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Supplementary webappendix

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Web extra material for 'Ranking elimination feasibility among malaria endemic countries'

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1: Deriving malaria elimination feasibility indicators

1.1 Deriving technical feasibility indicators

1.1.1 Estimating the relative intensity of endemic *P. falciparum* **transmission**

1.1.1.1 Datasets

The publication of (i) the revised global spatial limits of *P. falciparum* transmission¹ and (ii) a contemporary, model-based geostatistical description of P. falciparum malaria endemicity within these limits² by the Malaria Atlas Project (MAP), has resulted in a substantially improved evidence-base from which to derive estimates of baseline endemic transmission (R_0) . The models used to translate this malaria endemicity map into a map of R_0 are described in the main manuscript. While this MAP-derived R_0 map is useful for quantifying the relative variations in transmission between countries, it does not take into account population distribution, and it is the transmission intensity where people live that is epidemiologically important. Therefore, the Global Rural Urban Mapping Project (GRUMP) *alpha* gridded population surface³ was used to obtain a population weighted average for each country to provide a mean measure of the relative baseline R_0 between countries. This was preferred to a simple areal mean, since transmission levels in populated areas are more informative when assessing feasibility of elimination, whilst the incorporation of large unpopulated areas produces a skewed picture. These data are shown in Figure S1.1 and Table S1.1.

Figure S1.1. Population-weighted national estimates of MAP 2007 world malaria map derived R_0 for each *P*. *falciparum* endemic country in 2007.

Figure S1.1 (and Figure 2 in the main manuscript) identifies the level of additional control required on top of the contemporary patchwork of intervention coverage^{4, 5} to achieve elimination. The measurement of technical feasibility, however, requires estimates of baseline transmission intensity (see main paper). For instance, contemporary R_C values for Saudi Arabia and coastal Kenya are similarly low, but this is likely to be primarily due to the intensive control efforts presently underway in Kilifi⁶. Differences between the two areas, principally related to biological factors, such as the vectorial capacity, mean that baseline endemic transmission intensity (*R0*) for Kilifi is substantially larger than for Saudi Arabia. These differences are generally reflected in Figure S1.1, given that (i) the map is derived from both contemporary and older community prevalence surveys, (ii) recent intervention scale-ups will take time to show significant reductions in transmission, and (iii) intervention coverages for much of the world remain relatively $low⁴$. However, it could be argued that, for some areas, Figure S1.1 may not reflect baseline transmission intensity, and thus we test the use of an alternative transmission map here.

The only global map of pre-intervention malaria endemicity comes from a 1968 study by Lysenko⁷ (Figure S1.2). Endemicity as used by Lysenko was defined by the parasite rate (the proportion of a population sample with parasite in their blood) in the 2-10 year age cohort (hypoendemic <0.1; mesoendemic 0.11-0.5; hyperendemic 0.51-0.75), except for the holoendemic class (>0.75), where the parasite rate refers to the one-year age group⁸. This map was a major synthesis of historical records, documents and maps of a variety of malariometric indices (records of disease and vector presence and absence, spleen rates, parasite rates, sporozoite

rates and biting rates) used to record malaria endemicity until the late 1960s. These data were interpolated globally for malaria at the peak of its assumed historical distribution around 1900, using a combination of expert opinion, global elevation, temperature and rainfall isohyets^{7, 9}. Development, urbanization, aggressive vector control, chemotherapy and deforestation, amongst others, over the past century will have altered the malaria risk levels shown substantially, making the map a poor reflection of absolute present day transmission intensity. However, our focus here is on the examination of contemporary *relative* malaria elimination feasibility between nations and thus it is likely to present a feasible alternative for assessing relative differences between baseline transmission levels.

Figure S1.2. Pre-intervention *P. falciparum* endemicity (c. 1900) as defined by Lysenko⁷. Light gray: no risk; light blue: epidemic risk (note that this class refers to areas with very low prevailing risk and is restricted to the temperate regions - the term "epidemic risk" is used differently today); light green: hypoendemic risk (PR of less than 0.10); medium green: mesoendemic risk (PR ≥0.10-<0.50); dark green: hyperendemic risk (PR ≥0.50-<0.75); very dark green: holoendemic risk (PR \geq 0.75). PR here relates to the 2-10 year age cohort, except for the holoendemic class, where it relates to the one-year age group.

The Lysenko map was scanned from the original publication and geo-referenced using ERDAS Imagine 8.5 (Leica Geosystems GIS & Mapping, Atlanta, USA). The map was then digitised on-screen with MapInfo Professional 7.0 (MapInfo Corp., New York. USA) and converted to a 1 x 1 km gridded version. The values were then reclassified to represent the midpoint of each parasite rate class, thus hypoendemic $= 0.05$, mesoendemic $=$ 0.3, hyperendemic = 0.625 holoendemic = 0.875. Comoros, Solomon Islands and Vanuatu were not covered in the original Lysenko map, therefore transmission estimates were substituted in from the recently published 2007 world malaria map² for these nations. This adapted Lysenko map was then converted to a map of R_0 using the models outlined in the main manuscript, and population-weighted national estimates were produced as described above. These data are shown in Figure S1.3.

Figure S1.3. Population-weighted national estimates of Lysenko derived R_0 for each *P. falciparum* endemic country in 1900.

1.1.1.2 Testing the sensitivity of dataset choice

Figure S1.4 shows the relationship between baseline transmission rankings derived from the MAP 2007 map and the Lysenko map. The statistics and visual examination indicates that a significant relationship between the two exists, but some substantial differences are present, particularly at the lowest rankings. Therefore, the difference in overall results when the two alternative maps were used to derive baseline transmission rankings was examined.

Figure S1.4. Scatterplot of *P. falciparum* malaria endemic country rankings for MAP-derived versus Lysenko-derived R_0 estimates ($r^2 = 0.389$, $p \ll 0.01$).

The overall feasibility analyses were re-run using (i) the MAP 2007 derived R_0 estimates, and (ii) the Lysenko derived R_0 estimates, keeping all other factors the same. The results of these comparisons are shown in Figure S1.5, and demonstrate zero or little change in average ranking for the majority of countries, with an average absolute rank change of just 2.02. This results principally from substantial differences in endemicity estimates for east Asia, particularly Afghanistan and Pakistan. These results demonstrate

that, while neither map is a definitive source for derivation of baseline transmission estimates, and that the use of either could be argued for, the consequences of this choice result in minimal changes to overall conclusions.

Figure S1.5. Change in average rank for each *P. falciparum* malaria endemic country when switching from using MAP 2007 to Lysenko in order to derive R_0 estimates.

1.1.2 Estimating relative imported *P. falciparum* **malaria rates**

Malaria is constantly being exported and imported around the world and, in areas of high R_0 , malaria importation is generally a minor concern. As local transmission is reduced, however, the importance of imported malaria increases. Moreover, after R_0 has been pushed below a value of one and malaria has been eliminated from a region, importation becomes the primary concern. Importation risk can be defined as the probability of malaria reintroduction based on the flux of infected humans or infected *Anopheles* mosquitoes; the relevant quantities are the rate of infected and infectious hosts that are imported into a country each year.

In general, parasites can be imported in one of three ways: (i) the migration of an infected mosquito, (ii) infected humans visiting or migrating from an endemic area, (iii) residents visiting an endemic area and becoming infected, then returning. While mosquitoes can occasionally travel long distances though wind-blown or accidental aircraft or ship transport, typically they will only fly short distances¹⁰. Human carriage of parasites therefore represents the principal risk, and is to blame in many past instances where malaria has resurged¹¹⁻¹⁴. It can also be shown to be the cause of sustained transmission in low endemic areas^{15, 16}. Imported malaria cases carry parasites, including resistant strains, even if they are asymptomatic¹⁷. Quantifying human movements both temporally and spatially, and their resulting imported infection risks, represents an important task if elimination feasibility is to be assessed and if effective, evidence-based planning for elimination is to be undertaken¹⁸.

Rigorous examination of the role of human movement across different scales will significantly improve understanding of malaria transmission at low levels, which will be critical in increasing the effectiveness of elimination programs. At the global scale, implementation of such approaches is hampered by a severe lack of data. Ideally, data on international population flows at the range of spatial and temporal scales relevant to malaria transmission^{11, 16} are required to fully quantify importation risks. These include regular cross-border travel for work, social visits and seasonal migrations, but such data are non-existent for most of the world. Moreover, basic, inter-comparable data on population flows are lacking for a large number of countries (particularly malariaendemic countries), and are both patchy and extremely variable for the remainder of countries, even in highly developed settings.

The recent construction of a bilateral database of international migration¹⁹ provides valuable information on the relative strength of movements of people between nations. Wherever possible, these data were derived from the latest round of censuses, as these were considered most comparable at the global level. Where unavailable, population registers were drawn upon, and in the cases of missing data, a variety of techniques and tests were employed to create and validate a complete matrix of international bilateral migrant stocks¹⁹. Finally, all data prior to 2000 were scaled to the United Nations mid-year totals of migrant stocks for 2000 (United Nations 2004). For each country or territory, the completed dataset represented the number of foreign-born and foreignnationality people in residence in 2000-2, and which country/territory they were born in or had come from 19 . These foreign-born and foreign-national population stock data may include long-term migrants and seasonal workers, and may, therefore, more readily accord to the actual movements of people than any other globally comparable measures $^{19, 20}$

To obtain a surrogate measure of relative *P. falciparum* importation rates, the population-weighted *Pf*PR (*Pf*PRpw) for each country was calculated using the same approach, based on the GRUMP population surface, as in the previous section. The product of this *Pf*PRpw and each of the outgoing migration counts were calculated for each *P. falciparum* malaria endemic country (*Pf*MEC). Then, for each country the sum of the incoming *Pf*PRpwscaled migrant counts was calculated. This produced an index that accounted for both the relative number of incoming migrants to a country, and the *P. falciparum* endemicity in the country from which they had arrived. The index is high when a country has high incoming population flows from high *P. falciparum* endemicity countries, and the index is low when either it has relatively low numbers coming in, or those arriving are from low endemicity countries. The imported *P. falciparum* malaria index scores for each endemic country are shown in Figure S1.6 and Table S1.1.

Figure S1.6. *P. falciparum* malaria importation index for each endemic country for 2007. Large values indicate high numbers of imported *P. falciparum* carriers and low numbers indicate relatively low numbers of incoming carriers.

1.2 Deriving operational feasibility indicators

1.2.1 Government stability, effectiveness and commitment

1.2.1.1 Datasets

The WHO noted that of the 108 countries that have been successful in eliminating malaria, an absence of conflict and effective organization were common factors²¹. For any malaria elimination campaign to be successful, an enabling environment is required where political stability and an absence of conflict are central. Moreover, strong and effective organization and infrastructure are required to achieve elimination. This includes the capacity to implement and run a near-perfect surveillance system and a strong health system, to provide effective information and education programs, to construct a legal framework adapted to the needs of an elimination program, and to facilitate excellent inter-agency, community and cross-border collaboration. Quantifying these aspects is a difficult task, since political stability can change rapidly, and the organizational and technical infrastructure set up to eliminate malaria will be constructed once any decision to eliminate has been made. However, indices measuring the perceptions of a range of organizations and individuals on both political stability and the effectiveness of governments in delivering services and policy can be obtained from the World Bank's 'Aggregate and Individual Governance Indicators^{$22, 23$}.

The World Bank indicators cover 212 countries and territories and measure six dimensions of governance between 1996 and 2007: Voice and Accountability, Political Stability and Absence of Violence, Government Effectiveness, Regulatory Quality, Rule of Law, and Control of Corruption^{22, 23}. The indicators are based on hundreds of specific and disaggregated individual variables measuring various dimensions of governance, taken from 35 data sources provided by 32 different organizations, and they are described in detail by Kaufmann *et al*²². In brief, answers to 365 questions on the perceptions of governance by firms, qualified individuals, commercial risk rating agencies, non-governmental organizations, and a number of multilateral aid agencies and other public sector organizations were compiled. The questions were assigned to one of the six dimensions of governance outlined above, with final indices calculated through weighted averages of the responses. The two dimensions which best capture the political stability and effectiveness of organization aspects that are so relevant to malaria elimination are the Political Stability and Absence of Violence index and the Government Effectiveness index.

The Political Stability and Absence of Violence index is defined as being a measure of the "perceptions of the likelihood that the government will be destabilized or overthrown by possibly unconstitutional and/or violent means, including domestic violence and terrorism" $^{22, 23}$. Low scores for this variable mean that citizens cannot count upon the continuity of government policy or the ability to peacefully select and replace those in power. These data were extracted for every *P. falciparum* and *P. vivax* malaria endemic country for the most recent year of data available: 2008^{23} . These do not therefore capture more recent changes, such as the decline in stability in Madagascar, post-election violence in Kenya or the end of conflict in northern Sri Lanka. While it represents a key component of assessing malaria elimination feasibility, political stability remains a difficult factor to predict. With annual iterations of the governance indicators, however, updates can easily be incorporated. The 2008 data are shown in supplemental Figure S1.7 and Table S1.1.

Figure S1.7. World Bank political stability and absence of violence index for each malaria endemic country in 2008. The most politically stable countries have high index scores, while those that are unstable or in conflict have low scores.

 The Government Effectiveness index is defined as a measure of "the quality of public service provision, the quality of the bureaucracy, the competence of public servants, and the independence of the civil service from political pressures"22, 23. These data were again obtained for every *P. falciparum* and *P. vivax* MEC for the most recent year available: 2008²³, and are shown in supplemental Figure S1.8 and Table S1.1.

Figure S1.8. World Bank government effectiveness index for each malaria endemic country in 2008. High scores indicate effective governance, while low scores indicate ineffective governance.

The majority of countries will need to strengthen their health systems to achieve and sustain zero transmission, requiring strong political and financial commitment. Future health system performance and commitment to elimination are very difficult factors to measure, however, since governmental, political, and financial motivation for malaria elimination in the majority of countries is hard to gauge and harder to predict on the multiple-decade timeline which a malaria elimination plan implies^{24, 25}. Nevertheless, existing data on public health spending by both the government and private health sector provides an indicator of how committed a nation is presently, both financially and politically, to the health of its citizens, and this would be likely to correlate with a commitment to malaria elimination. To ensure comparability of expenditure between countries, accounting for both population size and differing costs, data on *per capita* total US\$ expenditure on health at average exchange rates for the most recent year available, 2006, were acquired. These data were obtained from the World Health Report 2009 of the WHO²⁶ and are shown in supplemental Figure S1.9 and Table S1.1.

Figure S1.9. Overall per capita health expenditure in US\$ at average exchange rates for every malaria endemic country in 2006.

1.2.1.2 Testing the sensitivity of dataset choice

Given that changes in governments and political stability can occur rapidly, we here examine the effects on overall rankings of using the 2007 data on political stability and government effectiveness to assess the magnitude of effects on overall results through one year of change. The 2007 Political Stability and Absence of Violence index data, and the 2007 Government Effectiveness index data were obtained for each *P. falciparum* endemic country. The overall feasibility analyses were then re-run using (i) the 2007 political stability data rather than the 2008 data, keeping all other factors the same, and (ii) the 2007 government effectiveness data rather than the 2008 data, keeping all other factors the same. The absolute average rank difference for the political stability change was just 1.03, while the same measure for government effectiveness was just 0.45. The breakdown of these changes by country can be seen in figures S1.10 and S1.11, and demonstrates that the overwhelming majority of countries displayed little or no change in rank. Just four countries showed average rank changes greater than 10, and all these were due to changes in political stability, demonstrating the need to update results with new information when available, in order to capture these outliers.

Figure S1.10. Change in average rank for each *P. falciparum* malaria endemic country when switching from using the 2008 to 2007 political stability and absence of violence indices.

Figure S1.11. Change in average rank for each *P. falciparum* malaria endemic country when switching from using the 2008 to 2007 government effectiveness indices.

1.2.2 Health systems

The performance and infrastructure of the health system within a country is integral to the success of malaria elimination, and needs to be capable of providing near-universal access to high quality diagnosis and treatment. These qualities are important to guarantee sufficient coverage and specificity for passive case detection. Countries that have previously been successful in eliminating malaria all had well developed general health services with extensive human and physical resources, and a firm financial commitment to sustaining and improving these services²¹.

There exist a wide range of national health system related indicators of varying levels of completeness and comparability²⁷, and a range of studies that attempt to compare differing aspects of the quality and capacity of national health systems using these e.g.²⁸⁻³⁰. The World Health Report 2000³⁰ defined a health system as including all organizations and people whose primary role is to promote, restore or maintain health, and identified four key functions of a national health system: (i) stewardship (often referred to as governance or oversight), (ii) financing, (iii) human and physical resources, and (iv) organization and management of service delivery. With governance, financing and organization examined in the previous section, we focus here on contemporary indicators of the relative resources, processes and impacts of health systems in each country.

With only a select few basic indicators measured in a relatively comparable, reliable and consistent way across all malaria endemic countries^{26-28, 31}, measures of relative health system performance that are specifically relevant for malaria elimination (access to treatment, diagnosis quality, drug supply and health management information system quality) are generally unavailable or incomplete. Moreover, the majority of well reported health statistics are relatively static resource-based measures, such as physicians or hospital beds *per capita*²⁶, which do not inform on the contemporary performance of the health system. Thus, the use of more process and impact-based measures has been advocated as part of recent thinking on conceptualizing health systems within countries as dynamic systems³², and here we examine two types: immunization coverages and antenatal/birth attendance coverages.

Bos and Batson³³ outline the usefulness of immunization coverage data as a proxy for health system performance. Firstly, immunization coverage data can serve as an indicator of a health system's capacity to deliver essential services to the most vulnerable members of a population and has been shown to be significantly related to health worker densities e.g.³⁴. Secondly, immunization is a health output with a strong impact on child morbidity, child mortality and permanent disability. Information on coverage levels provides not just a measure of the implementation of one health intervention, but a proxy for the overall capacity of the health system to support priority health interventions. Thirdly, the target group consists of zero- to one year old children, and the members of the group consist of the cohort of children born each year. Immunization coverage is therefore a sensitive indicator: if measured annually, it can provide timely evidence of improvement and deterioration in current services. Fourthly, the measurement of immunization coverage can be relatively straightforward and inexpensive, and results in valid and verifiable information, while definitions used in surveys and health information systems to measure immunization coverage can be precise and objective, enabling comparisons across countries and over time. Finally, immunization coverage rates are useful (i) to monitor progress in expanding essential health services in adverse health settings, and (ii) as "safeguard" indicators when health system reforms are changing delivery or financing of health services in settings in which immunization coverage is already high. While not all immunization coverage data are reliable or precise, and comparability over time is sometimes limited, these five aspects highlight the value of immunization coverage data and, as such, this measure was adopted here as a dynamic indicator of successful health system processes and impacts.

Data on coverages for a range of immunizations were obtained for every *P. falciparum* and *P. vivax* MEC for the period 2000-2008³⁵. These included the proportion of 1-year olds given the first and third dose of diphtheria and tetanus toxoid with pertussis vaccine (DTP1 and DTP3), the measles-containing vaccine (MCV), the third dose of polio vaccine (Pol3), third dose of hepatitis B vaccine (HepB3), the bacille Calmette-Guérin (vaccine against tuberculosis, BCG) and the third dose of Haemophilus influenzae type b vaccine (Hib3). The Hib3 and HepB3 statistics included missing data for many countries, and were thus not given further consideration. Further, the coverage for delivery of DTP3 was chosen as a more representative measure of health system performance than DTP1, which showed lower variance in values between countries. The data for the remaining immunizations are shown in Figures S1.12-15, and a scatterplot showing the relationship between country rankings for each immunization coverage is shown in Figure S1.16.

Figure S1.12. Proportion of 1-year olds given Measles Containing Vaccine (MCV).

Figure S1.13. Proportion of 1-year olds given third dose of diphtheria and tetanus toxoid with pertussis vaccine (DTP3).

Figure S1.14. Proportion of 1-year olds given third dose of Polio vaccine (POL3).

Figure S1.15. Proportion of 1-year olds given bacille Calmette-Guérin (vaccine against tuberculosis) (BCG).

Figure S1.16. Scatterplot of malaria endemic country rankings for four types of immunization coverage. All relationships are significant at the $p \le 0.01$ level.

Figure S1.16 shows that BCG has the weakest relationship with the other immunization types. An examination of the variance of coverage levels between malaria endemic countries showed a substantially lower value for BCG (BCG = 134, DTP3 = 276, MCV) $= 245$, Pol3 = 263), with values uniformly high, meaning that it represented a less sensitive variable in quantifying differences between health systems and was therefore not considered for further analysis. Finally, to test the sensitivity of results to the choice of the remaining three EPI coverage statistics used, we examined the average overall elimination feasibility rankings produced for each country by holding all factors constant except the EPI statistics. We examined the effects on results of using all possible combinations of EPI coverage statistics, including the use of each type individually and averages of two and all three types. Figure S1.17 shows the maximum range of average ranks that were produced for each country. In general, this shows that the results are relatively insensitive to EPI coverage statistic choice, except for a few countries where individual coverage rates for differing immunizations vary widely. In these cases, the use of averages of coverage statistics for different immunizations produced more stable results and therefore an average of the coverage statistics for all three types was used in the final analyses (figure S1.18).

Figure S1.17. Maximum difference in average rankings for each *P. falciparum* malaria endemic country when using all combinations of EPI coverage statistics.

Figure S1.18. Average coverage percentages of the third dose of diphtheria and tetanus toxoid with pertussis vaccine (DTP3), the measles-containing vaccine (MCV) and the third dose of polio vaccine (Pol3) for each malaria endemic country in 2008.

Antenatal care and birth attendance by skilled personnel represent a second set of essential services to vulnerable populations and are both health outputs with strong impacts on maternal mortality³⁶. Moreover, both are sensitive indicators which, by being measured annually, provide timely evidence of the state of current maternal services. While, like EPI coverage, births attended by skilled personnel (PERS) indicates the ability of a health system to deliver services, antenatal care coverage (ANCC) provides more of a complimentary indicator of health system access and utilization through data on the percentage of women who used antenatal care provided by skilled health personnel for reasons related to pregnancy at least once during pregnancy, as a percentage of live births 2000-08.

 Data on ANCC and PERS were obtained for every *P. falciparum* and *P. vivax* MEC for the period 2000- 200835. ANCC by country is shown in figure S1.19, and PERS by country is shown in figure S1.20, while a scatterplot showing the relationship between the two is shown in Figure S1.21.

Figure S1.19. Antenatal care coverage percentages for each malaria endemic country for the period 2000-08.

Figure S1.20 Births attended by skilled health personnel (%) 2000-08 (PERS).

Figure S1.21. Scatterplot of *P. falciparum* malaria endemic country rankings for antenatal care coverage (ANCC) versus births attended by skilled health personnel (PERS) ($r^2 = 0.444$, $p \ll 0.01$)

Figure S1.21 shows that a significant relationship between ANCC and PERS exists, but that there are some substantial differences, particularly in the mid-range rankings. Therefore, the magnitude of the effects of using each dataset on overall results was examined.

Figure S1.22. Change in average rank for each *P. falciparum* malaria endemic country when switching from using the ANCC to PERS indicators.

The overall feasibility analyses were re-run using (i) ANCC, and (ii) PERS, keeping all other factors the same. The results of these comparisons are shown in Figure S1.22, and demonstrate zero or little change in average ranking for the majority of countries, but larger changes for a selection of countries. These results demonstrate that either statistic could be used and that the consequences of this choice result in minimal changes to overall conclusions for the majority of countries. Given that ANCC provides more of a complimentary indicator to EPI of health system access and utilization, this was chosen over PERS, which, like EPI, is more reflective of service delivery.

1.2.3 Populations at risk

The feasibility of elimination will be affected by (i) the number of people at risk, which determines the scale of the problem to be tackled; (ii) the proportion of the total national population that are at risk, which determines the ability of the government to deal with eliminating transmission in these populations; and (iii) the difficulty in accessing populations at risk, which presents a logistical and financial obstacle to success in achieving elimination. The requirement for these three demographic indicators can be illustrated by considering the situation in Brazil. Compared to other MECs, Brazil has a large population at risk of stable *P. vivax* transmission (12.9 million) presenting an operational challenge in terms of numbers requiring intervention coverage and treatment, but these make up just 6.9% of the total population, presenting less of a burden to the government than MECs where the entire population is at risk. However, with the majority of those at risk situated within the Amazon or on its frontier^{37, 38}, accessing these populations to deliver the required level of intervention and treatment dictated by technical feasibility assessments presents challenges, as has been encountered previously³⁹.

An evidence-based map outlining the global extent of stable *P. falciparum* transmission¹ enabled the estimation of the total populations at risk of stable *P. falciparum* malaria transmission in each country. Similar approaches were followed to create an evidence-based map for *P. vivax*, and a full description can be found in⁴⁰. In brief, 105 countries where *P. vivax* transmission is occurring were identified by cross-referencing information from the Global Malaria Action Plan⁴¹ with the CDC Health Information for International Travel 2010 book⁴² and a range of national surveys and personal communications. Ten of these countries: Algeria, Armenia, Egypt, Jamaica, Mauritius, Morocco, Oman, Russian Federation, Syrian Arab Republic and Turkmenistan, have either interrupted transmission or are extremely effective at dealing with minor local outbreaks, and we did not classify these nations as malaria endemic. Information on *P. vivax* free areas was extracted from international travel health guidelines and mapped. Annual parasite incidence (API) data were then used to identify stable and unstable transmission areas (as defined by Guerra et al¹), as well as to further refine the spatial mapping of *P. vivax* free areas. Using *P. vivax* specific temperature - sporogony relationships, areas where transmission is temperature limited were then excluded. The resulting limits of *P. vivax* transmission are shown in Figure S.1.23.

Figure S1.23. *P. vivax* malaria risk, with areas defined as no risk, unstable or stable transmission.

These maps were overlaid onto the GRUMP *alpha* gridded population surface³ and total populations residing in *P. falciparum* and *P. vivax* stable transmission zones per country were extracted. The population at risk of *P. vivax* transmission is modulated by the frequency of Duffy negativity⁴³, since such individuals are refractory to infection. A model-based geostatistical map of the proportion of Duffy negative individuals (Fya and Fyb antigen) in prevalence surveys (*n*=244) was thus created (Figure S1.24), and used to rescale the *P. vivax* populations at risk, where population at risk = population residing in stable transmission zones \times (1 - frequency of Duffy negative individuals).

Figure S1.24. A model-based geostatistical map of the proportion of Duffy negative individuals (Fya and Fyb antigen) in prevalence surveys (*n*=244).

These are shown in supplemental figures S1.25 and S1.26, and Table S1.1. Further, the proportions of the total national population that these numbers represented were calculated and are shown in supplemental figures S1.27 and S1.28, and Table S1.1.

Figure S1.25. Numbers of people residing in areas of stable *P. falciparum* transmission for each endemic country in 2007.

Figure S1.26. Numbers of people residing in areas of stable *P. vivax* transmission for each endemic country in 2007.

Figure S1.27. The percentage of the total national population who lived in areas of stable *P. falciparum* transmission in 2007.

Figure S1.28. The percentage of the total national population who lived in areas of stable *P. vivax* transmission in 2007.

Accessibility can be measured in units of time taken to reach a location of interest from any other location. Gridded estimates of time taken to reach the nearest substantial settlement (defined as population >50,000) using land or water based travel were recently estimated globally to produce a world map of accessibility⁴⁴ (Figure S1.29). This global map was computed using a cost-distance algorithm that computed the "cost" of travelling between two locations on a regular raster grid. This cost was measured in units of time, and the cells in the grid contain values which represent the cost required to travel across them, hence this raster grid is often termed a friction-surface. The friction-surface accounts for information on road quality; rail, river and sea transport; and environmental factors such as topography, geographical barriers and land cover types that affect travel times between locations. For Vanuatu, Comoros and Timor-Leste, where the largest settlements used were smaller than 50,000 people, the accessibility map was recalculated based on the largest settlement in each country.

The global accessibility map provides a consistent and comparable basis for measuring the per-country accessibility to populations at risk of *P. falciparum* or *P. vivax* malaria. This accessibility is measured from the nearest substantial settlement, at which primary health facilities are based and from which intervention and control efforts are coordinated and launched. For each country the limits of *P. falciparum*¹ and *P. vivax* (Figure S1.23) malaria transmission were used in combination with the GRUMP *alpha* population surface³ to map all populations living in areas of either *P. falciparum* or *P. vivax* malaria transmission. The global accessibility surface was then overlaid and for each country and the average population-weighted accessibility value was calculated. This provided indicators of the relative level of difficulty that will be faced in accessing populations at risk of *P. falciparum* and *P. vivax* malaria in a country. These are shown in figures S1.30 and S1.31, and Table S1.1.

Figure S1.29. Travel times to reach the nearest settlement of size $> 50,000$ people in 2007 (adapted from ⁴⁴). The darkest colours show the least accessible regions.

Figure S1.30. Mean population-weighted accessibility index score for the areas of *P. falciparum* transmission in each endemic country in 2007. High scores indicate poor accessibility.

Figure S1.31. Mean population-weighted accessibility index score for the areas of *P. vivax* transmission in each endemic country in 2007. High scores indicate poor accessibility.

2. Combining indicators

2.1 Introduction

Composite or summary measures are increasingly being recognised as a useful tool in policy analysis and public communication. They provide simple comparisons of entities of interest that can be used to illustrate complex and sometimes elusive issues in wide ranging fields, e.g. environment, economy, society, health or technological development⁴⁵. Composite indicators are now widely used in public policy and health policy debates⁴⁶. Familiar examples include the Human Development Index^{47} and deprivation indices⁴⁸. Few would claim that these examples reveal everything of importance concerning state of development or wealth. Yet because of their comprehensibility and the advantages of simplicity of communication and concision, composite measures have become as much an established part of the policy debate in health as in other fields.

In general terms, an indicator is a quantitative or a qualitative measure derived from a series of observed facts that can reveal relative positions (e.g., of a country) in a given area. When evaluated at regular intervals, an indicator can point out the direction of change across different units and through time. They can also be helpful in setting policy priorities and in benchmarking or monitoring performance. A composite indicator is formed when individual indicators are compiled into a single index on the basis of an underlying model. However, composite indicators can send misleading policy messages if they are poorly constructed or misinterpreted. Their "big picture" results may invite users (especially policy makers) to draw simplistic analytical or policy conclusions. Instead, composite indicators must be seen as a starting point for initiating discussion and attracting public $interest⁴⁵$.

The strengths and weaknesses of composite indicators largely derive from (i) the quality of the underlying variables, and (ii) the subjectivity involved in their construction. Ideally, variables should be selected principally on the basis of their relevance, analytical soundness, timeliness and accessibility. Here, the variables used and their criteria for selection are outlined in detail in supplemental information 1. Composite indicators and their construction often face a degree of scepticism among statisticians, economists and other groups of users. This scepticism is partially due to the lack of transparency of some existing indicators, especially as far as methodologies and basic data are concerned. To avoid these risks, in this study we make available the full input datasets used and in the remainder of this document, we describe the benefits and drawbacks of approaches for weighting indicators in composite ranking methods.

A range of methodologies for constructing composite measures exist, each with their own advantages and disadvantages. The strongest justification for a composite indicator lays in its fitness to the intended purpose and its acceptance by peers^{45}. A new era of global spatial data means that planning for malaria elimination programmes can now rely on a strong evidence base to complement and guide strategies, rather than being driven by subjective or political decisions. Sufficient, comparable data on a broad range of factors common to all countries that have ever been successful in eliminating malaria now exist (see section 1), enabling construction of composite rankings of current malaria endemic countries by elimination feasibility. However, a range of methodologies for constructing such composite measures exist, each with their own advantages and disadvantages, as well as levels of appropriateness for malaria elimination feasibility assessment. Here we describe four categories of approach, providing an example of each. We restrict our focus here to broad categories of approaches that are most relevant to the assessment of elimination feasibility, and briefly discuss their appropriateness. Further details and wider discussions on composite indicators and their construction and alternatives to ranking can be found elsewhere $45, 46, 49.53$.

2.2 **Methods for composite ranking creation**

2.2.1 Equal weightings

One of the simplest approaches to composite ranking is to define the composite as a linear aggregate of the key factor values, or the ranks of the key factors. Most existing composite indicators rely on equal weighting, i.e., all factors are given the same weight. This can correspond to the case in which all factors are "worth" the same in the composite but it can also disguise the absence of statistical or empirical basis, e.g. when there is insufficient knowledge of causal relationships or a lack of consensus on the alternative. In any case, equal weighting does not mean "no weights", but implicitly implies that the weights are equal⁴⁵.

The Human Development Index⁴⁷ represents an example of this approach and is simply a linear aggregrate of rescaled life expectancy, income per capita and literacy, where the weights are one-third for each. This additive

form has the advantage of simplicity of calculation and ease of communication and comprehension. Often, as with the human development index, the use of more complex options for defining composite measures is not pursued because there is no theoretical or empirical basis to postulate alternative forms. However, the approach inherently assumes that each factor considered is equally important and can give undue influence to extreme values in a single factor. For instance, consider countries x, y and z, measured using a composite index of equal weightings of factors A, B and C (table 2.1).

Country	Factor A	Factor B	Factor C	Composite
	0.43			
			0.58	
		N 99		

Table 2.1. Hypothetical data illustrating equal weighting composite construction

Here we see that country *x* scores higher than *y* and *z* on all three factors, so any reasonable ranking method would rank x higher than y and $z - i.e.$ country x is intrinsically better than y and z according to these data. A different picture emerges when comparing *y* with *z*. Country *y* is better on factors A and C, but *z* is better on factor B. The approach described above equally weights each factor to create a composite index to decide that country *y* is better overall. Thus, a subjective decision is made that factors A, B and C are equally important in defining the composite index. A different composite ranking approach might have *z* out-ranking *y* if it was found that factor B was more important (for instance, through methods outlined in sections 2 and 3 below). Alternatively, it could be deemed that countries *y* and *z* are not intrinsically comparable with respect to the three factors (for instance through methods outlined in section 4 below). An alternative example is presented in Box 2 of the main manuscript, illustrating a linear aggregation of the ranks of factors.

Equal weighting represents the simplest and most straightforward methods for obtaining a simple ranking of malaria endemic countries (MECs) by elimination feasibility. However, we have no prior information on the relative importance of each key factor in determining elimination feasibility (though it can also be argued that we can attempt to acquire some – see sections 2.2.2 and 2.2.3 below), and therefore, assuming that each factor should be definitively given an equal weighting ultimately represents an undesirable approach.

2.2.2 Expert consultation based weightings

The choice of the weightings for each factor can be based on some arbitrary choice, as described above, or 'expert' opinion can be sought. Participatory methods that incorporate various stakeholders, experts, citizens and politicians, can be used to assign weights. An example of such an approach was taken for the World Health Report 2000³⁰, with weights based on survey of preferences of informed individuals (1007 individuals from 121 countries⁵⁴) summarized into five chosen factors (See below and Evans et al⁵⁵); health, health inequality, level of responsiveness, distribution of responsiveness and fairness of financial contribution. The results of this survey in terms of the weights for the five key factors overall were 0.24 for health, 0.25 for health inequality, 0.13 for level of responsiveness, 0.16 for distribution of responsiveness and 0.22 for fairness of financial contribution. To make the definition of the composite easier to understand, these survey results were rounded to the nearest one-eighth so that the final weights used were 0.25 for health, 0.25 for health inequality, 0.125 for level of responsiveness, 0.125 for distribution of responsiveness and 0.25 for fairness of financial contribution. Before applying these weights to calculate the composite, each component measure was rescaled on a 0 to 100 scale. The overall composite was, therefore, a number on the interval 0 to 100, with 100 being the highest possible level of attainment⁵⁶. The expert consultation aspect of the approach produced a range of opinions on the importance of each feature, and this was exploited to provide accompanying measures of uncertainty in the final scores and rankings. Moreover, this range of opinions also enabled a sensitivity analysis to be undertaken to assess how much the rankings changed given the range of opinions expressed.

The expert consultation approach is feasible and often ideal when there is a well-defined basis for e.g. a national policy. For international comparisons, such references are often not available, or they deliver contradictory results⁴⁵. The approach does have some attractive features for assessing malaria elimination feasibility, including the provision of a 'consensus' viewpoint, and the valuable by-product of diverse opinions for sensitivity analysis. However, there remain many key issues which make the adoption of the approach misaligned with the aims of this study, and each of which lends additional subjectivity to the analyses: (i) it is much more unclear how to define an 'expert' here than it is for other analyses where it has been employed, e.g. health system performance; (ii) the importance of differing factors in determining, for instance, a strongly performing health

system, is likely to be much more widely agreed upon than the importance of differing factors in achieving malaria elimination; (iii) a large sample of opinions is needed for such an approach to be robust - whether there are enough people qualified to judge the importance of each of a wide range of spatially varying factors across the world in determining elimination feasibility is unclear.

2.2.3 Past study based weightings

One of the most robust and justifiable approaches to defining weightings and compositing indicators relies on past case studies on the issue being examined to empirically determine factor weightings. Examples of its application can be found in a range of recent work that attempts to define empirically the best set of indicators and weightings for a wide area assessment of deprivation through to local intensive surveys of key factors determining deprivation. An overview can be found in Capellari and Jenkins⁵⁷. The success of the approach relies on the assumptions that (i) important factors today are measured equally as well as in the past, and that (ii) the relationship between the desired outcome index and the factors used to construct it are maintained through time. The approach is only covered briefly here, since these assumptions mean it likely represents the least applicable to malaria elimination feasibility assessment.

For malaria elimination feasibility assessment, this approach would build on the fact that malaria has been eliminated from numerous countries in the past, and that we can learn how important individual factors were from studying these past examples. The potential range of weightings found would also enable sensitivity analyses to be undertaken. The principal drawback with this however is data inter-comparability. The majority of these previous national eliminations occurred in the mid-20th century, when global datasets comparable to those used in these analyses on factors such as political stability, immunization coverages and migration did not exist. Though it may be possible to find comparable information on, for instance, common measures such as GDP or health expenditure for the specific countries and times of elimination, it is unlikely that data on all important factors could be captured. Moreover, the control tools available, the spatial distribution and size of populations at risk, health systems and human movement patterns, amongst other factors, were all significantly different.

2.2.4 Partially ordered sets.

As discussed already, the choice of weights can have a significant effect on the overall composite rankings. The partially ordered sets (posets) approach⁵⁸ is based on the notion that there will be no consensus on the importance, and thus weightings, of different factors in determining elimination feasibility. The more conventional solutions outlined above assign a composite numerical score to each object by combining information on each factor in some fashion. Consciously or otherwise, every such composite involves judgements (often arbitrary and thus controversial) about tradeoffs or substitutability among factors. The posets approach takes the more conservative view that the relative positions in factor space determine only a partial ordering, and that a given pair of countries may not be inherently comparable 46 .

Box 2 in the main manuscript provides a brief example to illustrate the use and benefits of the posets approach. Formally, for factors *i* and *j* of countries *a*, *b* and *c*, if $a_i \leq b_i$ and $b_j \leq a_j$ then $a = b$, and if $a_{i,j} < b_{i,j}$ and $b_{i,j} < c_{i,j}$ then $a < b < c$. Thus, initial outputs of the posets methodology are ranked groups of countries, with countries assigned to each group only when there is clear information to do so. Given our relatively poor understanding of the importance of differing factors in determining malaria elimination feasibility, these features of the posets approach overcome some of the disadvantages outlined for approaches 2.2.1-3.

A finite poset can be visualized through its Hasse diagram⁵⁸, which depicts the ranking relations between pairs of elements and allows one to examine the whole partial order structure. Figure S2.1 below shows the Hasse diagram for the data presented in Box 2 of the main manuscript.

Figure S2.1. Hasse diagram illustrating the partial order structure for the example data presented in Box 2 of the main manuscript.

The factor values in Box 2 of the main manuscript for the Dominican Republic are unambiguously more favourable in terms of elimination feasibility than they are for Burundi, Somalia and Equatorial Guinea, so it is positioned in a set of its own above the three countries and connected to them to demonstrate this relationship in figure S2.1. There exists no evidence to inform on the relative elimination feasibility for Burundi, Somalia and Equatorial Guinea, so these are positioned alongside each other in a second set. Conflicting evidence exists for Ghana, meaning that it cannot unambiguously be ranked above or below any other country, so it remains unconnected. Though variations exist, generally Hasse diagrams display the highest ranked object at the top and the lowest ranked at the bottom, and those where no clear ranking decision can be made are listed alongside each other. The partial order structure means that multiple linearizations of the partial ordering can be produced by extracting all the possible rankings of countries that fit the relationships described by the partial ordering (and hence, the Hasse diagram). From these, an average ranking can be obtained for each country to arrive at a single index to quantify relative differences between countries. Calculating all linearizations from 107 malaria endemic countries and the range of indicators considered is incredibly computationally intensive, thus an algorithm based on a local partial order model can be applied⁵⁹, and was used here to estimate average rankings.

Finally, the ranking of the objects is sensitive to the set of attributes. To quantify the importance of an attribute on ranking, posets obtained by different attribute sets are compared with each other. The approach outlined here enabled the sensitivities of the calculated relative technical, operational and overall feasibility posets to the removal and additions of the different indicators to be examined and quantified. The ranking result (Hasse diagram) by means of all factors was compared with the results when omitting step by step each single factor or pairs of factors. The greater the difference respectively, between the results, the greater is the influence of the omitted factor on the posets structure. This difference was measured using distance metrics outlined by Bruggemann *et al.*⁶⁰ and implemented using the software package ProRank (www.prorank.biz). In principle, a high value means a high influence of the factor on the ranking result. Omitting such a factor leads to significant changes of the Hasse diagram, whereas a zero value indicates no effect when omitting the factor in question.

3: Elimination feasibility factor sensitivity results

3.1 Introduction

The calculation of the partially ordered sets (posets) and average ranks are sensitive to the set of factors used. To quantify the importance of each factor on posets definition, we compared posets obtained from different sets of factors with each other. Comparing posets means that an appropriate metric must be found, by which the distance between any two posets can be calculated⁶¹. Here we use the approach outlined by Bruggemann⁶⁰ to calculate distances, and this is described in detail in the paper. The distances calculated serve as a guide to highlight important or less important factors and to identify any internal correlations among them. Relatively large values correspond to a relatively large distance between the poset constructed using all factors, and the poset constructed through the removal of an individual factor or pair of factors, equating to a relatively large effect on results. Relatively small values correspond to a relatively small distance, equating to a small effect on results.

 In the following sections we present the sensitivity results in the form of tables of distance measures calculated to show the effects of the removal of one or a pair of factors on the overall poset definitions, and to highlight which factors have the biggest influence.

3.2 Technical feasibility

3.2.1 *P. falciparum*

Table S3.1 shows the sensitivity of factors in the relative *P. falciparum* technical feasibility partially ordered sets definition. As described above, the numbers represent the size of the effects of partially ordered set change caused by the removal of each factor (top row of values) or pair of factors (remaining rows). The similar numbers for the removal individually of R0 and imported malaria highlight, unsurprisingly, that each has an equal effect on set definitions.

Table S3.1. The sensitivity of factors in relative *P. falciparum* technical feasibility partially ordered sets definition.

3.3 Operational feasibility results 3.3.1 *P. falciparum*

Table S3.2 shows the sensitivity of factors in the relative *P. falciparum* operational feasibility partially ordered sets definition. As described in the introduction, the numbers represent the size of the effects of partially ordered set change caused by the removal of each factor (top row of values) or pair of factors (remaining rows). The largest effects are consistently caused by the removal of the accessibility factor, highlighting that this has the strongest influence on the resulting partially ordered set definitions and may thus be a constraining factor for more countries than any other factor listed. An example of this is Brazil, where all factors are relatively favorable for operational feasibility except for accessing those relatively remote populations at risk distributed throughout the Amazon basin.

Table S3.2. Sensitivity of factors in relative *P. falciparum* operational feasibility partially ordered sets definition.

3.3.2 *P. vivax*

Table S3.3 shows the sensitivity of factors in the relative *P. vivax* operational feasibility partially ordered sets definition. As described in the introduction, the numbers represent the size of the effects of partially ordered set change caused by the removal of each factor (top row of values) or pair of factors (remaining rows). As above, the largest effects are consistently caused by the removal of the accessibility factor, highlighting that this has the strongest influence on the resulting partially ordered set definitions and may thus be a constraining factor for more countries than any other factor listed. Political stability was the factor with the second largest influence, emphasizing that many countries could substantially improve their relative positioning for *P*. *vivax* operational feasibility if a more stable situation arose.

Table S3.3. Sensitivity of factors in relative *P. vivax* operational feasibility partially ordered sets definition.

3.4 Overall feasibility results 3.4.1 *P. falciparum*

Table S3.4 shows the sensitivity of factors in the relative *P. falciparum* overall elimination feasibility partially ordered sets definition. As described in the introduction, the numbers represent the size of the effects of partially ordered set change caused by the removal of each factor (top row of values) or pair of factors (remaining rows). Again, the largest effects are consistently caused by the removal of the accessibility factor, highlighting that this has the strongest influence on the resulting partially ordered set definitions and may thus be a constraining factor for more countries than any other factor listed. Here, imported malaria showed the second largest influence, highlighting that for many countries, such as South Africa or Thailand particularly, proximity to neighbouring higher transmission countries and the levels of cross border movement from these countries, are an obstacle to *P. falciparum* elimination at present.

Table S3.4. The sensitivity of factors in relative overall *P. falciparum* elimination feasibility partially ordered sets definition.

4: Table of all elimination feasibility indicator values

The table presented on the next 12 pages shows the indicator values used in the study for all malaria endemic countries.

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