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The prevalence of *Plasmodium falciparum* in sub Saharan Africa since 1900

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Abstract

Malaria transmission is influenced by climate, land use and deliberate intervention. Recent declines have been observed in malaria transmission. Here, we show that the continent has witnessed a long-term recession in the prevalence of *Plasmodium falciparum* since 1900-29 (40%) to 2010-15 (24%), interrupted at different times by periods of rapidly increasing and decreasing transmission. The cycles and trend over the last 115 years are inconsistent with simplistic explanations in terms of climate or intervention alone. Previous global initiatives had minor impacts on malaria transmission, and a historically unprecedented decline has been observed since 2000. However, there has been little change to the continued high transmission belt covering large parts of West and Central Africa. Previous efforts to model the changing patterns of *P. falciparum* transmission intensity in Africa have been limited to the last 15 years1,2, or have used maps of historical expert opinion3. We provide quantitative data comprising 50,424 surveys at 36,966 geocoded locations to cover 115 years of malaria history in sub-Saharan Africa.

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Authors contributions

RWS assembled the data, designed the experiment and wrote the paper, BS undertook the statistical analysis, PB provided support for data interpretation and AMN provided support for data assembly and analysis. DK, JM, PA, CWM all provided assistance in locating survey reports, abstraction of data and geo-coding. All authors have access to the data and have reviewed the paper and SI.

The authors declare they have no conflict of interest. The authors declare no competing financial interests.

Requests for reprints can be obtained from Professor Bob Snow at rsnow@kemri-wellcome.org

Ethics statement

Our research centre considered the work as secondary use of aggregate survey data to be non-human research for which individual informed consent was not applicable

Code availability

The WINBUGs code for both the negative binomial and Poisson models have been made freely accessible. No restrictions apply. The code can be found at the following link http://dx.doi.org/10.7910/DVN/Z29FR0

Data availability

The full database of survey data that support the findings of this study are available open access from the KEMRI Wellcome Trust Research Programme's Population Health page in the Harvard Dataverse, http://dx.doi.org/10.7910/DVN/Z29FR0 (Snow, 2017), under a CC-BY 4.0 license.

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Short term seasonal cycles are a fundamental aspect of the epidemiology of malaria. Longer-term climate anomalies, changing environmental and intervention landscapes also alter the likelihoods of mosquito-human contact or the duration of host infection. The supra-seasonal, long-term cycles of transmission are poorly defined for *P. falciparum* malaria in Africa.

To provide an empirical basis to define the long-term nature of malaria transmission cycles, we used data on the *P. falciparum* parasite rate, the proportion of persons positive for malaria infection among those examined. These data were assembled as part of an intensive search lasting 21 years (SI 1). The data represent the largest ever assembled repository of any parasitic disease in Africa and provide information on over 50,000 community-based surveys across SSA since 19004 (SI 1; Extended Data 1; Extended Data 2), the data are released with this publication. We have used the space-time cube of data to leverage power from neighbouring areas and preceding data points in time5, within a conditional autoregressive spatial and temporal model to compute a smoothed median estimate for approximately five-year intervals since 1900 across 520 sub-national administrative polygons (Extended Data 3) within the changing limits of *P. falciparum* transmission (Figure 1).

The median posterior predictions of *P. falciparum* prevalence provide a summary of several important cycles in the history of malaria transmission across the continent (Figure 2). The impact of interventions and/or climate can only be assessed by temporal plausibility rather than quantitative analysis. Between 1900 and 1944, efforts to control malaria focused on areas of European economic influence, largely targeting vector larvae or mass quinine administration campaigns targeting the parasite6, and we did not observe declines in transmission.

We observed two precipitous declines in infection prevalence in 1945-49 and in 2005-2009. Dichlorodiphenyltrichloroethane (DDT) and chloroquine were introduced in 1945-1949, and the widespread introduction of insecticide treated bed nets (ITN) and artemisinin-based combination therapy (ACT) in 2005-2009 (Figure 2). Indoor residual house-spraying (IRS) with DDT was introduced through comparatively small projects during the 1950s and expanded in the 1960s only in southern Africa, Ethiopia, Sudan, Somalia and Madagascar. Expansion to national scales of ITN took over a decade following successful trial projects to reach moderate levels of coverage in Africa before 20107.

Both precipitous declines in malaria prevalence followed rises in prevalence. The rise in median malaria prevalence during the period 1985-2004 led to a return to the prevalence witnessed fifty years earlier, before the introduction of DDT (Figure 2). This period also included: a) a rapid expansion of chloroquine resistance across Africa9; b) climate anomalies on the continent with changes in sea surface temperatures in the pacific10 (Figure 2); and c) failure of many national health agencies to prioritize the growing malaria epidemic because of lack of international donor assistance12.

The period 1960 to 1984 was characterised by a slow decline in malaria prevalence across Africa (Figure 2). Remarkably, this coincided with a cessation of malaria elimination ambitions across much of SSA13, emerging resistance to organochloride insecticides14 and

a period where malaria was integrated into broader health agendas, focussed on the presumptive treatment of fevers with choroquine (cheap, widely available and efficacious). This period also included drought across much of the Sahel10 (Figure 2) rendering some areas unsuitable for malaria transmission15. Hence several interventions may have influenced the observed trends, but no single factor appears sufficient.

Despite impressive gains in the coverage of effective interventions since 2005, the rate of malaria prevalence reduction has slowed during the interval 2010-2015 (Figure 2). Continued challenges to malaria control include difficulties in ensuring access to ACTs and the threat of drug resistance, rapidly emerging insecticide resistance, and inadequate funding planning to replace long-lasting insecticide treated nets16.

There has been an overall recession in malaria transmission intensity over the last 115 years. Independent abiotic factors related to economic growth may have contributed to this overall recession, but the constant growth in GDP17, urbanization18 or female education17, cannot explain the emerging malaria epidemic 1985-2004. Conversely, minimum temperatures across SSA have risen by over 1°C since the 1970s10 (Figure 2), and the linear phenomena of global warming cannot explain the precipitous declines in malaria prevalence witnessed after 2004. The interplay between malaria, climate, effective or failing intervention, human settlement and development is inevitably complex. Our analysis highlights that a focus on one factor alone is too simplistic and fails to adequately explain the cycles of parasite prevalence.

The reduction in malaria transmission intensity has not occurred equally between countries or within countries (Figure 1), with more substantive declines and “shrinking of the map” at the margins of the historical range of *P. falciparum* transmission compared to the heartland of Africa’s most efficient vector species *Anopheles gambiae* s.s and *An. colluzi*, that forms a densely populated belt from West Africa, through central Africa down toward Mozambique. This remains the most significant part of the malaria endemic world today, was ignored after 196019,20 and risks being ignored today21. Our previous, and current, armoury of interventions did not, and will not, eliminate malaria in this part of the world.

Caution is required in predicting a complex future, but if the future is consistent with the past we would predict further reductions in the range of and intensity of malaria transmission in Africa but punctuated with resurgences. We show the implausibility of simplistic explanations for temporal trends over the last 115 years, and therefore caution against simplistic explanations for the trend of the last 15 years (e.g. ascribing the trend to human intervention alone). The unique endemicity that prevails in Africa cannot be ignored in any global effort to eliminate *P. falciparum*, nor should we wait for a future storm to re-galvanize interest in a parasite that remains entrenched in across large parts of the continent.

Methods

Data Assembly

Over 21 years we sourced unpublished and published materials related to community-based malaria infection prevalence at European, United Nations and African national libraries,

archives and ministry of health repositories. We undertook standard electronic data searches of peer-reviewed publications, and contacted malaria scientists, regional health research institutes, government and non-government agencies involved in the delivery and monitoring of malaria interventions (SI 1.3 and SI 1.4). The minimum data requirements for the survey included the date and location, age range, numbers examined, infection prevalence by species and parasite detection method. A total of 50,424 parasite prevalence surveys since 1900 were included4 (SI 1.5; Extended Data 1; Extended Data 2).

Spatial limits and resolution of malaria predictions

We excluded previously endemic north African countries (Morocco, Algeria, Tunisia, Libya and Egypt), off-shore islands and countries where malaria has not been described (Western Sahara and Lesotho). We used current national and sub-national first-level administrative boundary units used by the UNs GAUL project22, with adaptations for the margins of natural *P. falciparum* risk, disputed boundaries, dissolving small urban municipalities and to ensure contiguous shapes between sub-national units. Rwanda, Burundi, Djibouti, Swaziland and The Gambia were treated as single polygons (SI 2.1; SI 2.2; Source Data Figure 1). The natural spatial limits of *P. falciparum* risk were derived from expert opinion national maps and biological constraints (SI 2.2; Source Data Figure 1). The selection of 520 spatial polygons at the natural range of *P. falciparum* transmission is shown in Extended Data 3. Changing limits were mapped using data from national reports of malaria incidence since the 1960s (SI 2.3; Source Data Figure 1).

Statistical methods

We employed a Bayesian hierarchical binomial model that simultaneously estimates stable spatial and temporal structured patterns and departures from these stable components5. The input data were as follows: observed number of *P. falciparum* positive children aged 2-10 years, $PfPR_{it}$, and total number of tested children aged $_{2\text{-}10}$,n_{it}, for subnational region $i = 1, \ldots, 520$, and period $t = 1, \ldots, 16$ (1900-1929, 1930-1944, and five year periods from 1945-1949 to 2010-2015). The model was fitted using Markov Chain Monte Carlo simulation using non-informative priors. Posterior distributions of parameters were obtained using WinBUGS software (SI 3; Source Data Figure 1). Gelman-Rubin statistics was used to assess model convergence (Extended Data 4). Observed versus fitted $PfPR_{2\text{-}10}$ from the full model was used to validate output (Extended Data 5).

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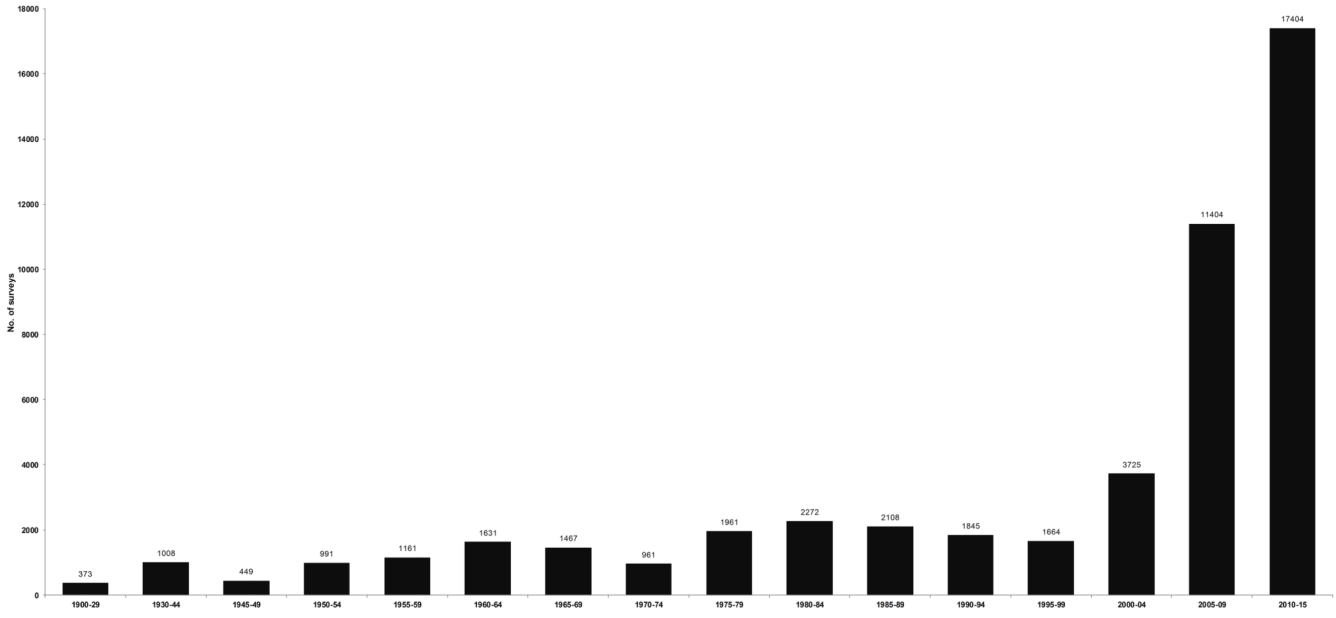
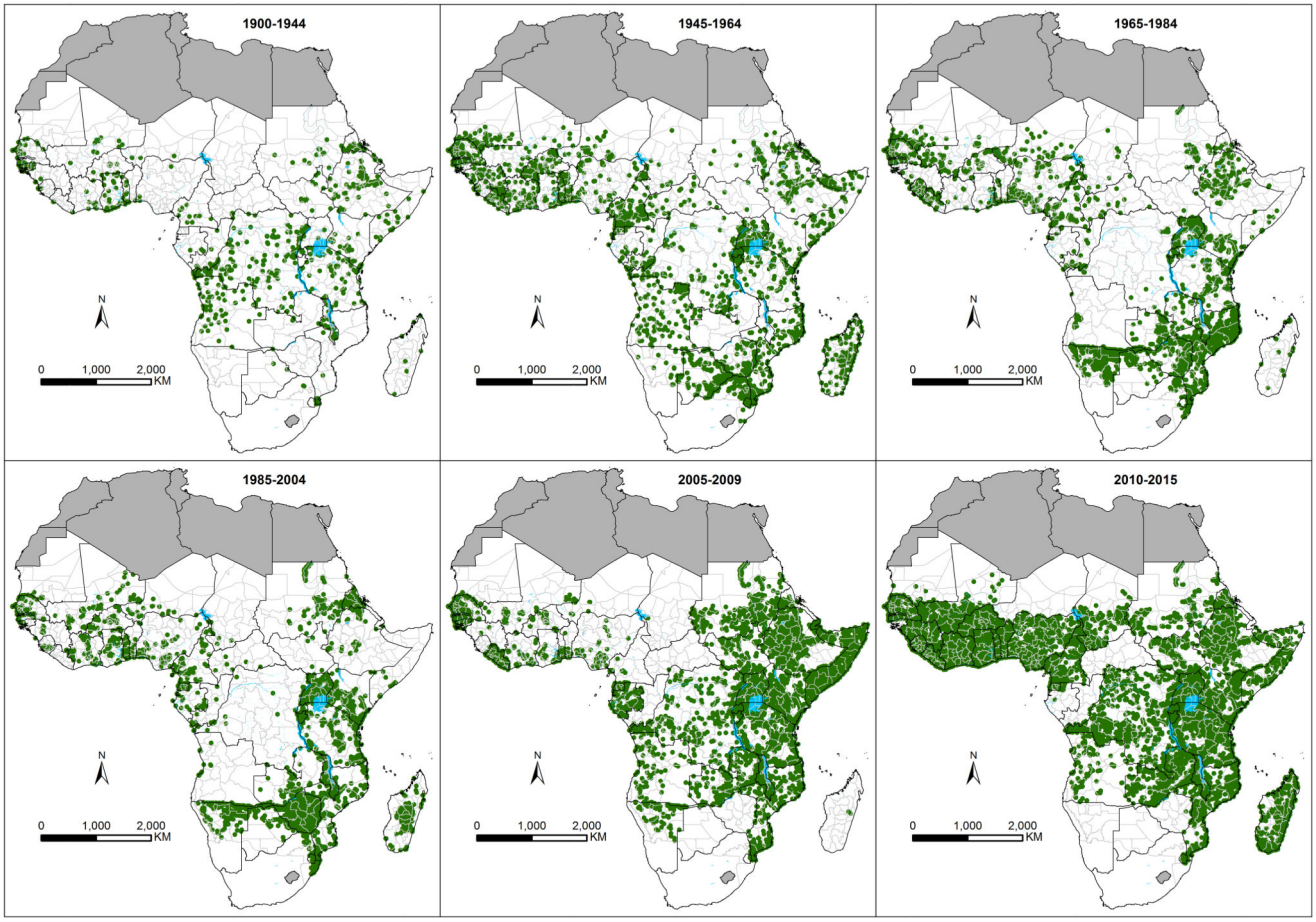
Extended Data



Extended Data 1.

Survey data in time: The temporal distribution of survey data per intervals selected for analysis (number of surveys shown on top of bars)



Extended Data 2.

Survey data in space: Location of 53,529 *P. falciparum* parasite surveys undertaken at 39,033 locations by time intervals from 1900-44 to 2010-15

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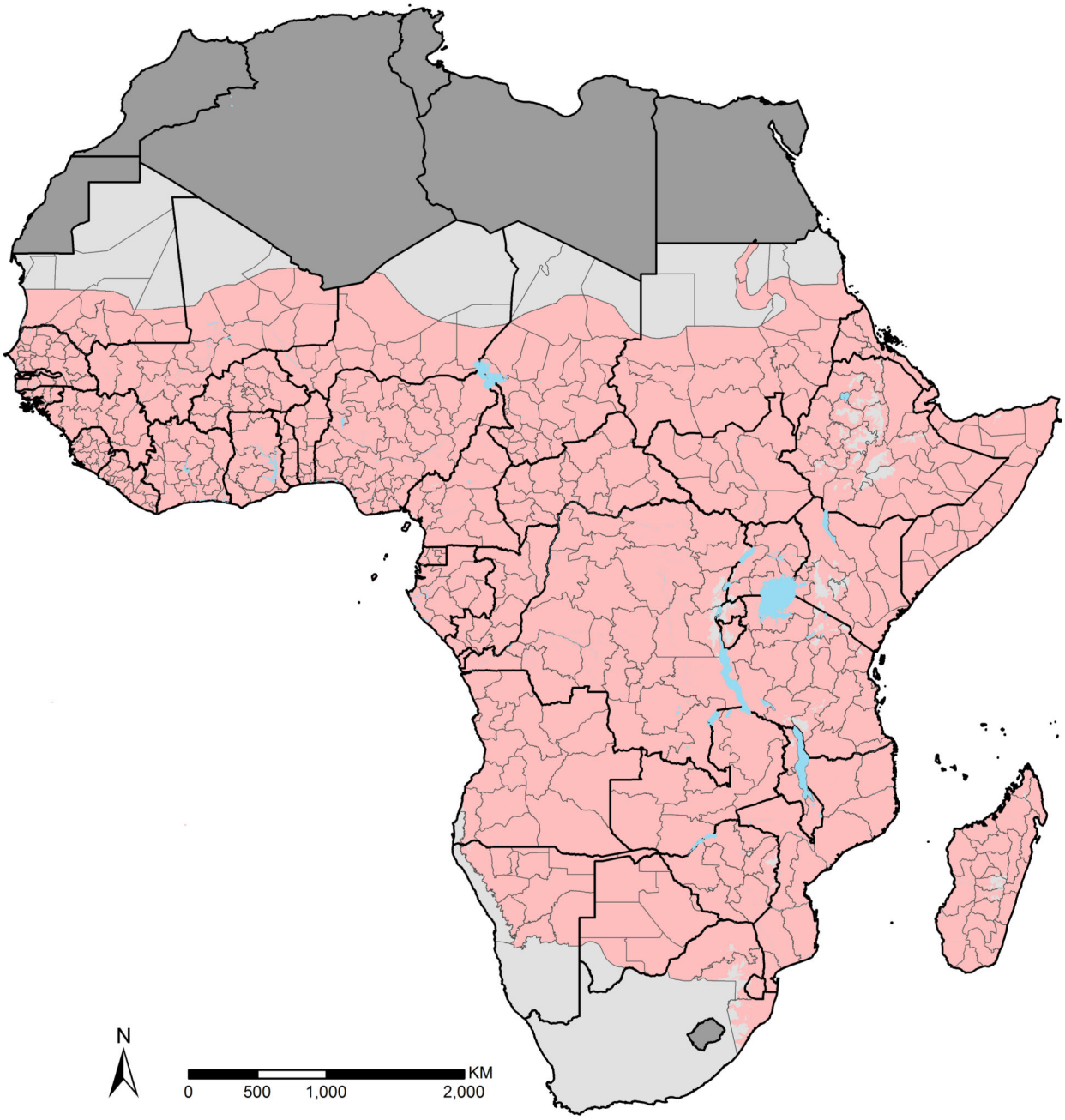

Extended Data 3.

The spatial range of *P. falciparum* Africa in between 1900-1950: light grey represents absence of natural *P. falciparum* transmission; pink is the natural extent of transmission; dark grey represents countries not included in the analysis

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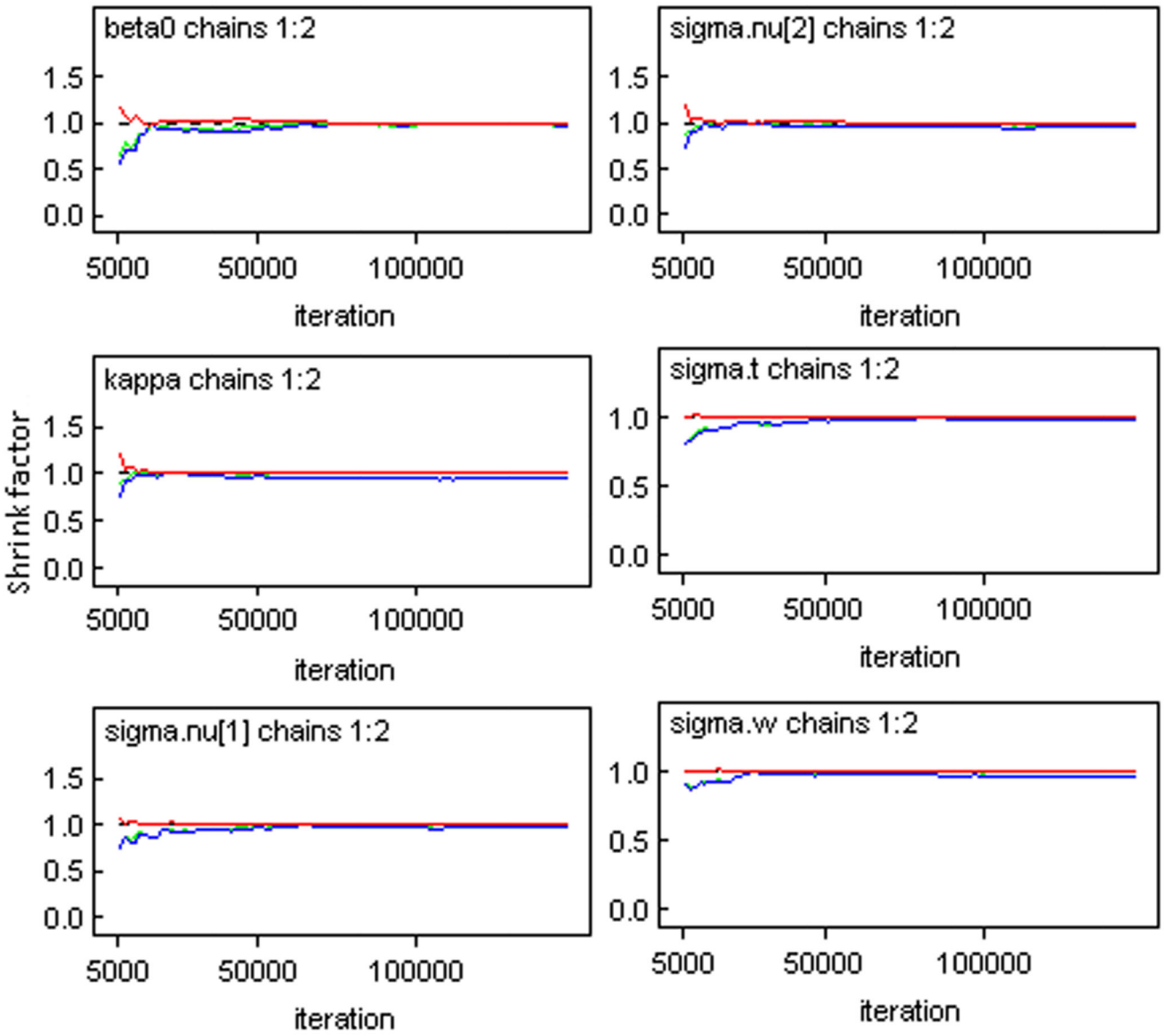

Extended Data 4.

Model Convergence: Gelman-Rubin-Brooks plots demonstrating convergence during MCMC simulation for key model parameters. Black line represents ratio of within chain variability to between chain variability, the dark grey line represents the within-chain variability (pooled) and the light grey line represents the between-chain variability (average)

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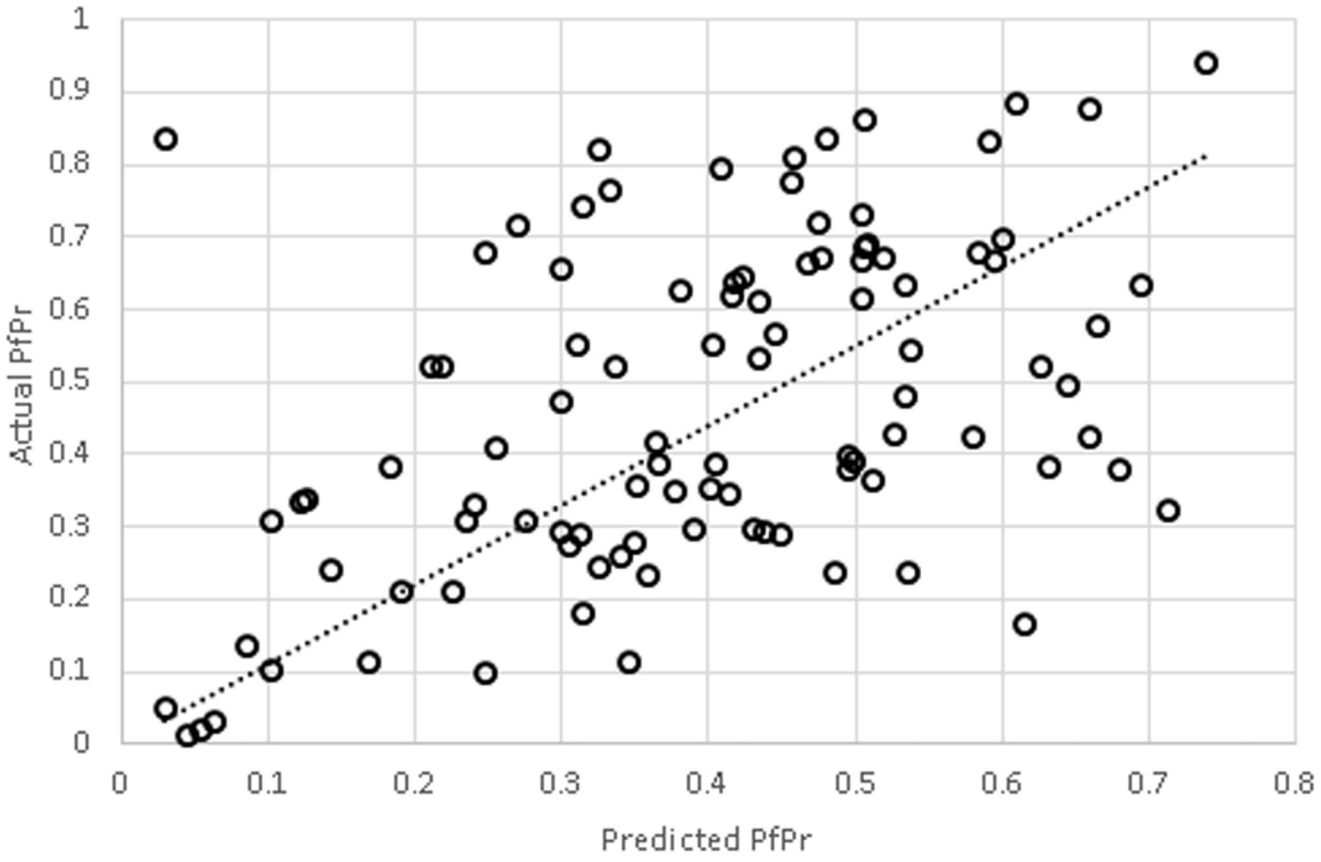

Extended Data 5.

Model Validation: Predicted *Pf*PR$_{2-10}$ versus observed *Pf*PR$_{2-10}$ for 100 randomly selected data points. 99% of data points are within 95% credible interval (CI); Spearman Rank Correlation 0.46, P <0.001 (two-sided test)

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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17. World Bank. [accessed 8th April 2017] World Development Indicators. http://data.worldbank.org/ mean GDP for SSA during the period 1960-65 was $144 per capita, rose to $631 per capita by 1980-85, plateaued through to 2000-04 and then rose linearly to over $1600 per capita in the period 2010-15; from 1970-74 the percentage of females completing primary education was 40% and rose linearly to 65% by 2010-15
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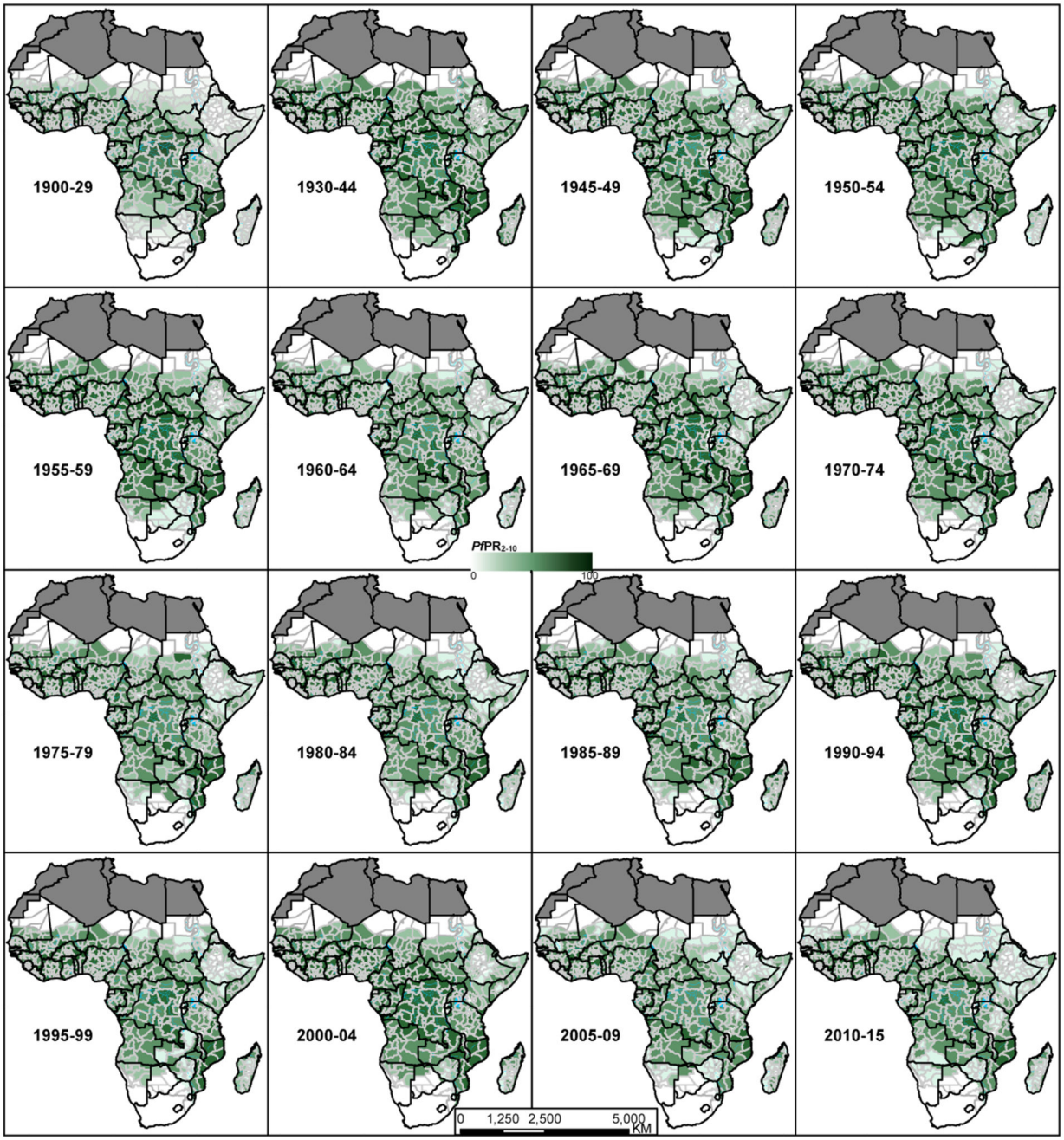

Figure 1. Changing spatial patterns of *P. falciparum* endemicity in sub-Saharan Africa since 1900.

Predicted posterior predictions of age standardised *P. falciparum* prevalence (*Pf*PR_{2-10}) per administrative unit on mainland SSA and Madagascar and masked (white) according to biological or control related absence of transmission (Methods and SI 2.2) and the reported changing spatial extents (Methods, SI 2.3, Source Data Figure 1).

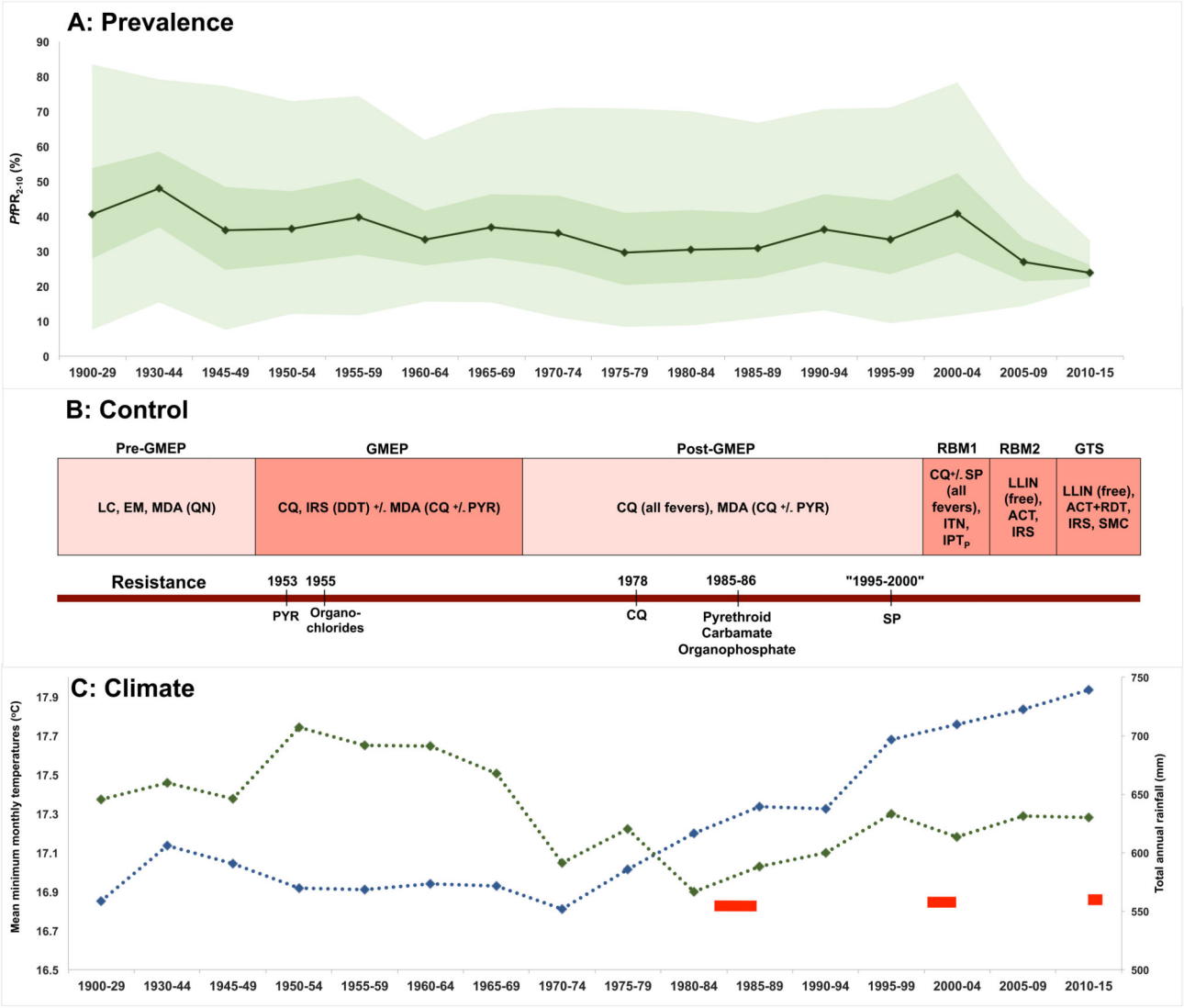

Figure 2. Summary and plausibility framework of *P. falciparum* transmission cycles in sub-Saharan Africa since 1900

Panel A: The median, (central dark line) and 25-75% (medium green boundaries) and 2.5-97.5% (light green boundaries) interquartile credibility range of the posterior predictions of *Pf*PR_{2-10} (Source Data Figure 2). ***Panel B***: Six periods of major intervention: 1) 1900-1949: restricted efforts through larval control (LC), environmental management (EM) and mass drug administration (MDA) using Quinine (QN); 2) 1950-1969; launch of Global Malaria Eradication Programme (GMEP) in 1955, introduction of DDT and drugs (e.g. chloroquine (CQ) and pyrimethamine (PYR)) and pilot elimination projects involving indoor residual house-spraying (IRS) accompanied later by MDA using CQ and PYR; 3) 1970-1999: end of most vector control efforts, presumptive treatment of fevers with CQ, use of CQ as MDA for school children; 4) 2000-2004: the Roll Back Malaria (RBM) initiative with Insecticide Treated Nets (ITN) for vulnerable children and pregnant women, expansion of Intermittent Presumptive Treatment of malaria in pregnancy (IPTp) and failing first line

treatment with Sulphadoxine-Pyrimethamine (SP) and/or CQ; 5) 2005-2010; large scale Long-Lasting Insecticide Treated Nets (LLIN) distributions, IRS expanded and switch from CQ or SP to Artemisinin-based Combination Therapy (ACT); 6) 2010-2015: increased IRS in many countries, scale-up of Rapid Diagnostic Tests (RDTs); the Global Technical Strategy (GTS) was launched in 2012, re-invigorating a global ambition for eradication and seasonal malaria chemoprevention (SMC) in West African countries. Vector resistance to Organochorines detected in 1955 in Nigeria, organophosphate, carbamate and pyrethroid resistance detected in the late 1980s and have expanded rapidly since the late 1990s8; CQ resistance detected in 1978, SP resistance in 1953 with significant clinical failure rates in 20009. **Panel C**: Climate - mean annual rainfall across the Sahara (Green line)10, El Niño events leading to serious climate anomalies including flooding in 1997-1998 in East Africa and drought in the horn of Africa in 2014-2015 (Red bars)11, monthly minimum temperature (Blue line)10.

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