continuum between the two. As software becomes increasingly powerful and new datasets become available and GIS is increasingly used to understand and forecast the dynamics of (particularly environmental) disease, this evolution is likely to continue. A parallel exists between GIS and epidemiology. In the same way that epidemiology evolved into a science in its own right in the 1970s [77], GIS is beginning to be recognised as a science. Like epidemiology its tenets have been established piecemeal [77] with contributions coming from a number of different disciplines, in particular the earth sciences. It is now time to draw the different facets of GIS together under the umbrella of geographic information science.

Computer hardware is becoming increasingly cheaper and more powerful, so that even complex analyses of GIS and image data can be carried out on a desktop computer. At the same time, commercial software has been developed into stand-alone solutions capable of performing increasingly complex tasks through increasingly user-friendly interfaces. Whilst there is an increasing amount of
free software, the commercially available comprehensive packages remain expensive [11].

Since the 1st May 2000 the accuracy of off-the-shelf global positioning systems (GPS) has improved by an order of magnitude. Low cost units can now perform tasks that they previously weren’t suitable for. This development is likely to result in a sharp increase in the number of geo-referenced health projects making use of GPS technology in the near future.

**Obstacles to the advancement of GIS in health in Africa**

The paucity of qualified staff, which has prevented many GIS projects from surviving the donor involvement phase, is a major problem in Africa [78]. GIS applications in Africa are often found to be initiatives funded or supported by international aid agencies and many are pilot or research projects as opposed to operational systems. They also tend to be controlled by outsiders, not by African scientists [79]. If GIS are to be useful and effective, then they must be introduced by local scientists who understand both the technological and the socio-economic context in which the systems are to operate. Training creates capacity and leads to an increase in terms of data needs. It however also provides the capacity to fulfil these needs and the new products that result are often of value to many other sectors. Capacity development of African staff should therefore be prioritised.

In addition to lack of capacity, a lack of suitable GIS data sets is a major impediment to the growth of GIS in Africa. The access to spatial data (which are fundamental to any GIS application) continues to be difficult and expensive [10]. This is not specific to health but to all sectors that utilise GIS. There are similarities in the field requirements for using GIS between forestry, ecology, archaeology and epidemiology that could provide substantial benefits by the sharing of experiences and the pooling of resources [11]. However, much of the spatial data collection efforts within Africa have been conducted in a decentralised and uncoordinated manner. Inter-sectoral collaboration initiatives should therefore be encouraged and receive funding priority. Africa could usefully build projects such as the Global Spatial Data Infrastructure [80] (embedded within which is the SDI – Africa project) and the EIS – Africa [81] projects which aim to support ready access to geographic information to support decision making at all scales for multiple purposes. Geographic datasets are being developed for some countries in Africa through these initiatives, but a systematic programme is required to make geographic data readily available for the continent as a whole. A major programme (funded by an international body) is needed to take up this challenge. Priorities include, for example, the digitalisation of 1:250 000 and 1: 50 000 cartographic maps for countries that have them.

Similarly, national geo-referenced health facility databases should be established. Inexpensive African data sets include the African data sampler (topographic, boundary and place data) [82], long-term rainfall and temperature data [83] and raster population data [84]. Development of such data sets are of paramount importance to ensure the growth of all sectors of GIS in Africa.

Widespread availability of small scale digital data (< 1: 50 000) for many countries within Africa is unlikely to ever become a reality. The most cost-effective answer to the data deficit and poor vital registration and health statistics problem in Africa is the establishment of sentinel geo-referenced demographic and health surveillance systems [85]. This will enable the elucidation of small-scale disease patterns (e.g. diffusion dynamics) that could be modelled using coarser resolution data and the coverage extended. The INDEPTH network is a network of these sentinel surveillance sites, 23 of which are in Africa [86]. The sites follow up a designated population intensively over time collecting highly accurate demographic, vital event (e.g. births, deaths, migrations) and health data on a routine basis. So far only a small proportion of the sites are fully geo-referenced but this is likely increase with the increase in GPS accuracy, falling prices and the obvious operational and research advantages of fully geo-referenced data. These sites can especially contribute (and have already contributed) to our understanding of diseases with ill-defined relationships to the environment due to the detailed longitudinal collection of disease covariates. A recent spatial initiative in health is the West African Spatial Analysis Prototype (WASAP) that used geo-coded demographic and health survey (DHS) data to study the effects of climate on children’s nutritional status, and the relationship between economic diversity and reproductive behaviour, as well as study the subnational geographic variation in health indicators at a regional level [87, 88].

Following the success of WASAP, more DHS sites have begun to geo-code their survey data in an effort to facilitate cross-disciplinary analyses. The increasing availability of regional geo-referenced DHS data will facilitate a more comprehensive understanding of the patterns and processes of demographic and health changes and will lead to an increasing amount of GIS-based analyses of this important data in the near future.

In addition to the geo-coded household datasets outlined above, a large number of remotely sensed data sets, which have been already used extensively in health are available free of charge or at nominal cost. With the emergence of new technologies and techniques within remote sensing, there is likely to be a great improvement in the quality of such data sets and parallel improvement of GIS and related research products [89]. Nevertheless, it is also true to say that so far, our ability to extract meaning and make
useful decisions from remotely-sensed data has not kept pace with the developments in this field.

The issue of scale is one that is poorly understood in the disease arena. Disease patterns and processes evident at one scale are not necessarily evident at another. Moreover, correlations between explanatory variables and outcomes may even be (seemingly) reversed at different scales. This has led to a significant amount of confusion when hypotheses are rejected at one scale and not at another. Sometimes it is advisable to use coarser resolution data to mask out small scale heterogeneity. For example, the malaria modelling at a continental level used climatic data at a resolution of 0.05° [32,34]. Higher resolution satellite data (sub kilometre) may obscure continental malaria patterns by exposing unnecessary small area variation. Ideally the resolution of the data should be driven by the application. However, given Africa's geographic data deficits, future research is needed to establish how applicable coarse resolution data sets are to modelling high resolution disease-specific dynamics and vice-versa. The above issues are as applicable to temporal resolution as they are to spatial resolution.

Another obstacle remaining to the growth of GIS in health in Africa is to convince role players (often from cash-strapped organisations) of the proven cost-effectiveness of GIS in the health arena[90]. Even amongst the international scientific community, significant scepticism still exists surrounding the use of GIS technology in health. This problem will diminish in size as GIS continues to evolve. The parallel with epidemiology again warrants mentioning: In the same way that scepticism greeted epidemiologists who hypothesised that a relationship existed between smoking and lung cancer in the 1950s [77], so to will scepticism continue to plague GIS until it is firmly established as a science.

It is encouraging to note that several of the issues cited as obstacles to the growth of GIS in Africa a decade ago [91] have been overcome to some degree. These included the incompatibility of different software formats (data conversion problems), the non user-friendly interfaces of many systems and the lack of good inexpensive/free GIS software. Other obstacles such as the prohibitive costs of hardware have also become less of an issue. Perhaps a review in a decade's time will describe the increasing availability of inexpensive spatial data sets for Africa?

The 'mapping malaria risk in Africa' (MARA) research collaboration is an African research endeavour that makes extensive use of GIS technology. The collaboration has been highly successful in collating malaria data from around the continent, and producing a large number of scientific publications on a limited budget. The outputs of the research were then disseminated to countries throughout Africa in the form of digital (via the stand-alone MARA lite software) and hard copy maps. The collaboration overcame significant data deficits by creating its own base data sets and created a significant amount of GIS capacity in its five regional centres throughout the continent. During the setting up of the collaboration, significant scepticism was expressed by influential malaria scientists as to the ultimate value of a GIS approach, its logistical feasibility and cost-effectiveness[33]. The collaboration is a testament to the fact that successful GIS initiatives can be undertaken in Africa.

### Viable GIS health applications in Africa

The current software and hardware trends in combination with the realities faced in Africa have given rise to essentially, two broad categories of long-term feasible GIS health applications in Africa. The outputs of the categories will inform one another and are not mutually exclusive and may overlap. The first category involves the use of GIS as a research tool. These applications should seek to provide new insights into the spatial dimensions of disease and new methodologies to more cost-effectively allocate resources to health services. These types of applications will normally use high-end systems with significant analytical functionality and will usually involve a significant amount of additional data collection.

The second category of long-term viable GIS application concerns the use of GIS as a health planning and management tool and for exploratory data analysis. Generally speaking this kind of system will involve a low-end GIS. The primary goal of such a system will be to simply display and overlay basic health data concerning both health care facilities and disease patterns. These systems (normally vector-based) permit rapid manipulations of spatial data and display of the results so that the decision makers can use them for policy decisions. A further step could involve limited spatial queries and analysis such as buffering.

The outputs of the different categories of application will inform one another. As the data is geographically displayed using a management GIS and research questions are derived, collaborations can be initiated with institutions undertaking GIS research to test hypotheses and model disease distributions. Similarly, research GIS applications will inform GIS management applications to plan optimal resource allocation and intervention strategies, for example. The MARA collaboration is a successful example of this type of approach and is embedding several of its research outputs in the freely available GIS software HealthMapper (developed by WHO) for intervention planning in Africa at a district level.
Conclusions
A review of the health literature in Africa reveals the GIS bias towards so-called 'environmental' diseases. In certain diseases, such as the vector-borne diseases (e.g. malaria, schistosomiasis, human helminth infections and trypanosomiasis) the environmental component in the determination of factors such as transmission intensity is extremely high. In other diseases, especially in the non-communicable category (e.g. multiple sclerosis) links to the environment are weak or non-existent. Some infectious diseases such as HIV and tuberculosis have moderately strong links to the environment. Thus there exists a continuum of diseases, on the one hand they are those diseases in which GIS has limited research application and on the other there are those in which GIS is highly applicable. This continuum does not relate to the availability of ancillary data sets but rather to the inherent nature of the disease itself.

Not only does Africa have the highest burden of disease of all the continents[18], but it is the continent in which the greatest component of the burden is contributed by so-called 'environmentally dependent' diseases. In addition, the phenomenon of climate change is likely to hit hardest in Africa [15] on account of its greater rainfall variability and the proportion of 'ecothermic infectious diseases'. This makes the potential applications of GIS in health particularly relevant to Africa, i.e. GIS in health has greater relevance and inherent potential in Africa than it does in the United States or Europe for example. Unfortunately, this reality is not reflected in the literature or in practice. Thus, we concur with authors [92,93] who have concluded that GIS is an appropriate technology for developing countries (despite the fact that in some ways GIS appears to contradict the principles of appropriate technology because of its sometimes high cost and often high levels of expertise required) since many issues of poverty relate to large scale problems requiring integration of large spatial datasets. Furthermore, the success of participatory approaches for the transfer of GIS technology by the MARA project and in other developing country settings [94] could serve as a useful framework for future projects.

The ability to map spatial and temporal variation in disease risk is more important than ever given the ever-increasing disease burden in Africa. GIS allows the planning of control strategies and the delivery of interventions where the need is greatest, and sustainable success is most likely. Despite some obstacles, GIS holds considerable promise for health research and development in Africa. The global trend towards faster, more powerful computers, user-friendly software and falling prices combined with the magnitude and nature of Africa’s disease burden and lack of reliable disease statistics makes it a viable, relevant and powerful technology for health research and management in Africa.

List of abbreviations
DHS – Demographic and Health Survey
DOT – Directly observed treatment
EIS – Environmental Information Systems
GPS – Global Positioning System
HIV – Human Immunodeficiency Virus
MARA – Mapping Malaria Risk in Africa
SDI – Spatial Development Initiative
WASAP – West African Spatial Analysis Prototype
WHO – World Health Organisation

Authors’ contributions
The authors contributed equally to the conceptualisation and writing of the manuscript.

Acknowledgements
David le Sueur died unexpectedly during the advanced stages of manuscript preparation. Frank Tanser wishes to acknowledge him for conceiving and driving the Mapping Malaria Risk in Africa (MARA) initiative and for his unsurpassed lifetime contribution to the field of malaria mapping and modelling and to GIS in health in general. This research was jointly funded by the South African Medical Research Council and the Wellcome Trust.

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