The global distribution and population at risk of malaria: past, present, and future

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Abstract

The aim of this review was to use geographic information systems in combination with historical maps to quantify the anthropogenic impact on the distribution of malaria in the 20th century. The nature of the cartographic record enabled global and regional patterns in the spatial limits of malaria to be investigated at six intervals between 1900 and 2002. Contemporaneous population surfaces also allowed changes in the numbers of people living in areas of malaria risk to be quantified. These data showed that during the past century, despite human activities reducing by half the land area supporting malaria, demographic changes resulted in a 2 billion increase in the total population exposed to malaria risk. Furthermore, stratifying the present day malaria extent by endemicity class and examining regional differences highlighted that nearly 1 billion people are exposed to hypoendemic and mesoendemic malaria in southeast Asia. We further concluded that some distortion in estimates of the regional distribution of malaria burden could have resulted from different methods used to calculate burden in Africa. Crude estimates of the national prevalence of *Plasmodium falciparum* infection based on endemicity maps corroborate these assertions. Finally, population projections for 2010 were used to investigate the potential effect of future demographic changes. These indicated that although population growth will not substantially change the regional distribution of people at malaria risk, around 400 million births will occur within the boundary of current distribution of malaria by 2010: the date by which the Roll Back Malaria initiative is challenged to halve the world's malaria burden.

"While keeping in mind the realities one can nevertheless be confident that malaria is well on its way towards oblivion. Already as a malariologist, I feel premonitory twinges of lonesomeness, and in my own organisation I am now a sort of 'last survivor'. So perhaps it is fitting that I should take this backward glance at the fascinating pages of malaria history."[1]

This extract from the 1955 preface of Paul Russell's *Man's Mastery of Malaria*[1] now seems astonishing. In the 50 years that have passed since the series of lectures on which this book is based was given we have become less sanguine about the prospects for global malaria control. The purpose of this review is to document what happened to the global spatial limits

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of malaria risk during the past 100 years and use this to examine the task facing the global malaria-control community at the turn of this century.

Spatial distribution of malaria through time

The human race and malaria parasites have had a long evolutionary host–parasite association.[2–4] Advances in bioinformatics[5,6] largely support hypotheses inferred from changes in human ecology that around 10 000 years ago *Plasmodium falciparum* populations rapidly expanded in Africa and spread worldwide, coincident with human population growth and subsequent diasporas facilitated by the dawn of agriculture.[7,8] It has also been suggested that this expansion followed an earlier smaller wave of migration in the pleistocene.[4] The probable maximum preintervention distribution of malaria (around 1900)[9–11] is shown in figure 1, reaching latitudinal extremes of 64° north and 32° south[18] (corresponding approximately with the theoretical 15°C July and January isotherms, respectively, supporting *Plasmodium vivax* transmission).[19] These maps represent risk from one or more of the four species of *Plasmodium* that cause malaria in human beings, hereafter referred to as all-cause malaria risk.[20] We extend previous inquiry into this area[7,21–24] by quantifying recorded changes in the global malaria distribution over a longer period of time, at more frequent intervals, and relating this distribution to the intensity of malaria risk.

Human efforts to control malaria have markedly restricted its distribution during the 20th century.[12–17] Distribution maps have been compiled largely from country reports and expert opinion arising from the network of regional offices of the WHO. Despite these maps being imperfect representations of global malaria-infection risk distribution in space and time, they nevertheless facilitate some insight into the progress of malaria control in the 20th century. We present results that were obtained using summary procedures in geographic information systems (GIS) on digitised (electronically redrawn and geographically referenced) versions of original maps, the exact methodology for which is explained in the relevant figure and table legends. These procedures show that since preintervention (about 1900–2002) development and control efforts have reduced the area of human malaria risk by around half, from 53% to 27% of the Earth's land surface (table 1). The number of countries and territories (with populations of more than 100 000 inhabitants) exposed to some level of malaria risk fell from 140 to 88 during this period.

Despite a resurgence in the interest in mapping malaria endemicity in Africa,[26–29] which has been used as an empirical basis to help estimate malaria burden,[30,31] the only global map of malaria endemicity[9] dates from Lysenko's efforts in 1968 (figure 2). Endemicity as used by Lysenko[9] was defined by the parasite rate in the 2–10-year age cohort (hypoendemic <0·1; mesoendemic 0·11–0·5; hyperendemic 0·51–0·75), except the holoendemic class (>0·75) where the parasite rate refers to the 1-year age group.[32] This map was a major synthesis of historical records, documents, and maps of several malariometric indices (records of disease and vector presence and absence, spleen rates, parasite rates, sickle cell incidence, sporozoite rates, biting rates, etc) used to record malaria endemicity up until the late 1960s. These data were then interpolated globally for malaria at the peak of its assumed historical distribution, using a combination of expert opinion, global increase, temperature, and rainfall isohyets.[9,33] The map is used here in its original form to frame a discussion on the regional variation in control effectiveness, since there is no modern global equivalent.

Using the contraction in the limits of all-cause malaria transmission (figure 1), assumed as a consequence of control efforts and development, and subdividing these changes by endemicity class (figure 2) shows that these gains have been most radical at lower endemicity rates with reductions of the epidemic, hypoendemic, and mesoendemic areas of 100%, 66%, and 45%, respectively, between 1900 and 2002 (table 2 and figure 3a).

Conversely, there were negligible effects in areas of hyperendemic and holoendemic malaria with reductions of only 16% and 0%, respectively (table 2 and figure 3a). These numbers and the decreasing relative effect on the distribution over time (table 2) provide support for hypotheses of the increasing difficulty of malaria control with increasing intensity of malaria transmission.[34–39] We now investigate how human populations have changed alongside this global restriction in the area of all-cause malaria.

Human populations at risk through time

The global human population has grown geometrically during the 20th century from approximately 1 to 6 billion (table 1). These demographics have important implications for the percentage of the human population exposed to all-cause malaria risk through time. The percentage of the global population at risk has decreased from 77% at the turn of the 20th century to a low of 46% in 1994. This figure increased to 48% in 2002 due to population growth in an unchanged geographic distribution. In absolute terms the numbers of people at risk have increased consistently from 0·9 to 3 billion over the same period (about 1900–2002; see table 1 for data and methods). At the turn of the 21st century, therefore, we estimate that 48% of the global population remain exposed to the risk of malaria, a situation that has deteriorated since the early 1990s and a figure substantially higher than the 40% widely cited.[40–42]

The changes in populations exposed to various rates of endemicity from around 1900–2002 are shown stratified by WHO region in figures 4a–g. These WHO regional groupings (figure 4g) are largely administrative but were originally defined to capture environmentally and epidemiologically coherent zones for public-health management.[24] Certain anomalies exist, however, that make interpretation of regional malaria risk problematic, such as the inclusion of Somalia and Sudan in the Eastern Mediterranean Regional Office (EMRO). The European region (EURO) is the only grouping of countries to show a consistent decrease in populations at risk through time (figure 4d). The American region (AMRO) remained approximately stable in terms of populations at risk, as population growth compensated for substantial control gains during the 20th century (figure 4b). Limited growth in populations at risk are shown in the EMRO area (figure 4c), but the most striking changes are the sharp growth in populations at risk in the African Regional Office (AFRO) area (figure 4a) and particularly the South East Asia Regional Office (SEARO) area (figure 4e). In the AFRO area the population at risk grew from 0·06–0·65 billion during the 20th century, more than 80% of whom remain in areas of hyperendemic and holoendemic malaria. The SEARO area (dominated by India) has experienced even more dramatic growth from 0·2–1·5 billion people at risk, but unlike the AFRO area has only 37% of these populations in places defined as hyperendemic.[9] Consistent growth in population at risk is not a feature of the Western Pacific region (WPRO; figure 4f) due to the marked reduction in the limits of transmission in China since 1975 (figure 1).[44] These estimates of populations at risk, derived from crude maps of malaria endemicity, mask the very different public-health consequences of infection with *P falciparum* and *P vivax*,[45] but do draw attention to a huge potential burden that is hard to quantify directly from official statistics.[46] Furthermore, despite current emphasis on the AFRO area[47] these analyses suggest that the SEARO region warrants greater international attention, an issue to which we return later. Finally, that much of this population growth will have been concentrated in urban areas is a significant confounder to global burden of malaria estimates and is the subject of significant contemporary research effort.

Global malaria control from ~1900 to 2002

During the 19th century great improvements in the control of several communicable diseases were realised, chiefly as a result of environmental improvements.[48–52] In parallel, improved social conditions (particularly housing) and changing land use (particularly agricultural practices) contributed significantly to the global reduction in the distribution of malaria.[8,21,53–56] These gains from malaria control were often coincidental with economic and social development, forces that although spatially heterogeneous, have remained undiminished throughout the 20th century. Our analyses (figure 1 and table 1) show that, counterintuitively, all-cause malaria is not an obligate tropical disease but more precisely one that we have progressively restricted to the tropics in the 20th century through development and control.[1,3,8,21,37,40,57–59] This global reduction followed several distinct phases.

The first "sanitation era" of malaria intervention focused primarily on environmental control of mosquito breeding sites,[1,60–63] once Ross[64–66] had discovered the importance of anophelene mosquitoes in the life-history of avian malaria in 1898 and Grassi showed the full transmission cycle of the human malarias later that year.[67–69] The well-documented success in mosquito control in the Panama Canal,[70–72] Indonesia,[73] Malaysia,[74] the mines and plantations of the Zambian copper belt,[75,76] and the eradication of A*nopheles gambiae* in Brazil[77,78] and Egypt[78,79] validated such approaches (despite some conspicuous failures in Sardinia,[80] Sierra Leone, and India[1,57,64]). To generalise, the species sanitation approach was generally adopted where it was logistically feasible and there was a commercial incentive for investment.[53,54,81] This type of intervention was broadly responsible for the preintervention (about 1900) to 1946 contraction in the global malaria distribution (figure 1 and table 1).

The discovery of the residual insecticide properties of dichlorodiphenyltrichloroethane (DDT) in the 1940s enabled, for the first time, large-scale, wide-area approaches to malaria control[82] and its effect on those engaged in malaria interventions should not be underestimated. The WHO endorsed this approach through the global malaria-eradication programme (from approximately 1955–1969)[83] using DDT to interrupt transmission in an "attack phase" and chemoprophylaxis to eradicate malaria in the later "consolidation phase" of intervention.[36,84–87] The successes, long-term benefits, and problems of consolidation and maintenance have been well documented,[57,81,88] along with the subsequent resurgence of malaria in India[89] and the complete disregard of sub-Saharan Africa in the "global" eradication efforts.[84] The shrinkage in the global malaria distribution from 1946–1965 (figure 1 and table 1) largely coincides with this eradication era.

Since 1965 the further restriction of the global distribution of malaria has resulted from continued national efforts in the developing economies of meso-America and South America, the latitudinal extremes of Africa,[90] the middle east, and China.[44] Despite these local successes no significant impact was made on the global limits of malaria risk between 1992 and 2002 (figure 1 and table 1).

In 1998 the Roll Back Malaria movement was launched as a mentoring, coordinating, and advocacy vehicle for international malaria control.[91–94] Its widely publicised mandate is to reduce the global malaria burden of risk, morbidity, and mortality by half by 2010. To realise this bold ambition Roll Back Malaria has four main targets: to achieve a 60% coverage of children and pregnant women with insecticide treated nets (ITNs), to have 60% of malaria cases receive effective treatment within 24 h of the onset of symptoms, for 60% of pregnant women to receive intermittent presumptive therapy (IPT), and for 60% of epidemics to be detected within 2 weeks of onset and then responded to appropriately within

a further 2 weeks.[47] Implicit in the strategy used to formulate these targets is a focus on malaria in the highly endemic areas of sub-Saharan Africa where most of the remaining global burden of malaria is thought to be.[95,43] We explore this assumption and its implication for international malaria-control priorities in the following section.

The consequences of changing global population at risk

Malaria burden

There has been a renewed interest in establishing precise estimates of morbidity and mortality as part of the Global Burden of Disease Programme.[96,97] Almost all of this work, including studies on acute respiratory-tract infections,[98] HIV/AIDS,[99] and malaria,[30,31] has been driven by the use of empirical survey data, modelled and extrapolated to wider areas. These studies are all critically dependent on the denominator population at risk. For a vector-borne disease such as malaria, the population at risk is a function of the coincidence of human population and malaria infection risk and endemicity.[30,31] Because such an empirical approach has not been developed for regions outside AFRO, the most widely cited estimate of the global proportion of malaria morbidity and mortality borne by AFRO is 90%,[43,95] with estimates ranging from 62 to 93%.[24,43,100,101] The variation in these estimates has wide-ranging implications for policy and the strategic emphasis of the Roll Back Malaria movement.

To highlight this issue we extended our descriptions of populations at risk of all-cause malaria to make preliminary estimates of regional variation in malaria exposure globally. To achieve this it is necessary both to assess regional variation in populations exposed to the various rates of malaria endemicity and to quantify the important distinction between *P falciparum* and *P vivax* burden.[45] Using the 2002 malaria distribution (figure 1),[17] the 1968 Lysenko malaria endemicity map (figure 2),[9] and population distribution projected to 2002 (table 1) a national prevalence index has been computed. This national prevalence index was estimated at the country level by assuming each endemicity class was described by its midpoint parasite rate value as follows: (population exposed to hypoendemic × 0·05) + (population exposed to mesoendemic × 0·305) + (population exposed to hyperendemic × 0·63) + (population exposed to holoendemic × 0·875). We then used the product of the national prevalence and a *P falciparum* index (the proportion of malaria cases reported nationally in 1993 that were due to *P falciparum*)[15,102] to create a national falciparum prevalence (N*f*P). This approach makes several assumptions: first, that the underlying maps used to generate these metrics are relatively precise; second, that the national prevalence may be based on the total population (since national data on the variation in age-specific infection rates are not readily available); third, that the *P falciparum* index estimated in 1993 is compatible with endemicity estimates from the late 1960s; and fourth, that the *P falciparum* index is the same across all endemicity classes in a country. Given these assumptions we use the N*f*P metric to explore malaria-risk distribution only at the regional level (table 4) and have displayed the resulting N*f*P metric as a cartogram,[103] a graphic that depicts countries in proportion to some attribute other than area, to help visualise these variations (figure 5).

It is hard to be unimpressed by the scale of the problem in AFRO (53% of global N*f*P). The absolute magnitude of the *P falciparum* malaria-infection burden in SEARO (33% of global N*f*P) is also compelling (table 4 and figure 5) and not incompatible with recent analyses, which report a significant proportion of global childhood mortality in the SEARO area.[104] The implications of such analyses cannot be dismissed simply by arguing that control and development have changed so fundamentally the endemicity in regions outside AFRO since the late 1960s. If we hypothesise this to be the case and recalculate N*f*P by assuming that in all areas outside AFRO endemicity has been so radically reduced by development and

control that all areas have stepped down one endemicity class[9] (ie, from hyperendemic to mesoendemic, from mesoendemic to hypoendemic, and from hypoendemic to zero risk), we still have 25% of the N*f*P outside AFRO (table 4, scenario b).

There are differences between *P falciparum* malaria risk and resulting morbidity and mortality outcomes experienced in different populations of the world.[105] It is beyond the scope of this review to attempt to model morbidity and mortality globally. Reconciling N*f*P estimates with national level malaria reporting is a logical and important extension of this work. It is perhaps worth noting, however, that while mortality rates from *P falciparum* infection are on average nine per 1000 in the under-five populations of AFRO,[31,106] they range from 0·1–1 per 1000 and 0·01–0·1 per 1000 (in all age groups) in SEARO countries such as Myanmar (Burma) and Sri Lanka, respectively.[105] This order of magnitude difference in mortality risk means that most malaria mortality is likely still to be in AFRO. The absolute magnitude of populations at risk outside of AFRO (table 2 and table 4), however, indicate that malaria-attributable mortality will not be trivial, particularly in SEARO, and that morbidity is likely to be substantial. What these analyses suggest therefore is that reliance on WHO country reports for disease-burden estimates outside AFRO in calculating the global malaria burden must be augmented with alternative approaches used to estimate the burden in AFRO[30,31] to enable sensible comparisons. The two most important implications of regional variations in the distributions of risk relate to the current status of antimalarial drug management and the extent to which vector control is likely to be effective outside AFRO.

Drug resistance

The idea that populations living in areas of low malaria transmission are catalysts for the development of antimalarial drug resistance is now supported on both theoretical[107–109] and empirical grounds.[110–113] These analyses have shown that almost 30% of the global population at risk from malaria reside in areas of hypoendemic and mesoendemic transmission in the SEARO region (table 3), including Thailand, the focus for the origin of drug-resistant malaria.[6,114,115] The spread of drug-resistant malaria parasites from SEARO to AFRO has provided an explanation for the rising mortality from malaria in this region since 1990.[106,116–118] It is possible therefore that aggressive efforts to limit transmission outside of AFRO might have a larger than expected global effect on public health by helping delay the development of drug resistance.

Types of vector control

The difficulty of malaria intervention in areas of high transmission is a tenet of malariology[34–39,119,120] and the debate has often centred on the holoendemic areas of sub-Saharan Africa. The relatively high anthropophily,[121] longevity, and density of the *A gambiae* complex and *Anopheles funestus* and their resulting efficiency as malaria vectors in sub-Saharan Africa[3,122–124] results in an average annual entomological inoculation rate for the continent (based on 159 samples of malarious areas) of 121 infected bites per person per annum.[29,125] Furthermore, these high rates of transmission combined with the dominance of *P falciparum* in sub-Saharan Africa[15,102] warn against naive extrapolation of control successes in temperate and subtropical parts of the world, before considering a host of other economic, logistic, and social constraints to control.[126]

Despite the widely accepted intransigence of malaria in holoendemic areas, opinions on appropriate control strategies in such areas differ.[34,37,39,61,78,127,128] We do not attempt to reignite this debate but several aspects of these analyses are noteworthy. First, any optimistic prospect derived from the reductions in the total area malarious by endemicity class is confounded by demographic changes. Numbers at risk have increased relentlessly in all

endemicity classes except the epidemic one (table 3 and figures 3a–b). Second, more than half of the 2002 malaria distribution is hypoendemic (19·5%) or mesoendemic (32·2%; table 3). Regardless of the position adopted on the choice of eradication versus control in hyperendemic or holoendemic areas (and/or the exact suite of interventions that could be applied), more than 50% of those at risk of malaria live in areas where sustained control is inherently epidemiologically feasible. In the SEARO area such control has a strong historical precedent for success[89] and more ready access to the resources needed to implement control than the AFRO area.

Implications for rolling back malaria

Despite the international support and political will for malaria control having improved in the past 5 years,[91–94,129–131] doubts about the efficacy, focus, and particularly the financing of international initiatives have been raised[132–134] with a concomitant push for strategic changes in the direction and emphasis of research and control.[135–137] The Commission for Macroeconomics and Health has estimated that an immediate injection of at least US$1 billion per annum is needed to enable the Roll Back Malaria movement to start to work towards its goals[138] and that this should be boosted to between $1·5–2·5 billion annually by 2007 if it is to have any chance of meeting them. Recent analyses of donor expenditure suggest that these financial targets are far from being met.[133,134]

In this environment, the central goal of the Roll Back Malaria movement[91–94] to decrease by 50% the global malaria burden (risk, infection, morbidity, or mortality?) by 2010 by meeting targets on ITN distribution, IPT in pregnant women, prompt and effective treatment and epidemic preparedness, looks increasingly difficult. We emphasise here that its implementation and effect monitoring are made more problematic by a lack of accurate information on the global distribution of populations and risk at various stages of malaria endemicity and the resulting distribution of malaria mortality and morbidity. Addressing this issue is a priority. We have also presented here, through analyses of the NfP distribution between WHO regions (table 4 and figure 6a), a preliminary attempt to define the problem facing Roll Back Malaria in the future. Such analyses have illustrated how human demographics continually shift public-health goalposts.

Extending these analyses of the regional distribution of NfP to 2010 in a hypothetical world where population has grown according to current projections (and all else is equal including risk and control) we have also made various predictions (table 4 and figure 6b). The higher population growth rates in the tropics will increase the percentage of the global population exposed to infection risk to above 50% (table 1), but, surprisingly, the proportion of the NfP outside AFRO will remain largely unchanged at approximately half (46%; figure 6b).

Conclusions

No recent global maps of malaria endemicity have been developed since those of Lysenko in 1968,[9] despite significant advances in the collection of empirical data, global environmental information from satellites, and the statistical techniques that can be used to integrate them.[28,29] In addition, given the poor health information systems in the AFRO area it is paradoxical that some of the best information on malaria endemicity and burden exists for this region.[27–29] We suggest therefore that updating global maps of malaria endemicity is a priority and that it would provide regionally consistent measures of population at risk that could contribute to continuing efforts to refining global burden of disease estimates for malaria. Preliminary analyses of existing endemicity maps indicate the probable extent of malaria infection risk outside the AFRO area, and particularly in the SEARO region, conclusions that remain robust even under very optimistic scenarios of endemicity reduction. These populations are of particular political importance given the historical

success of aggressive vector control in areas of low-to-medium malaria endemicity and the dangers of inaction in facilitating the emergence of drug-resistant malaria parasites. We stress, however, that the global burden of malaria is still dominated by the AFRO countries which are least able to raise financial resources to tackle their high rates of malaria death and disability.[31] In summary, while international priorities seem broadly justified in their focus on the AFRO area, there is an urgent need to define the global extent of malaria risk and disease to enable effective and equitable prioritisation of investment and strategic direction by Roll Back Malaria and others.

Acknowledgments

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Search strategy and selection criteria

Data for this review were identified through PubMed Medline, the Bodleian library at Oxford, manual searches of the WHO's *Weekly Epidemiological Record* (http://www.who.int/wer/en/), suggestions of reviewers (formal and informal), and the bibliographies of the resulting articles. We used the following Boolean search statement: "malaria" and ("distribution" and "maps"), "malaria" and ("burden" or "risk"), "malaria" and ("control" and "campaign"). Articles in all languages were selected and Lysenko (1968) translated from Russian.
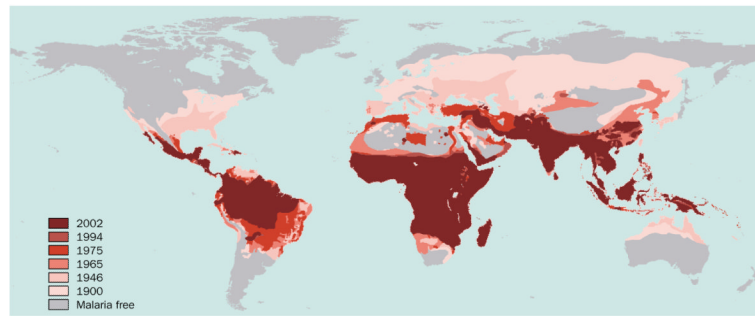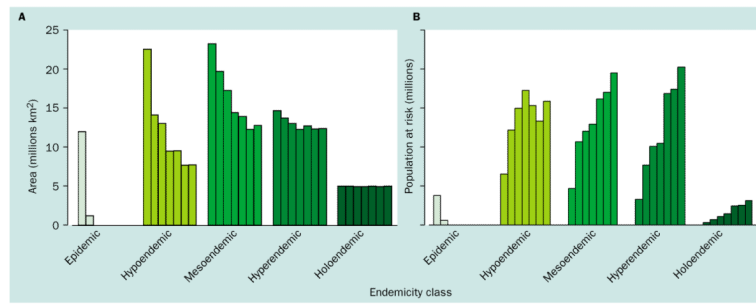
Figure 1.
The global distribution of malaria since preintervention (~1900–2002). All-cause malaria distribution maps for the preintervention distribution (circa 1900)[9] and for the years 1946, 1965, 1975, 1992, 1994, and 2002[12–17] were georeferenced using ERDAS Imagine 8.5 (Leica Geosystems GIS & Mapping, Atlanta, GA, USA). Maps were then digitised on screen with MapInfo Professional 7.0 (MapInfo Corp, NY, USA). Areas of high and low risk were merged throughout to establish all-cause malaria transmission limits. The only modification of original maps was infilling areas labelled as unknown in China in the 1975 map[14] with the distribution recorded in 1965.[13] Each map was then overlaid to create a single global distribution map of malaria risk which illustrates range changes through time. Note that the 1992 distribution is excluded from the figure for clarity because it was so similar to that of 1994.
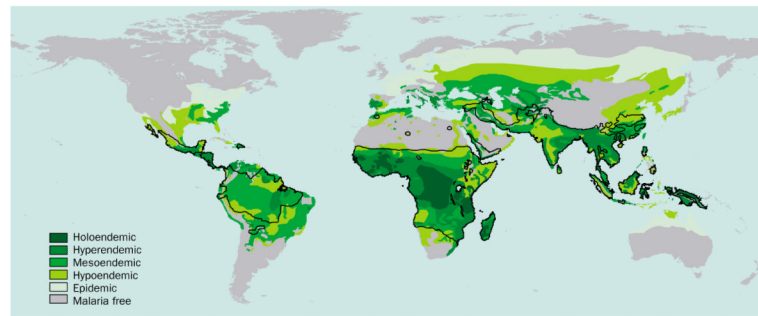
Figure 2.
The Lysenko map of global malaria endemicity. This map was digitised from the original source[9] using the method outlined in figure 1. Endemicity as used by Lysenko[9] is defined by the parasite rate (PR) in the 2–10-year age cohort (hypoendemic <0·1; mesoendemic 0·11–0·5; hyperendemic 0·51–0·75) except the holoendemic class (0·75) where the PR refers to the 1-year age group.[32] The black line represents the 2002 limit of malaria risk[17]. Note that the "epidemic" class is restricted to the temperate regions in these maps and that this term is used differently today.

Figure 3.
A histogram of (A) the global area (km^2) and (B) population at risk of all-cause malaria risk subdivided by endemicity class (~1900–2002). Derivations of area and population at risk estimates are described in tables 1–3. The bars in each endemicity class show data for the years (left to right) 1900, 1946, 1965, 1975, 1992, 1994, and 2002.
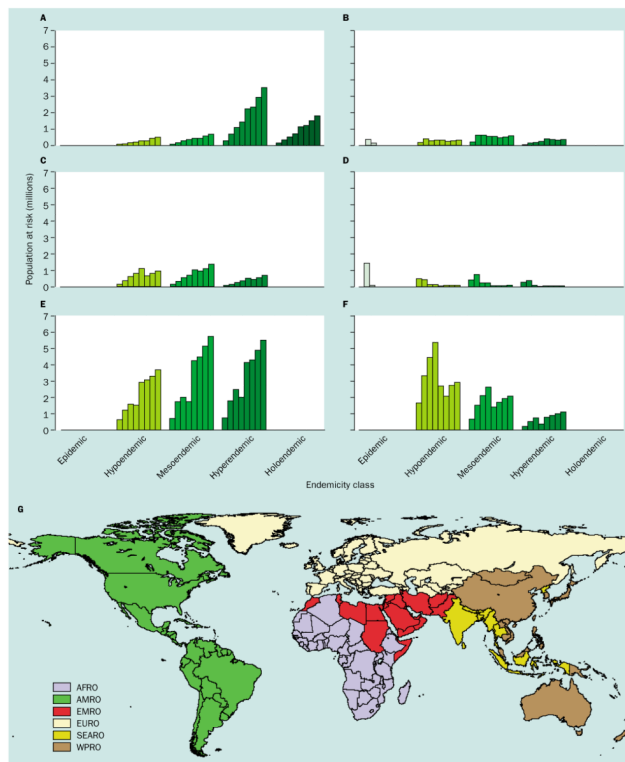
Figure 4.
Histograms of population at all-cause malaria risk (~1900–2010) subdivided by malaria endemicity and WHO regional grouping. (A) AFRO, (B) AMRO, (C) EMRO, (D) EURO, (E) SEARO, (F) WPRO, and (G) a map of WHO regional groupings. Derivations of area and population at risk estimates are described in tables 1–3. The WHO regional grouping map was generated from global administrative boundaries (Environmental Systems Research Institute Inc, Redlands, CA, USA) and county tables in annexes of the 2002 World Health Report[43]. The bars in each endemicity class show data for the years (left to right) 1900, 1946, 1965, 1975, 1992, 1994, and 2002.
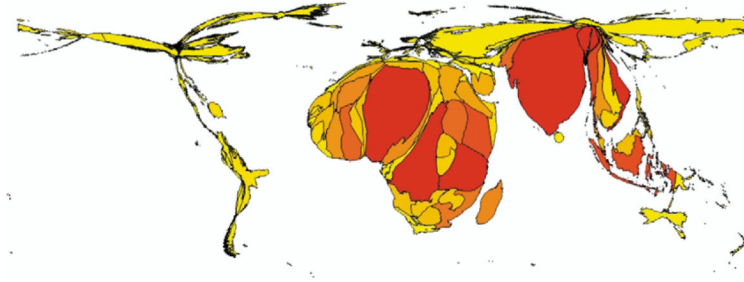
Figure 5.
The national falciparum prevalence (NfP) cartogram for 2002. The NfP was calculated using the method outlined in table 4. These continuous area cartograms[103] were generated using MAPresso (http://www.mapresso.com), a public domain Java applet. Ten iterations were used.
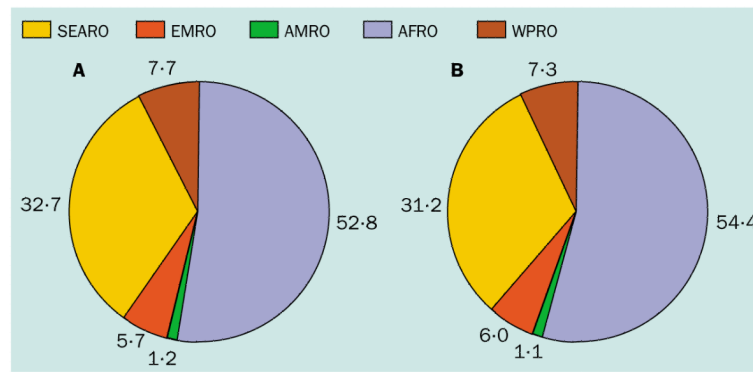
Figure 6.
Pie charts of the national falciparum prevalence (NfP) by WHO region for 2002 (A) and projected to 2010 (B). Data derived as for figure 5 and estimated using population projected for 2010 as described in table 1.

Table 1

Global population at risk from malaria from preintervention to 2010 (~1900–2010)

Time	Global population	Land area malarious		Countries at risk	Population exposed	
Years	n	km²	%	n	n	%
1900	1 158 409 472	77 594 480	53·16	140	892 373 056	77·03
1946	2 391 400 960	58 565 752	40·12	130	1 635 815 808	68·40
1965	3 363 417 344	53 492 988	36·65	103	1 924 360 320	57·21
1975	4 085 759 488	48 075 780	32·93	91	2 121 086 592	51·91
1992	5 419 255 808	43 650 812	29·90	88	2 565 702 144	47·34
1994	5 582 432 256	39 537 020	27·08	87	2 570 555 136	46·05
2002	6 204 095 488	39 758 172	27·24	88	2 996 419 584	48·30
2010	6 807 085 056	39 758 172	27·24	88	3 410 862 080	50·11

The area totals were generated using the maps of all-cause malaria risk distribution through time (figure 1). The percentage of Earth malarious was calculated from a total global land surface area of 145 975 899 km². To estimate countries at risk territorial designations for 2002 were used throughout (Environmental Systems Research Institute, Inc, Redlands, California, USA). Country-specific "medium variant" population growth rates from the World Population Prospects database (http://esa.un.org/unpp) between 1950 and 2010 were applied to the Gridded Population of the World (GPW) v2.0[25] to generate population distribution maps for 1900, 1946, 1965, 1975, 1992, 1994, and 2002 to match with the malaria risk distribution maps (figure 1) and were also projected to 2010 to enable evaluation of potential future changes in global malaria risk. Global summary counts of these population distribution maps give accuracy to within 5% of the UNDP global population estimate (http://esa.un.org/unpp) for all calculated years. All area and population summaries from these polygons were processed in Idrisi Kilimanjaro (Clark Labs, Clark University, Worcester, MA, USA).

Table 2

The global area of malaria subdivided by endemicity class (1900–2002)

Date	Epidemic		Hypoendemic		Mesoendemic		Hyperendemic		Holoendemic	
Year	km²	%	km²	%	km²	%	km²	%	km²	%
1900	11·99	15·45	22·57	29·08	23·30	30·03	14·69	18·94	5·05	6·50
1946	1·26	2·15	14·14	24·14	19·71	33·66	13·75	23·47	5·05	8·62
1965	0·02	0·04	13·04	24·38	17·25	32·25	13·07	24·42	4·98	9·31
1975	0	0·00	9·47	19·71	14·48	30·12	12·31	25·61	5·00	10·41
1992	0	0·00	9·55	21·88	13·94	31·94	12·75	29·21	5·00	11·47
1994	0	0·00	7·73	19·56	12·32	31·15	12·35	31·22	4·96	12·55
2002	0	0·00	7·75	19·50	12·81	32·21	12·39	31·17	5·01	12·60

These figures were derived as outlined in table 1 by subdividing the limits of all-cause malaria risk (figure 1) by endemicity class (figure 2). Area figures are in millions and the percentage figures express the proportion of the total global area at risk occupied by that endemicity class.

Table 3

Population by malaria endemicity class (1900–2010)

Date	Epidemic		Hypoendemic		Mesoendemic		Hyperendemic		Holoendemic	
Year	n	%	n	%	n	%	n	%	n	%
1900	183·81	20·60	313·22	35·10	223·14	25·01	158·51	17·76	13·76	1·54
1946	22·38	1·37	583·46	35·67	512·56	31·33	366·47	22·40	34·30	2·10
1965	0·07	0·00	720·21	37·43	577·78	30·02	484·30	25·17	52·62	2·73
1975	0·09	0·00	830·13	39·14	619·08	29·19	503·21	23·72	69·64	3·28
1992	0	0·00	736·74	28·72	775·70	30·23	811·34	31·62	115·77	4·51
1994	0	0·00	638·86	24·85	815·08	31·71	836·36	32·54	122·55	4·77
2002	0	0·00	761·72	25·42	937·52	31·29	974·30	32·52	150·28	5·02
2010	0	0·00	849·95	24·92	1 051·86	30·84	1 126·52	33·03	181·95	5·33

These figures were derived as outlined in table 1 by subdividing the limits of all-cause malaria risk (figure 1) by endemicity class (figure 2). The population figures are in millions and the percentage figures express the proportion of the total global population at risk in each endemicity class at each time interval. The percentages do not sum to exactly 100% because of problems in extrapolating endemicity classes from preintervention[9] to later distributions, as some areas could not be allocated an endemicity class. Since the total population by endemicity class is calculated relative to the total population exposed to malaria in each period, percentages are 100% only for 1900. The percentages for unallocated areas are very small, however, so the global/regional conclusions remain robust.

Table 4

Estimates of malaria morbidity and mortality by WHO administrative region

Year		AFRO	AMRO	EMRO	EURO	SEARO	WPRO	Total
		WHO regions						
WHO (2002) [43]								
2001	Morbidity	342 814 347	3 798 292	14 894 969	0	32 930 363	2 238 314	396 676 285
	Percentage	86·4	1·0	3·8	0·0	8·3	0·6	100·0
	Mortality	962 736	1 445	54 570	160	94 380	10 474	1 123 764
	Percentage	85·7	0·1	4·9	0·0	8·4	0·9	100·0
Scenario A								
2002	NP	334 028 822	38 504 919	73 799 354	4 736 720	482 235 352	134 712 740	1 068 042 048
	Percentage	31·3	3·6	6·9	0·4	45·2	12·6	100·0
	NfP	334 028 822	7 475 574	35 976 263	0	206 563 944	48 408 818	632 453 421
	Percentage	52·8	1·2	5·7	0·0	32·7	7·7	100·0
2010	NP	403 084 278	43 575 514	90 974 069	5 186 586	541 603 144	146 320 691	1 230 774 481
	Percentage	32·8	3·5	7·4	0·4	44·0	11·9	100·0
	NfP	403 084 278	8 310 592	44 297 793	0	231 365 224	54 311 995	741 369 882
	Percentage	54·4	1·1	6·0	0·0	31·2	7·3	100·0
Scenario B								
2002	NP	334 028 822	12 810 398	22 857 751	1 633 218	175 340 349	40 328 276	586 998 814
	Percentage	56·9	2·2	3·9	0·3	29·9	6·9	100·0
	NfP	334 028 822	1 706 170	10 709 060	0	75 602 014	17 938 499	439 984 565
	Percentage	75·9	0·4	2·4	0·0	17·2	4·1	100·0
2010	NP	403 084 278	14 613 880	28 530 282	1 778 624	197 290 551	44 128 430	689 426 046
	Percentage	58·5	2·1	4·1	0·3	28·6	6·4	100·0
	NfP	403 084 278	1 901 788	13 405 644	0	84 798 879	20 150 770	523 341 360
	Percentage	77·0	0·4	2·6	0·0	16·2	3·9	100·0

Using the 2002 malaria distribution[17] (figure 1) stratified by endemicity classes defined by Lysenko[9] (figure 2) and population distribution projected to 2002 (table 1), a national prevalence (NP) was estimated by: (population exposed to hypoendemic × 0·05) + (population exposed to mesoendemic × 0·305) + (population exposed to hyperendemic × 0·63) + (population exposed to holoendemic × 0·875). The product of the NP and the 1993 *P falciparum* index[15,102] then gives a national falciparum prevalence (NfP). NP and NfP are estimated for 2002 and 2010 assuming that endemicity[9] and the *P falciparum* index[15,102] are unchanged (scenario A) or that development and control has been so successful outside of AFRO that all endemicity values were reduced by one class (scenario B). The WHO estimates for global morbidity and mortality from malaria in 2001 are also shown for comparison.[43]