Global malaria mortality between 1980 and 2010: a systematic analysis

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Summary

Background **During the past decade, renewed global and national efforts to combat malaria have led to ambitious goals. We aimed to provide an accurate assessment of the levels and time trends in malaria mortality to aid assessment of progress towards these goals and the focusing of future efforts.**

Methods **We systematically collected all available data for malaria mortality for the period 1980–2010, correcting for misclassification bias. We developed a range of predictive models, including ensemble models, to estimate malaria mortality with uncertainty by age, sex, country, and year. We used key predictors of malaria mortality such as *Plasmodium falciparum* parasite prevalence, first-line antimalarial drug resistance, and vector control. We used out-of-sample predictive validity to select the final model.**

Findings **Global malaria deaths increased from 995 000 (95% uncertainty interval 711 000–1 412 000) in 1980 to a peak of 1 817 000 (1 430 000–2 366 000) in 2004, decreasing to 1 238 000 (929 000–1 685 000) in 2010. In Africa, malaria deaths increased from 493 000 (290 000–747 000) in 1980 to 1 613 000 (1 243 000–2 145 000) in 2004, decreasing by about 30% to 1 133 000 (848 000–1 591 000) in 2010. Outside of Africa, malaria deaths have steadily decreased from 502 000 (322 000–833 000) in 1980 to 104 000 (45 000–191 000) in 2010. We estimated more deaths in individuals aged 5 years or older than has been estimated in previous studies: 435 000 (307 000–658 000) deaths in Africa and 89 000 (33 000–177 000) deaths outside of Africa in 2010.**

Interpretation **Our findings show that the malaria mortality burden is larger than previously estimated, especially in adults. There has been a rapid decrease in malaria mortality in Africa because of the scaling up of control activities supported by international donors. Donor support, however, needs to be increased if malaria elimination and eradication and broader health and development goals are to be met.**

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Background

During the past decade, a range of organisations have led a global movement to combat malaria. In 2007, the Bill & Melinda Gates Foundation renewed a call, originally set forth by the WHO in 1955, for malaria eradication; in 2011, the UN Secretary-General declared a goal of reducing malaria deaths to zero by 2015.[1] Development assistance for tackling malaria increased from US$149 million in 2000 to almost $1·2 billion in 2008,[2,3] which led to a rapid scaling up of malaria control in Africa.[4,5] Accurate assessments of the levels and time trends in malaria burden are crucial for the assessment of progress towards goals and the focusing of future efforts.

Many efforts have been made to quantify the burden of malaria[4,6–19] with different approaches leading to highly variable results. Hay and colleagues[11] estimate almost twice as many cases of malaria in 2007 than was reported in the World Malaria Report (figure 1). Global malaria death estimates in the 1980s and 1990s range from 800 000 to almost 2·5 million; in the 2000s, the range is from 650 000 to more than 1 million (figure 1). Dhingra and colleagues[22] estimate 205 000 annual deaths from malaria in India in 2002, a large proportion of which are in adults, compared with the WHO's estimate of 15 000 deaths. These conflicting estimates triggered intense debate.[23,24] Less analysis has been done for time trends; only the World Malaria Reports for 2010[4] and 2011[21] produce estimates over time with both suggesting reductions in malaria mortality compared with the previous decade (figure 1).

Several developments make the reassessment of malaria mortality timely. First, the scale-up of malaria control is likely to be changing the pattern of malaria mortality rapidly. Second, as part of the Global Burden of Disease 2010 Study, all available data for mortality by cause from 1980 to 2010 is being systematically collated. Third, the Malaria Atlas Project (MAP) has produced comparable estimates at a fine geographical resolution of the *Plasmodium falciparum* parasite rate (*Pf*PR) for all countries.[25] Fourth, cause-of-death estimation is improving with the use of new modelling methods.[26–28] Fifth, the availability of low-cost computation power makes more objective assessments of the performance of any proposed model possible with out-of-sample predictive validity. We used a large database that included vital registration (VR) and published and unpublished verbal autopsy (VA) studies to develop empirical models for malaria mortality by age, sex, and country for 1980 to 2010.

Methods

Study design

Our objective was to predict levels and trends over time in malaria mortality and not to causally attribute changes in malaria mortality to explanatory factors. Other study designs provide a more appropriate way to do this.[29,30] Our approach follows that developed[31] and applied for other causes of mortality.[26,28,29,32] We systematically identified all data for the event of death coded as malaria, correcting for known bias such as misclassification of deaths to causes that cannot be a true underlying cause of death (known as garbage codes), such as fever. Using this empirical database, we developed and tested many different models. We used out-of-sample predictive validity to assess model performance and choose the final model.

Data collection and processing

We restricted our analysis to 105 countries with local malaria transmission[33] during the period Jan 1, 1980, to Dec 31, 2010. For countries that have eliminated malaria during this period, we identified the year of elimination[33] and estimated malaria deaths for the period in which malaria transmission occurred.

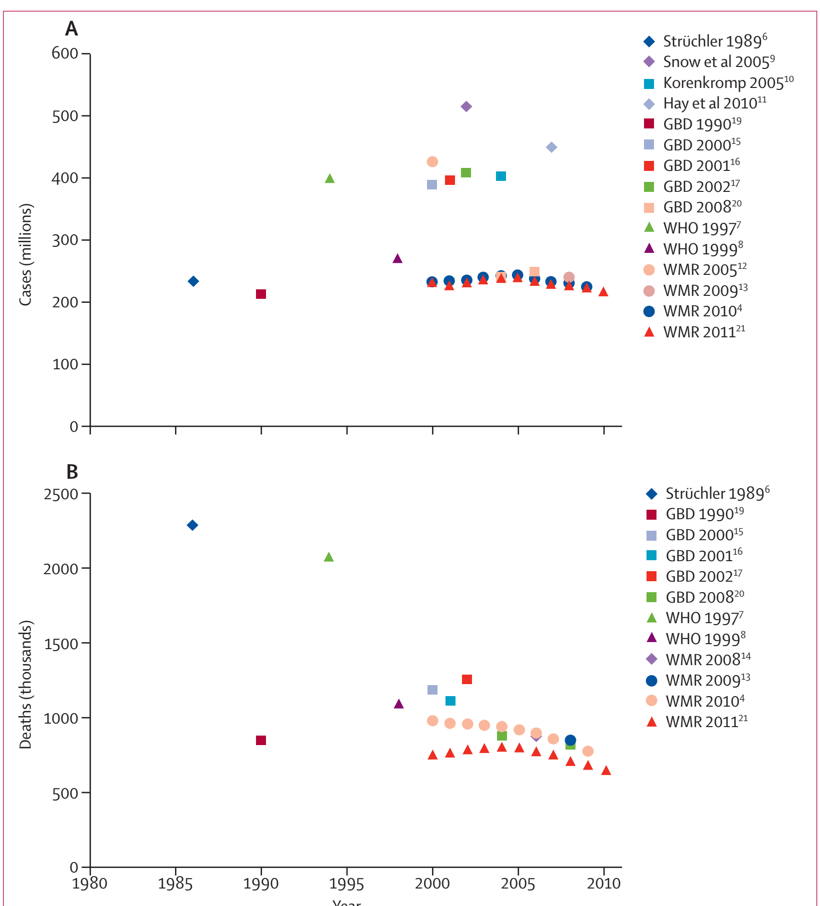

Figure 1: **Global estimates of malaria cases**
Comparison of previous estimates of global malaria cases (A) and deaths (B) in individuals of all ages, 1980 to 2010.

During the past 4 years, we have systematically developed a database of VR data since 1980 for all countries globally. In some countries, VR systems are incomplete;[34] we adjusted for completeness by assuming that the cause composition of all deaths is equal to the cause composition of recorded deaths. When VR completeness was less than 75%, we treated the VR as being subnational.

VR data have been supplemented through the systematic collation of VA studies. We identified VA studies, irrespective of cause, by searching PubMed and Google Scholar for all studies with the term “verbal autopsy”, and did country-specific searches on Google using the country name and “verbal autopsy”. We also identified studies from systematic reviews of malaria mortality[35,36] and updated them by searching for “‘malaria” and “mortality” in the following databases and languages: Google Scholar (English, French, and Spanish), PubMed (English and Spanish), LILACS (Spanish and Portuguese), SCIELO (Spanish), Horizon (French), BDSP (French), Cairn (French), and Santetropicale (French). We supplemented published sources by tracing references and identifying studies in the grey literature or in survey or census datasets. We reviewed 13 666 search results. We included only studies meeting three inclusion criteria: the study was population-based and covered a period of at least 1 year, used VA, and was open to any set of causes and provided the number of deaths due to at least malaria. All studies in special populations (eg, refugees) were excluded. Table 1 provides the number of site-years that include malaria as a cause of death by data type and decade across the 105 countries.

We used the approach developed by Naghavi and colleagues[37] to account for changes in the International Classification of Diseases and Injuries (ICD) and to redistribute deaths assigned to garbage codes. The following ICD (version 10) codes were identified as containing potentially misclassified malaria deaths: R50 (fever of other and unknown origin), D65 (disseminated intravascular coagulation), B99 (other and unspecified infectious diseases), B94 (sequelae of other and unspecified infectious and parasitic diseases).

For VA, we addressed two issues. First, some studies report results for large age categories—eg, 15 years and older. All reported age intervals were converted into results for 5-year age groups, assuming that the relative risk of death by age within the reporting age interval equals the globally observed relative risk of death by age for malaria. All studies of deaths of children younger than 5 years were converted into late neonatal, post-neonatal, and childhood age intervals; we excluded the early neonatal period. Second, for selected sites such as the Adult Morbidity and Mortality Project studies in

Tanzania, VA results reported deaths for categories such as fever. We obtained results from a validation study in these project sites that provided the proportion of deaths that were considered to be due to malaria on the basis of reviews of medical records. For VA studies that reported deaths broadly due to anaemia, we redistributed these deaths on the basis of the prevalence of underlying causes (malaria, iron deficiency, etc) and their respective effect on haemoglobin.

There were 21% more malaria deaths in the database after adjustment for misclassification of death codes. All data from VR and VA were converted to cause fractions. When rate models are used, cause fractions were multiplied by the relevant age-specific mortality rates.[27,28]

Model development

In view of the differential patterns of malaria mortality, we divide the world into three groups: countries with only *Plasmodium vivax* malaria (15 countries), countries from sub-Saharan Africa and Yemen (45 countries), and countries outside of sub-Saharan Africa (45 countries).

Because the recorded malaria death rate in countries with only *P vivax* is low—there are 2242 malaria deaths in the database for the 15 countries between 1980 and 2010—we used the median recorded death rate by age as a simple predictor of malaria mortality.

For the other two categories of countries, we developed and tested a diverse set of models—including different combinations of covariates and both mixed-effect and spatio-temporal forms— for the log of the death rate and for the logit of the cause fraction. We developed models separately for each sex and broad age group (<5 years and 5 years and older)—ie, a total of eight models.

A key predictor of malaria deaths is malaria transmission intensity such as *Pf*PR. However, available data are restricted to single time periods. To address this limitation, we specified models that include estimates of malaria transmission intensity for a reference period and then supplement this with time-series data for other factors (eg, rainfall), to capture changes in malaria mortality from the reference period. We tested only models that include a measure of malaria transmission intensity and at least one time-series predictor.

We tested three sources of malaria transmission intensity: the proportion of the population by endemicity zone defined by Lysenko and Semashko[38] for the assumed malaria transmission peak before the 1960s,[39] WHO's estimates of the proportion of the population at risk of malaria for 2006,[4] and the MAP estimates of *Pf*PR for the standardised age interval of 2–10 years in 2007.[25] For the MAP *Pf*PR, we tested continuous and categorical forms: the population-weighted average of *Pf*PR and the proportion of the population in three transmission zones (*Pf*PR <5%, 5–39%, ≥40%[40]). Because MAP provides high-resolution estimates, we also established the location-specific value of the MAP 2007 *Pf*PR for all subnational studies. We allowed models to include only malaria intensity measures from one reference period—ie, Lysenko and Semashko,[38] WHO, or MAP.

	1980–89	1990–99	2000–10	Total
Vital registration (national)	262	340	313	915
Vital registration (subnational)	15	7	2	24
Verbal autopsy (national)	0	2	12	14
Verbal autopsy (subnational)	41	44	64	149
Other	0	27	21	48

Table 1: Site-years of data, by decade

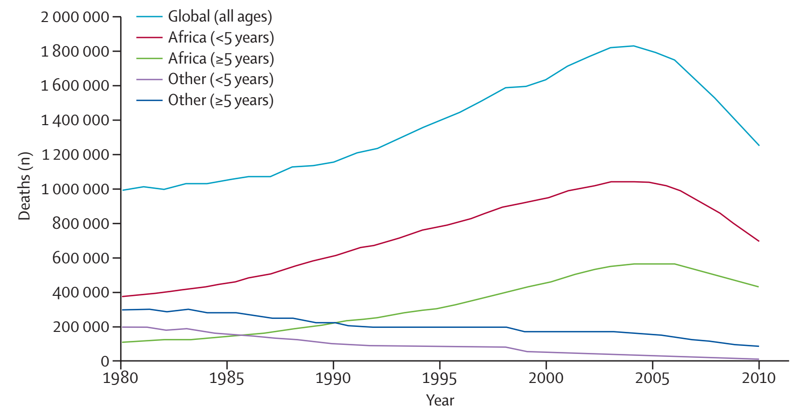

Figure 2: Trends in global malaria deaths by age and geographical region, 1980 to 2010

We tested the following time-series variables: rainfall, health-system access, first-line antimalarial drug resistance, insecticide-treated bednet coverage, indoor residual spraying coverage, income per head, and educational attainment.[41] First-line antimalarial drug resistance is a weighted average by country and year of the treatment efficacy of chloroquine, sulfadoxine-pyrimethamine, and artemisinin-combination therapy with weights based on the frequency of drug use. Treatment efficacy was estimated with a spatio-temporal model of in-vivo efficacy studies and WHO antimalarial drug resistance database reports.[42,43] Frequency of drug use was estimated with a spatio-temporal model of survey data for antimalarial drug use in children with fever, which was supplemented by programme data for supply of artemisinin-combination therapy, correcting for bias with survey data as the benchmark. Updated estimates of household bednet coverage and estimates for outside of Africa were produced with a previously described Bayesian statistical model.[5] Coverage of indoor residual spraying was based on a spatio-temporal model of survey data for reported household spraying in the previous 12 months and programme data reported to WHO, correcting for bias with survey data as the benchmark.

We tested all possible combinations of covariates and retained models if the coefficients on all covariates were in the expected direction, and with a less conservative p value <0·1, in view of the scarcity of data for malaria mortality. This approach yielded 145 models for boys younger than 5 years in Africa; 56 models for boys and men aged 5 years or older in Africa; 69 models for girls younger than 5 years in Africa; 41 models for girls and women aged 5 years or older in Africa; 119 models for boys younger than 5 years outside of Africa; 337 models for boys and men aged 5 years or older outside of Africa; 183 models for girls younger than 5 years outside of Africa; and 343 models for girls and women aged 5 years or older outside of Africa.

For each combination of covariates, we assessed both a mixed-effects linear model and a spatial-temporal Gaussian process regression version.[26–28] Spatio-temporal models provide a way to identify trends in the underlying data that are not captured by the available covariates to the extent that the data are correlated in time and space.

We also tested ensemble models, which are weighted averages of individual component models. Ensemble models generate predictions with smaller errors and more accurate uncertainty intervals than do single models.[44–46] We tested a range of ensemble models that differ in how the weights on component models are chosen.

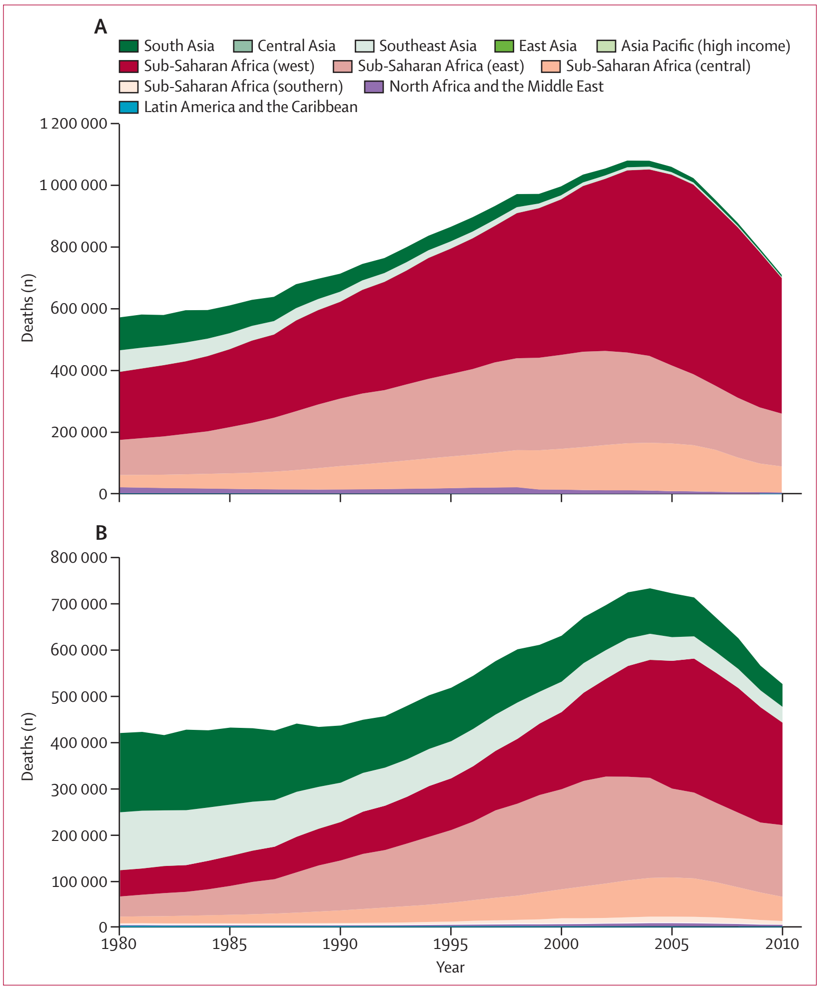

Figure 3: **Malaria deaths by Global Burden of Disease Study region for children younger than 5 years (A) and individuals aged 5 years of age or older (B), 1980 to 2010**

We assessed the ability of each of the models to make accurate predictions by creating 50 train-test-test splits. We randomly assigned 70% of the data to the train dataset, 15% to the first test dataset, and the remaining 15% to the second test dataset. For each train dataset, we re-estimated all of the proposed models. The test data are not included in the model estimation; the out-of-sample predictions for the test set are therefore a fair assessment of how each model will perform in the prediction of malaria mortality when data are missing. Individual component models are assessed in the first test set with the results used to construct the ensemble models. Both ensemble and individual component models are assessed in the second test set.

Predictive validity is assessed with three metrics. First, we assessed how well every model predicts age-specific death rates with the root mean squared error of the log of the death rate. Second, we established the proportion of the time the model correctly predicts whether mortality is increasing or decreasing when compared with the previous year. Third, we computed the percentage of the data in the test set included in the 95% prediction interval. On the basis of the predictive validity tests, for each of the eight groups we chose the final model with the lowest root mean squared error and best trend metric.

Verbal autopsy sensitivity analysis

A multisite VA validation study by Lozano and colleagues[47] shows that where malaria is not a common cause of death, physicians are more likely to assign malaria as the cause of death on the basis of the symptoms recorded. In areas where malaria is a common cause of death, physicians tend to underestimate it. On the basis of this study, we did a sensitivity analysis for malaria mortality, building on the same idea as in previous work.[35] Lozano and colleagues[47] compared cause-specific mortality fractions for malaria produced from physician-coded VA with gold-standard cause-of-death assignment based on predetermined clinical, diagnostic, and pathological criteria in 500 test datasets. These comparisons provide a functional relation and uncertainty between estimated cause-specific mortality fractions and true cause-specific mortality fractions. Using this relation, we adjusted the VA data in the database for misclassification bias and reran the analysis as outlined above—ie, all the steps from covariate selection through the final prediction.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had

	Number of deaths (95% uncertainty interval)				Cumulative probability of malaria death (per 1000 population)			
	1980	1990	2000	2010	1980	1990	2000	2010
Afghanistan	14 243 (5164–30 111)	9773 (3099–23 627)	9150 (3666–19 419)	2274 (1–7135)	23·9	15·7	9·2	1·9
Angola	4916 (404–14 269)	7241 (682–20 132)	13 652 (1420–33 841)	7777 (329–24 968)	16·1	16·9	23·7	11·1
Argentina	10 (0–58)	2 (0–9)	0 (0–1)	0 (0–0)	<0·1	<0·1	<0·1	<0·1
Armenia	2 (0–13)	0 (0–2)	0 (0–0)	··	0·2	<0·1	<0·1	··
Azerbaijan	7 (0–41)	2 (0–9)	0 (0–1)	0 (0–0)	0·3	<0·1	<0·1	<0·1
Bangladesh	16 365 (2852–50 138)	8317 (1681–22 499)	3021 (601–8928)	702 (108–2146)	5·6	2·5	·9	·2
Belize	1 (1–3)	1 (0–1)	0 (0–1)	0 (0–0)	0·2	<0·1	<0·1	<0·1
Benin	4554 (1887–9097)	5939 (2638–10 881)	8634 (4479–15 432)	8251 (3521–16 152)	32·6	31·8	35·2	26·2
Bhutan	89 (28–205)	45 (12–105)	13 (4–33)	2 (0–6)	5·9	2·5	0·9	0·1
Bolivia	99 (24–298)	66 (18–180)	20 (6–51)	6 (1–17)	0·5	0·3	<0·1	<0·1
Botswana	32 (3–148)	26 (1–184)	52 (0–309)	28 (0–225)	0·8	0·6	1·1	0·6
Brazil	374 (164–641)	211 (92–381)	55 (26–97)	16 (5–38)	0·1	<0·1	<0·1	<0·1
Burkina Faso	9037 (3842–18 217)	13 305 (6998–23 606)	28 211 (14 448–42 677)	24 656 (9417–42 206)	32·7	36·7	59·4	40·4
Burma	13 943 (1510–50 640)	8267 (627–38 823)	3760 (240–18 751)	1228 (64–7218)	14·1	8·3	4·2	1·5
Burundi	6386 (3125–11 544)	12 044 (6693–19 032)	17 875 (9074–28 618)	10 361 (4453–19 893)	41·7	55·2	77·9	41·1
Cambodia	6970 (2163–17 564)	6888 (2100–17 760)	2536 (736–6982)	301 (35–903)	28·8	17·9	7·7	1
Cameroon	7011 (2531–15 806)	9011 (2806–21 070)	19 935 (8995–35 211)	12 589 (5289–25 352)	20·7	20·3	38·3	19·7
Central African Republic	2257 (958–4493)	3584 (1829–6512)	6676 (3194–11 007)	5072 (2344–8664)	28·0	34·5	52·9	37·4
Chad	4194 (1392–8920)	5305 (1771–10 955)	9776 (3322–18 333)	9997 (3320–19 920)	24·2	23·3	30·5	23·3
China	72 (25–172)	32 (13–64)	12 (4–27)	3 (0–10)	<0·1	<0·1	<0·1	<0·1
Colombia	170 (70–311)	76 (34–155)	31 (13–55)	11 (1–27)	0·2	<0·1	<0·1	<0·1
Comoros	152 (13–378)	200 (21–488)	359 (51–761)	235 (24–555)	11·8	13·3	18·4	9·2
Congo	1193 (334–3196)	1746 (390–4301)	3001 (765–6939)	1869 (338–5302)	18·3	21·4	29·0	14·6
Costa Rica	1 (0–4)	0 (0–1)	0 (0–0)	0 (0–0)	<0·1	<0·1	<0·1	<0·1
Côte d'Ivoire	6538 (1305–18 735)	11 066 (2504–26 012)	16 911 (4971–32 479)	16 304 (5786–31 632)	19·2	24·8	31·5	26·5
Democratic Republic of the Congo	31 294 (12 171–58 555)	62 676 (31 553–100 859)	108 311 (66 928–177 521)	69 505 (28 858–134 616)	29·6	40·9	50·6	27·1
Djibouti	8 (1–49)	21 (2–118)	54 (5–237)	34 (3–142)	0·7	1·1	2·5	1·4
Dominican Republic	6 (3–12)	2 (1–5)	1 (0–2)	0 (0–1)	<0·1	<0·1	<0·1	<0·1
Ecuador	53 (20–113)	28 (11–51)	15 (6–28)	3 (1–6)	0·2	<0·1	<0·1	<0·1
Egypt	11 (1–52)	3 (0–12)	··	··	<0·1	<0·1	··	··
El Salvador	10 (0–56)	1 (0–6)	0 (0–1)	0 (0–0)	0·3	<0·1	<0·1	<0·1
Equatorial Guinea	174 (72–350)	516 (260–881)	564 (72–1529)	310 (0–1279)	24·7	36·1	32·0	14·5
Eritrea	1180 (256–2869)	1217 (264–3170)	1629 (399–4200)	1444 (307–4125)	13·2	11·1	13·0	8·3
Ethiopia	15 268 (4802–44 586)	35 585 (12 441–74 774)	46 918 (20 277–83 088)	22 165 (10 132–40 255)	11·6	19·2	19·4	9·1
Gabon	183 (0–746)	397 (0–1499)	465 (0–1717)	272 (0–1089)	8·3	12·6	12·7	7·2
Gambia	665 (343–1168)	971 (562–1343)	1334 (636–2287)	1594 (534–2980)	25·7	25·7	26·8	26·6
Georgia	2 (0–13)	0 (0–2)	0 (0–0)	0 (0–0)	0·1	<0·1	<0·1	<0·1
Ghana	10 335 (3954–20 092)	14 060 (6920–22 822)	15 560 (9706–23 164)	10 575 (5567–18 739)	24·8	27·4	26·1	14·8
Guatemala	90 (26–213)	48 (23–89)	21 (9–38)	6 (2–14)	0·3	0·2	<0·1	<0·1
Guinea	8532 (3549–16 517)	11 099 (5240–18 489)	17 868 (9923–27 723)	14 208 (8039–22 945)	49·8	51·0	58·2	40·8
Guinea-Bissau	1853 (893–3183)	2233 (1214–3628)	2447 (1352–3909)	2678 (858–5322)	61·1	58·2	55·0	52·6
Guyana	14 (3–38)	7 (3–14)	3 (1–5)	1 (0–3)	0·6	0·4	0·2	<0·1
Haiti	767 (305–1673)	488 (185–934)	290 (138–545)	94 (27–219)	4·0	2·1	1·2	0·4
Honduras	19 (8–39)	6 (3–12)	3 (1–6)	1 (0–2)	0·1	<0·1	<0·1	<0·1
India	85 283 (31 797–190 815)	47 077 (17 384–105 034)	24 026 (8272–50 319)	4826 (781–14 437)	4·0	1·9	0·9	0·2
Indonesia	43 636 (13 081–112 728)	14 543 (5409–30 623)	5637 (2378–11 451)	1724 (585–3712)	9·5	3·2	1·3	0·4
Iran	22 (5–61)	11 (5–23)	3 (1–5)	1 (0–2)	<0·1	<0·1	<0·1	<0·1
Iraq	18 (0–99)	3 (0–19)	1 (0–4)	0 (0–1)	0·2	<0·1	<0·1	<0·1
Kenya	5915 (2183–13 930)	15 372 (7733–28 107)	21 129 (11 909–31 093)	12 399 (5886–21 708)	8·5	17·0	19·8	8·9

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	Number of deaths (95% uncertainty interval)				Cumulative probability of malaria death (per 1000 population)			
	1980	1990	2000	2010	1980	1990	2000	2010
(Continued from previous page)								
Kyrgyzstan	6 (0–31)	1 (0–6)	0 (0–1)	0 (0–0)	0·2	<0·1	<0·1	<0·1
Laos	1850 (273–5929)	1455 (202–5210)	634 (59–2272)	156 (0–693)	16·0	9·7	4·1	1·2
Liberia	2052 (729–4434)	2905 (1253–5620)	5391 (2801–8931)	4593 (2167–7776)	27·6	34·2	54·9	33·3
Libya	3 (0–13)	1 (0–5)	1 (0–3)	..	<0·1	<0·1	<0·1	..
Madagascar	654 (303–1258)	1261 (705–1905)	1843 (865–3314)	1919 (491–5055)	2·0	3·0	3·3	2·9
Malawi	4983 (1825–10 777)	13 791 (6984–23 302)	11 029 (5591–19 000)	9106 (3778–18 325)	19·6	38·8	25·6	15·9
Malaysia	32 (10–71)	11 (4–22)	3 (1–7)	1 (0–2)	<0·1	<0·1	<0·1	<0·1
Mali	17 609 (10 552–27 696)	20 210 (11 236–33 352)	31 745 (16 653–54 758)	28 859 (7971–67 629)	63·2	58·5	69·6	46·8
Mauritania	307 (43–734)	393 (65–969)	810 (141–1855)	758 (120–1848)	5·5	5·5	9·2	7·1
Mauritius	1 (0–2)	0 (0–1)	..	..	<0·1	<0·1	..	..
Mexico	84 (0–470)	10 (0–54)	1 (0–7)	0 (0–1)	0·2	<0·1	<0·1	<0·1
Morocco	3174 (900–7311)	1179 (417–2528)	536 (193–1200)	..	4·7	1·7	0·9	..
Mozambique	23 088 (9362–44 120)	31 891 (15 027–52 651)	42 733 (25 307–62 361)	27 612 (14 964–43 477)	50·4	62·3	63·0	34·5
Namibia	52 (2–238)	64 (4–295)	104 (9–433)	66 (3–348)	1·3	1·3	1·9	1·2
Nepal	1172 (203–3659)	690 (136–2167)	270 (47–913)	72 (7–287)	2·3	1·1	0·4	0·1
Nicaragua	90 (23–238)	29 (13–54)	10 (4–18)	3 (1–7)	0·7	0·2	<0·1	<0·1
Niger	6949 (1596–18 103)	9735 (2344–24 650)	16 123 (4285–35 633)	22 984 (6988–44 167)	29·8	30·0	35·2	36·0
Nigeria	130 405 (55 159–240 421)	192 945 (96 552–327 766)	304 897 (163 914–482 748)	266 429 (111 177–467 137)	45·5	53·7	68·7	47·9
North Korea	10 (0–56)	2 (0–9)	0 (0–2)	0 (0–0)	0·1	<0·1	<0·1	<0·1
Oman	3 (0–10)	1 (0–3)	0 (0–1)	..	<0·1	<0·1	<0·1	..
Pakistan	4492 (1067–13 302)	2728 (967–6331)	1500 (531–3507)	581 (218–1233)	1·6	0·7	0·4	0·1
Panama	4 (1–11)	3 (1–7)	1 (0–4)	1 (0–2)	<0·1	<0·1	<0·1	<0·1
Papua New Guinea	848 (172–2787)	631 (103–2253)	507 (84–1874)	229 (26–957)	7·3	4·8	3·0	1·2
Paraguay	3 (0–18)	1 (0–3)	0 (0–0)	0 (0–0)	0·1	<0·1	<0·1	<0·1
Peru	35 (13–74)	18 (9–34)	5 (3–10)	1 (0–4)	<0·1	<0·1	<0·1	<0·1
Philippines	225 (82–472)	111 (39–243)	61 (29–119)	20 (6–46)	0·1	<0·1	<0·1	<0·1
Rwanda	3801 (876–8750)	6575 (1660–13 984)	9016 (2124–18 149)	4786 (817–14 142)	17·6	23·5	35·8	12·3
Sao Tome and Principe	40 (22–73)	52 (27–92)	52 (25–99)	41 (15–89)	12·0	13·2	11·3	8·2
Saudi Arabia	22 (0–82)	7 (0–27)	4 (0–13)	1 (0–6)	<0·1	<0·1	<0·1	<0·1
Senegal	2917 (1342–5840)	4359 (2135–6763)	7939 (3181–14 576)	4085 (1163–10 677)	13·6	15·9	23·5	9·6
Sierra Leone	5978 (2844–10 637)	7777 (4221–12 420)	14 101 (7273–23 201)	8516 (3650–16 007)	56·7	57·4	88·4	41·7
Solomon Islands	45 (3–197)	28 (1–133)	19 (1–110)	7 (0–56)	4·8	2·4	1·4	0·4
Somalia	5601 (1946–12 344)	11 108 (4737–21 964)	17 621 (7709–31 490)	13 910 (5518–25 712)	24·9	42·8	58·9	37·6
South Africa	13 (2–45)	13 (4–41)	31 (8–69)	13 (2–38)	<0·1	<0·1	<0·1	<0·1
South Korea	5 (0–30)	1 (0–4)	0 (0–1)	0 (0–0)	<0·1	<0·1	<0·1	<0·1
Sri Lanka	28 (12–52)	10 (4–19)	4 (2–10)	1 (0–3)	<0·1	<0·1	<0·1	<0·1
Sudan	6432 (1011–18 009)	11 212 (2282–30 671)	19 159 (3061–51 009)	9551 (1340–29 254)	8·5	11·6	16·5	7·3
Suriname	4 (1–8)	2 (1–5)	2 (1–4)	0 (0–1)	0·4	0·3	0·2	<0·1
Swaziland	37 (3–161)	83 (7–455)	88 (7–597)	47 (3–328)	1·5	2·5	2·7	1·5
Syria	35 (1–221)	10 (1–46)	4 (0–14)	..	<0·1	<0·1	<0·1	..
Tajikistan	21 (6–48)	18 (6–41)	11 (5–23)	4 (1–13)	0·2	<0·1	<0·1	<0·1
Tanzania	24 894 (10 921–51 471)	50 325 (29 249–75 203)	60 880 (41 810–98 044)	26 606 (10 928–49 663)	34·0	51·4	48·4	15·9
Thailand	1066 (424–2014)	282 (110–536)	52 (20–105)	14 (2–39)	0·9	0·3	<0·1	<0·1
Timor-Leste	587 (42–1981)	448 (28–1608)	369 (19–1542)	115 (3–663)	29·5	15·6	10·4	2·8
Togo	2982 (1229–6502)	3868 (1624–8883)	4987 (2319–9671)	4449 (1793–9418)	27·8	28·6	31·5	25·2
Turkey	92 (0–511)	10 (0–56)	1 (0–6)	0 (0–1)	0·4	<0·1	<0·1	<0·1
Turkmenistan	8 (0–43)	2 (0–10)	0 (0–1)	..	0·3	<0·1	<0·1	..
Uganda	11 271 (3869–25 952)	19 943 (9228–36 545)	39 411 (19 457–62 684)	23 126 (9818–42 642)	22·2	27·5	38·8	17·1
United Arab Emirates	0 (0–1)	0 (0–1)	..	..	<0·1	<0·1	..	..

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	Number of deaths (95% uncertainty interval)				Cumulative probability of malaria death (per 1000 population)			
	1980	1990	2000	2010	1980	1990	2000	2010
(Continued from previous page)								
Uzbekistan	22 (0–125)	5 (0–28)	1 (0–5)	0 (0–1)	0·2	<0·1	<0·1	<0·1
Vanuatu	7 (1–25)	2 (0–9)	2 (0–7)	1 (0–3)	1·7	0·4	0·3	0·1
Venezuela	8 (3–16)	9 (4–17)	5 (2–9)	2 (0–4)	<0·1	<0·1	<0·1	<0·1
Vietnam	1497 (266–5059)	482 (96–1371)	95 (16–265)	24 (0–120)	0·9	0·2	<0·1	<0·1
Yemen	1642 (9–5014)	2084 (14–6335)	3382 (26–10 087)	2305 (21–7878)	4·6	3·9	5·2	2·8
Zambia	4513 (1255–11 018)	9595 (3644–18 037)	16 332 (8169–27 114)	8751 (4120–15 213)	20·0	33·2	41·8	17·1
Zimbabwe	380 (132–864)	381 (149–745)	592 (233–1235)	631 (170–1543)	1·3	1·1	1·6	1·8

··=No malaria transmission.

Table 2: **Country-specific malaria mortality estimates for children younger than 5 years**

	Number of deaths (95% uncertainty interval)				Cumulative probability of malaria death (per 1000 population)			
	1980	1990	2000	2010	1980	1990	2000	2010
Afghanistan	688 (16–2259)	488 (16–1673)	1085 (23–4547)	597 (0–1893)	7·0	5·8	8·1	3·2
Angola	1937 (379–4305)	2706 (610–5599)	6947 (1366–12 738)	6737 (1015–14 375)	48·0	51·5	98·1	69·5
Argentina	61 (0–314)	15 (0–78)	4 (0–20)	1 (0–5)	0·3	<0·1	<0·1	<0·1
Armenia	5 (0–27)	2 (0–8)	0 (0–2)	··	0·2	<0·1	<0·1	··
Azerbaijan	13 (0–67)	3 (0–16)	1 (0–4)	0 (0–1)	0·3	<0·1	<0·1	<0·1
Bangladesh	6813 (942–20 306)	5607 (1065–15 245)	4041 (663–11 450)	2668 (302–8907)	14·6	9·2	4·9	2·6
Belize	7 (4–11)	5 (3–9)	4 (3–7)	3 (1–6)	7·1	4·9	3·0	1·4
Benin	1724 (790–3714)	2122 (1167–4365)	3414 (1852–6107)	6164 (3764–10 606)	72·0	71·3	88·1	115·1
Bhutan	64 (19–116)	46 (15–88)	25 (7–46)	10 (3–23)	24·1	13·3	6·5	1·9
Bolivia	112 (37–248)	91 (35–190)	38 (18–65)	20 (6–40)	2·7	1·8	0·6	0·3
Botswana	40 (6–103)	65 (8–173)	355 (27–996)	264 (17–738)	7·7	8·5	24·3	17·8
Brazil	581 (260–849)	605 (219–871)	190 (132–345)	102 (48–211)	0·5	0·4	0·1	<0·1
Burkina Faso	3109 (1207–7473)	4886 (2515–8875)	10 331 (7149–14 905)	16 074 (10 014–21 186)	78·7	99·1	155·5	149·7
Burma	55 985 (21 618–137 350)	39 471 (11 434–115 467)	34 652 (9732–103 502)	20 766 (5429–75 235)	238·0	138·1	99·5	51·8
Burundi	1601 (432–4420)	3183 (1284–6745)	7742 (2989–15 918)	5901 (2264–12 410)	61·0	90·5	179·1	104·8
Cambodia	4640 (1976–9185)	4768 (1893–10 066)	4107 (1889–8218)	1495 (246–3690)	86·7	67·2	40·9	12·4
Cameroon	3658 (1580–7786)	5616 (2616–9803)	14 750 (8940–24 927)	10 592 (5833–18 477)	63·3	73·8	142·1	81·5
Central African Republic	1226 (469–2897)	2370 (931–5015)	5076 (2968–8297)	3641 (2033–6194)	87·2	117·1	200·6	132·6
Chad	1442 (642–2761)	1820 (883–3054)	3548 (1640–6205)	4516 (2230–7523)	46·8	46·4	69·4	65·9
China	258 (123–509)	125 (79–238)	147 (65–211)	55 (14–119)	<0·1	<0·1	<0·1	<0·1
Colombia	229 (110–334)	120 (78–197)	99 (54–145)	43 (14–80)	1·1	0·4	0·3	0·1
Comoros	87 (13–218)	154 (23–320)	402 (42–790)	205 (30–473)	43·7	59·2	120·4	48·4
Congo	912 (322–2121)	2215 (1005–3569)	4481 (2068–7835)	2243 (784–4624)	88·9	155·6	225·4	91·7
Costa Rica	3 (0–13)	1 (0–4)	0 (0–1)	0 (0–0)	0·2	<0·1	<0·1	<0·1
Côte d'Ivoire	3112 (987–7494)	6855 (2883–12 757)	14 604 (6371–26 020)	15 360 (7049–27 588)	63·2	91·1	131·8	118·3
Democratic Republic of the Congo	10 146 (3257–27 652)	18 992 (9268–37 134)	44 004 (30 261–62 741)	38 045 (20 582–73 215)	74·8	105·1	180·6	121·9
Djibouti	16 (2–66)	47 (9–211)	159 (22–764)	145 (26–676)	8·1	14·7	35·9	25·2
Dominican Republic	20 (11–29)	13 (9–21)	10 (6–15)	9 (3–14)	0·5	0·3	0·2	0·1
Ecuador	54 (33–92)	55 (24–80)	44 (23–61)	12 (4–29)	0·8	0·6	0·4	<0·1
Egypt	37 (3–160)	21 (3–72)	··	··	0·1	<0·1	··	··
El Salvador	9 (0–45)	2 (0–11)	1 (0–3)	0 (0–1)	0·3	<0·1	<0·1	<0·1
Equatorial Guinea	125 (50–307)	301 (166–557)	650 (271–1296)	431 (98–923)	81·8	129·1	198·3	97·7
Eritrea	593 (192–1403)	760 (247–1815)	1602 (469–3632)	1403 (432–2985)	37·1	40·6	75·7	47·4

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	Number of deaths (95% uncertainty interval)				Cumulative probability of malaria death (per 1000 population)			
	1980	1990	2000	2010	1980	1990	2000	2010
(Continued from previous page)								
Ethiopia	7217 (2373–16 554)	21 285 (12 584–37 141)	40 244 (23 720–68 212)	25 342 (14 677–44 481)	28·9	63·4	86·0	42·0
Gabon	292 (57–713)	862 (231–1533)	1494 (388–2866)	1080 (231–2114)	58·3	134·6	177·5	105·5
Gambia	90 (51–145)	140 (81–224)	296 (174–477)	662 (322–1274)	23·7	26·3	41·2	68·5
Georgia	13 (0–66)	3 (0–17)	1 (0–3)	0 (0–1)	0·3	<0·1	<0·1	<0·1
Ghana	2400 (1111–4967)	4046 (2386–7070)	7805 (5233–11 947)	12 049 (6571–17 817)	38·1	47·0	68·7	83·1
Guatemala	320 (83–574)	169 (83–235)	62 (40–114)	33 (7–80)	8·4	3·2	0·8	0·3
Guinea	2005 (971–4304)	2831 (1557–5576)	5568 (3224–9240)	5299 (2904–10 204)	70·0	76·7	105·1	84·3
Guinea-Bissau	358 (161–746)	408 (183–907)	536 (244–1105)	941 (529–1580)	63·9	61·6	67·4	95·2
Guyana	27 (11–60)	25 (17–41)	27 (13–38)	14 (0–30)	5·4	4·1	4·3	2·1
Haiti	1152 (668–1888)	979 (535–1607)	1068 (654–1639)	667 (259–1200)	26·0	19·7	18·6	9·9
Honduras	27 (15–42)	17 (9–27)	14 (7–24)	11 (4–22)	1·4	0·7	0·4	0·2
India	154 492 (83 209–282 157)	110 134 (61 175–191 534)	88 083 (47 425–144 575)	42 145 (11 340–88 615)	33·3	18·9	11·8	4·7
Indonesia	36 506 (20 100–59 559)	20 156 (11 415–34 146)	15 495 (8884–23 786)	9201 (4078–15 482)	29·0	12·6	7·7	3·8
Iran	13 (5–26)	14 (8–23)	12 (5–17)	4 (1–10)	<0·1	<0·1	<0·1	<0·1
Iraq	19 (0–97)	5 (0–24)	1 (0–7)	0 (0–2)	0·3	<0·1	<0·1	<0·1
Kenya	3907 (1779–8282)	12 418 (7708–20 262)	24 611 (13 968–35 236)	14 766 (7909–25 990)	36·6	81·6	109·5	54·9
Kyrgyzstan	9 (0–46)	2 (0–11)	1 (0–3)	0 (0–1)	0·4	<0·1	<0·1	<0·1
Laos	1078 (172–3612)	949 (150–3311)	827 (90–2937)	479 (0–2044)	45·8	33·0	22·6	10·4
Liberia	802 (364–1757)	912 (479–2007)	2207 (1193–4158)	3042 (1733–5648)	68·9	70·7	128·7	129·2
Libya	1 (0–6)	1 (0–6)	1 (0–7)	..	<0·1	<0·1	<0·1	..
Madagascar	2232 (1304–4403)	4806 (2938–7116)	7149 (4232–11 971)	14 241 (6710–27 661)	41·3	67·6	77·5	108·2
Malawi	1106 (415–2902)	4679 (2028–8021)	4937 (2442–8654)	4847 (2450–8400)	28·8	78·3	60·0	51·8
Malaysia	175 (76–317)	88 (46–148)	43 (25–63)	20 (8–40)	2·1	0·8	0·3	0·1
Mali	3106 (1975–4362)	3690 (2379–5558)	6416 (4086–9662)	10 424 (6034–19 981)	68·7	71·7	99·1	128·9
Mauritania	189 (29–378)	266 (40–528)	593 (80–1199)	737 (104–1463)	21·8	23·9	41	37·3
Mauritius	23 (6–52)	11 (4–23)	..	..	3·8	1·6	..	..
Mexico	116 (0–589)	27 (0–136)	7 (0–35)	2 (0–12)	0·3	<0·1	<0·1	<0·1
Morocco	156 (50–316)	87 (39–152)	64 (34–110)	..	1·1	0·5	0·3	..
Mozambique	7865 (4445–14 118)	11 705 (7770–17 616)	27 608 (19 848–40 586)	24 577 (16 137–36 344)	99·1	128·8	213·5	146·7
Namibia	79 (16–195)	111 (25–274)	332 (68–848)	400 (59–1016)	13·5	13·8	24·9	26·1
Nepal	1633 (334–4282)	1389 (271–3593)	968 (163–3010)	640 (61–2321)	17·9	12·1	6·4	3·3
Nicaragua	51 (14–111)	24 (11–37)	14 (9–23)	10 (3–19)	2·3	0·9	0·4	0·2
Niger	1727 (702–2906)	2181 (878–3714)	3830 (1507–6801)	7428 (2639–13 568)	48·2	47·6	61·8	86·2
Nigeria	27 865 (13 485–58 460)	39 966 (23 215–72 947)	79 395 (49 059–127 629)	114 213 (67 302–204 773)	58·2	65·6	100	112·5
North Korea	25 (0–129)	7 (0–36)	2 (0–11)	1 (0–3)	0·3	<0·1	<0·1	<0·1
Oman	1 (0–4)	0 (0–2)	0 (0–2)	..	0·1	<0·1	<0·1	..
Pakistan	7865 (2237–19 916)	6134 (2109–14 125)	5935 (1765–13 692)	3669 (1151–8351)	15·0	8·6	6·2	3·1
Panama	3 (2–5)	2 (1–4)	2 (1–4)	2 (1–3)	0·2	0·1	0·1	<0·1
Papua New Guinea	1793 (687–3706)	1934 (608–4349)	1904 (589–4679)	1493 (344–3983)	81·4	66·4	50·6	30·4
Paraguay	4 (0–20)	1 (0–5)	0 (0–2)	0 (0–1)	0·2	<0·1	<0·1	<0·1
Peru	36 (19–60)	31 (18–47)	20 (11–28)	7 (3–12)	0·3	0·2	0·1	<0·1
Philippines	955 (364–1530)	657 (286–1017)	402 (275–624)	242 (91–484)	2·7	1·4	0·8	0·4
Rwanda	1761 (544–4438)	4491 (1715–8855)	7953 (2801–14 822)	6175 (2220–11 817)	59·4	104·7	155·2	97·8
Sao Tome and Principe	55 (37–85)	68 (46–104)	92 (64–139)	114 (73–180)	76·9	81·0	93·9	97·6
Saudi Arabia	4 (0–35)	4 (0–25)	3 (0–19)	3 (0–17)	<0·1	<0·1	<0·1	<0·1
Senegal	1971 (1156–3588)	3670 (2216–6247)	7186 (3625–14 182)	6066 (3113–12 301)	60·3	86·4	131·5	86·2
Sierra Leone	1566 (714–3520)	2088 (1122–4252)	3810 (2269–6525)	3827 (2295–6449)	75·7	84·0	157·4	115·2
Solomon Islands	87 (7–279)	77 (5–259)	64 (5–252)	55 (0–280)	62·3	41·9	25·2	16·0
Somalia	957 (266–2321)	2189 (461–4528)	4369 (819–9851)	3410 (872–6947)	23·7	54·3	98·3	62·4

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	Number of deaths (95% uncertainty interval)				Cumulative probability of malaria death (per 1000 population)			
	1980	1990	2000	2010	1980	1990	2000	2010
(Continued from previous page)								
South Africa	196 (51–496)	266 (95–665)	1293 (569–2356)	593 (201–1454)	1·1	1·1	3·6	1·4
South Korea	76 (0–396)	18 (0–89)	4 (0–19)	1 (0–5)	0·4	<0·1	<0·1	<0·1
Sri Lanka	93 (40–134)	40 (26–68)	57 (22–100)	24 (9–47)	0·8	0·3	0·4	0·1
Sudan	3012 (531–7086)	6006 (874–12 721)	12 605 (1340–33 281)	7772 (1062–20 352)	24·2	37·2	59·8	27·8
Suriname	7 (3–13)	8 (4–11)	13 (5–19)	3 (1–7)	2·5	2·2	3·1	0·7
Swaziland	45 (7–163)	205 (32–862)	486 (95–1750)	249 (41–1022)	14·3	46·7	66·7	29·8
Syria	14 (6–28)	8 (4–14)	7 (3–12)	..	0·3	0·1	<0·1	..
Tajikistan	13 (7–21)	12 (6–21)	15 (8–23)	9 (2–20)	0·5	0·4	0·4	0·2
Tanzania	6282 (2255–16 717)	17 809 (10 129–29 723)	31 524 (20 499–57 928)	17 825 (6659–45 865)	61·8	126·9	151·6	66·3
Thailand	4198 (1780–5927)	2041 (1083–2763)	949 (616–1495)	313 (103–740)	9·8	3·8	1·4	0·4
Timor-Leste	343 (22–1175)	323 (17–1198)	256 (14–1033)	195 (8–911)	95·7	76·5	56·0	31·5
Togo	1135 (537–2594)	1453 (736–3225)	2035 (993–3777)	3767 (1941–7245)	70·4	66·8	70·1	97·2
Turkey	77 (0–397)	22 (0–111)	5 (0–28)	1 (0–7)	0·3	<0·1	<0·1	<0·1
Turkmenistan	6 (0–32)	2 (0–8)	1 (0–3)	..	0·4	<0·1	<0·1	..
Uganda	4678 (2093–11 163)	10 976 (5294–20 602)	26 170 (15 532–42 654)	18 522 (10 743–31 383)	60·7	98·6	171·4	95·5
United Arab Emirates	0 (0–1)	0 (0–1)	..	..	<0·1	<0·1	..	..
Uzbekistan	35 (0–178)	9 (0–48)	3 (0–14)	1 (0–4)	0·4	<0·1	<0·1	<0·1
Vanuatu	9 (2–20)	7 (2–17)	5 (1–13)	4 (1–10)	11·1	6·9	4·0	2·1
Venezuela	16 (9–26)	33 (17–46)	25 (14–36)	17 (7–34)	0·1	0·2	0·1	<0·1
Vietnam	20 636 (3178–88 627)	16 224 (1830–75 301)	8877 (1164–40 131)	1084 (92–2376)	56·7	36·0	14·9	1·4
Yemen	848 (32–2165)	1213 (48–3084)	3645 (164–9817)	3298 (147–9115)	19·7	20·4	38·9	26·5
Zambia	2212 (1095–4055)	7036 (4231–10 202)	18 527 (9803–27 239)	9319 (6060–13 126)	57·3	119·1	218·1	98·2
Zimbabwe	1180 (606–2395)	2049 (1215–3935)	8218 (3553–17 456)	5424 (2602–10 593)	28·7	33·1	77·3	59·2

..=No malaria transmission.

Table 3: **Country-specific malaria mortality estimates for individuals aged 5 years or older**

full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between 1980 and 2010, global malaria deaths have increased from 995 000 (95% uncertainty interval 711 000–1 412 000) in 1980 to a peak of 1 817 000 (1 430 000–2 366 000) in 2004 (figure 2). This increase is explained by rising malaria death rates in the 1980s and early 1990s and a growth in populations at risk of malaria. In 2010, there were 1 238 000 (929 000–1 685 000) malaria deaths, a 32% decrease since 2004.

The rise and fall of global malaria deaths is largely driven by the pattern seen in sub-Saharan Africa. Malaria deaths in African children younger than 5 years increased by about three times from 377 000 (182 000–602 000) in 1980 to a peak of 1 047 000 (716 000–1 479 000) in 2004. Accelerated decreases in the past 5 years translate into 699 000 (415 000–1 112 000) deaths in 2010. Malaria deaths in individuals aged 5 years or older in Africa show a similar pattern with deaths increasing from 116 000 (62 000–230 000) in 1980 to 569 000 (422 000–867 000) in 2006. Since 2006, malaria deaths in those aged 5 years or older in Africa have also decreased at a similar rate to deaths in children younger than 5 years; in 2010 there were 435 000 (307 000–658 000) malaria deaths in those aged 5 years or older in Africa.

Outside of Africa, the trend in malaria deaths is much different. Malaria deaths in children younger than 5 years have steadily decreased from a peak of 199 000 (91 000–421 000) in 1980 to 15 000 (4300–31 000) in 2010. There are also more malaria deaths in those aged 5 years and older than there are in children, although malaria deaths in those aged 5 years and older have also steadily decreased from 303 000 (187 000–502 000) in 1980 to 89 000 (33 000 to 177 000) in 2010.

Most malaria deaths in both children and adults occur in western, eastern, and central Africa (figure 3). Malaria deaths in children in south and southeast Asia have been steadily decreasing since 1980 and account for a small proportion of the global deaths in this age group in 2010 (figure 3). By contrast with this trend, malaria deaths in south and southeast Asia in individuals aged 5 years or older account for a large proportion of global malaria deaths in this age group in 2010 (figure 3).

	Number of deaths (95% uncertainty interval)				Cumulative probability of malaria death (per 1000 population)			
	1980	1990	2000	2010	1980	1990	2000	2010
Afghanistan	14 931 (5484–30 999)	10 261 (3408–23 856)	10 235 (4147–20 520)	2870 (6–7832)	30·8	21·4	17·2	5·1
Angola	6853 (1750–16 482)	9947 (2740–23 480)	20 599 (5453–41 809)	14 514 (4016–33 976)	63·3	67·4	119·4	79·8
Argentina	71 (0–373)	17 (0–87)	4 (0–22)	1 (0–6)	0·4	<0·1	<0·1	<0·1
Armenia	7 (0–39)	2 (0–10)	0 (0–2)	..	0·4	<0·1	<0·1	..
Azerbaijan	20 (0–107)	5 (0–25)	1 (0–5)	0 (0–1)	0·6	0·1	<0·1	<0·1
Bangladesh	23 177 (5463–57 350)	13 924 (4294–29 509)	7062 (2380–15 548)	3370 (732–9222)	20·1	11·7	5·8	2·8
Belize	8 (5–13)	6 (4–10)	5 (3–8)	3 (1–6)	7·3	5·0	3·0	1·4
Benin	6278 (3366–11 070)	8061 (4498–13 337)	12 047 (7476–19 335)	14 415 (8955–22 942)	102·2	100·8	120·2	138·3
Bhutan	153 (65–278)	91 (38–167)	37 (15–66)	11 (4–27)	29·9	15·8	7·3	2·0
Bolivia	211 (76–438)	156 (69–303)	58 (29–95)	26 (9–47)	3·3	2·1	0·7	0·3
Botswana	72 (15–227)	91 (18–314)	406 (55–1066)	292 (28–783)	8·5	9·1	25·4	18·5
Brazil	955 (515–1361)	817 (377–1134)	245 (170–397)	117 (59–233)	0·7	0·5	0·1	<0·1
Burkina Faso	12 147 (6077–22 577)	18 191 (10 937–28 444)	38 543 (24 347–52 607)	40 730 (23 092–59 778)	108·8	132·1	205·7	184·1
Burma	69 928 (29 175–159 522)	47 738 (14 970–127 118)	38 411 (10 888–104 759)	21 995 (5995–75 367)	248·8	145·3	103·3	53·3
Burundi	7988 (4271–13 298)	15 227 (9147–22 591)	25 617 (14 509–39 154)	16 262 (8773–28 641)	100·2	140·7	243·0	141·6
Cambodia	11 610 (5333–23 343)	11 656 (5539–24 365)	6644 (3556–12 907)	1795 (426–4077)	113·0	83·8	48·3	13·4
Cameroon	10 669 (5287–20 494)	14 627 (7648–27 395)	34 685 (21 470–51 470)	23 181 (13 819–37 818)	82·8	92·7	174·9	99·6
Central African Republic	3483 (1841–6017)	5955 (3485–9492)	11 753 (7281–17 218)	8713 (5052–12 837)	112·8	147·6	242·9	165
Chad	5636 (2466–10 404)	7125 (3273–12 603)	13 324 (6079–22 306)	14 513 (6709–25 052)	69·9	68·6	97·8	87·7
China	331 (178–614)	157 (103–272)	159 (75–228)	58 (14–123)	<0·1	<0·1	<0·1	<0·1
Colombia	399 (229–581)	197 (131–292)	129 (75–180)	54 (20–92)	1·3	0·5	0·3	0·1
Comoros	240 (79–504)	353 (131–708)	760 (310–1388)	440 (136–879)	55·0	71·7	136·6	57·1
Congo	2105 (964–4323)	3961 (2008–6630)	7482 (3945–12 364)	4112 (1715–8217)	105·6	173·6	247·8	105
Costa Rica	3 (0–17)	1 (0–5)	0 (0–1)	0 (0–0)	0·2	<0·1	<0·1	<0·1
Côte d'Ivoire	9650 (3732–21 640)	17 921 (8455–34 322)	31 514 (15 856–49 638)	31 664 (16 310–51 504)	81·2	113·6	159·2	141·7
Democratic Republic of the Congo	41 440 (19 317–72 651)	81 669 (47 230–123 449)	152 316 (106 956–224 382)	107 550 (57 083–177 278)	102·1	141·7	222·1	145·8
Djibouti	24 (5–94)	69 (16–262)	213 (52–831)	180 (48–699)	8·7	15·8	38·3	26·6
Dominican Republic	26 (16–36)	15 (11–24)	11 (6–16)	9 (4–15)	0·6	0·3	0·2	0·1
Ecuador	107 (61–183)	83 (40–122)	59 (36–79)	15 (5–32)	1·0	0·7	0·5	0·1
Egypt	48 (5–175)	24 (4–76)	..	..	0·1	<0·1	..	..
El Salvador	19 (0–103)	3 (0–17)	1 (0–3)	0 (0–1)	0·5	<0·1	<0·1	<0·1
Equatorial Guinea	300 (153–521)	817 (516–1217)	1214 (510–2226)	741 (202–1679)	104·4	160·5	223·9	110·8
Eritrea	1773 (631–3593)	1977 (762–4106)	3231 (1322–6505)	2847 (1169–5693)	49·8	51·3	87·7	55·3
Ethiopia	22 485 (9487–50 438)	56 869 (28 979–97 706)	87 163 (54 578–130 693)	47 507 (30 363–74 830)	40·2	81·4	103·7	50·6
Gabon	475 (113–1172)	1259 (388–2507)	1959 (681–3747)	1352 (444–2582)	66·1	145·5	188·0	111·9
Gambia	754 (420–1271)	1111 (683–1512)	1631 (951–2560)	2256 (1206–3542)	48·8	51·3	66·9	93·3
Georgia	15 (0–80)	4 (0–19)	1 (0–4)	0 (0–1)	0·4	<0·1	<0·1	<0·1
Ghana	12 734 (6245–22 229)	18 106 (11 204–26 905)	23 365 (17 115–33 602)	22 624 (14 620–31 283)	61·9	73·1	93·1	96·7
Guatemala	410 (126–755)	218 (119–293)	83 (56–133)	39 (12–86)	8·7	3·4	0·9	0·3
Guinea	10 537 (5312–18 604)	13 930 (7754–21 656)	23 436 (15 216–33 685)	19 506 (12 222–29 140)	116·4	123·8	157·2	121·7
Guinea-Bissau	2211 (1141–3549)	2642 (1514–4048)	2984 (1716–4481)	3619 (1695–6148)	121·1	116·3	118·7	142·7
Guyana	41 (15–88)	32 (22–50)	30 (15–41)	14 (0–31)	6·0	4·5	4·4	2·2
Haiti	1919 (1186–2973)	1468 (873–2198)	1359 (905–1934)	761 (322–1318)	29·9	21·8	19·8	10·3
Honduras	45 (27–71)	24 (14–35)	17 (9–27)	12 (5–24)	1·5	0·7	0·4	0·2
India	239 775 (137 767–417 605)	157 211 (95 079–241 437)	112 109 (67 550–171 438)	46 970 (14 757–94 945)	37·2	20·8	12·7	4·9
Indonesia	80 142 (39 520–155 830)	34 699 (20 745–55 274)	21 132 (13 578–31 414)	10 925 (5420–17 211)	38·2	15·8	9·0	4·2
Iran	35 (13–80)	25 (15–40)	14 (8–20)	5 (2–10)	<0·1	<0·1	<0·1	<0·1
Iraq	36 (0–195)	8 (0–42)	2 (0–11)	1 (0–3)	0·5	<0·1	<0·1	<0·1
Kenya	9821 (4726–19 297)	27 790 (18 045–42 976)	45 740 (29 762–60 270)	27 165 (16 994–40 521)	44·8	97·2	127·2	63·4

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	Number of deaths (95% uncertainty interval)				Cumulative probability of malaria death (per 1000 population)			
	1980	1990	2000	2010	1980	1990	2000	2010
(Continued from previous page)								
Kyrgyzstan	15 (0–76)	3 (0–17)	1 (0–4)	0 (0–1)	0·6	0·1	<0·1	<0·1
Laos	2929 (670–8177)	2404 (540–6863)	1461 (298–4332)	634 (0–2427)	61·1	42·4	26·6	11·6
Liberia	2854 (1361–5453)	3817 (2027–6563)	7598 (4776–11 751)	7635 (4514–11 821)	94·6	102·5	176·5	158·2
Libya	4 (0–14)	2 (0–8)	2 (0–8)	..	<0·1	<0·1	<0·1	..
Madagascar	2885 (1873–4981)	6066 (4035–8314)	8992 (5600–14 136)	16 160 (7706–28 669)	43·2	70·4	80·6	110·7
Malawi	6089 (2673–11 861)	18 470 (10 996–28 387)	15 966 (9795–23 564)	13 953 (8171–23 286)	47·8	114·1	84	66·9
Malaysia	206 (104–358)	99 (57–161)	46 (28–67)	21 (9–41)	2·2	0·8	0·3	0·1
Mali	20 715 (13 581–30 765)	23 899 (14 700–37 620)	38 161 (22 742–60 292)	39 283 (19 774–77 017)	127·6	125·9	161·8	169·7
Mauritania	496 (157–984)	659 (213–1312)	1403 (472–2570)	1495 (500–2782)	27·2	29·3	49·8	44·2
Mauritius	23 (7–53)	11 (4–23)	..	..	3·8	1·6	..	..
Mexico	200 (0–1061)	37 (0–192)	8 (0–43)	2 (0–13)	0·5	<0·1	<0·1	<0·1
Morocco	3330 (1028–7549)	1266 (497–2634)	600 (246–1290)	..	5·8	2·2	1·2	..
Mozambique	30 952 (16 668–52 654)	43 596 (26 060–64 878)	70 342 (51 585–95 357)	52 189 (36 227–70 553)	144·5	183·1	263·1	176·1
Namibia	131 (37–372)	175 (48–497)	436 (115–1056)	466 (99–1183)	14·8	15·1	26·7	27·3
Nepal	2806 (831–6022)	2079 (644–4613)	1238 (338–3215)	712 (102–2356)	20·2	13·2	6·8	3·4
Nicaragua	140 (49–293)	54 (29–82)	23 (16–34)	12 (5–23)	3·0	1·1	0·5	0·3
Niger	8677 (2990–20 414)	11 916 (4140–26 737)	19 953 (7347–38 281)	30 412 (13 218–51 968)	76·6	76·2	94·8	119·1
Nigeria	158 270 (77 819–267 352)	232 910 (133 007–365 703)	384 292 (240 933–566 513)	380 642 (224 228–586 705)	101·0	115·8	161·8	155·0
North Korea	35 (0–181)	9 (0–45)	3 (0–13)	1 (0–3)	0·4	<0·1	<0·1	<0·1
Oman	4 (0–11)	1 (0–4)	1 (0–2)	..	0·2	<0·1	<0·1	..
Pakistan	12 357 (4428–25 720)	8862 (4192–17 021)	7435 (2965–15 199)	4250 (1539–9042)	16·5	9·3	6·5	3·2
Panama	7 (4–14)	5 (3–9)	4 (2–7)	2 (1–4)	0·3	0·2	0·1	<0·1
Papua New Guinea	2641 (1335–5232)	2565 (945–5394)	2412 (933–5464)	1722 (469–4204)	88·1	70·9	53·4	31·6
Paraguay	7 (0–37)	2 (0–8)	0 (0–2)	0 (0–1)	0·4	<0·1	<0·1	<0·1
Peru	71 (39–120)	49 (32–68)	26 (16–34)	8 (4–14)	0·4	0·2	0·1	<0·1
Philippines	1179 (547–1765)	768 (345–1181)	463 (326–681)	262 (104–508)	2·8	1·5	0·8	0·4
Rwanda	5561 (1978–11 156)	11 066 (4475–20 104)	16 970 (6437–28 722)	10 962 (4185–20 195)	75·9	125·7	185·5	108·9
Sao Tome and Principe	95 (66–138)	120 (84–172)	144 (100–207)	155 (101–221)	88·0	93·1	104·1	105
Saudi Arabia	27 (0–92)	11 (0–41)	7 (0–26)	4 (0–19)	0·1	<0·1	<0·1	<0·1
Senegal	4888 (2894–7862)	8029 (5240–10 859)	15 125 (9705–22 443)	10 150 (5871–15 924)	73·1	100·9	151·9	95
Sierra Leone	7545 (4152–12 114)	9864 (6045–14 533)	17 911 (10 973–27 066)	12 343 (6901–20 918)	128·1	136·5	231·8	152·1
Solomon Islands	132 (22–350)	105 (13–320)	83 (10–271)	62 (0–285)	66·9	44·2	26·5	16·4
Somalia	6557 (2668–13 316)	13 297 (6082–24 643)	21 990 (10 364–37 881)	17 321 (7953–30 258)	48·0	94·7	151·4	97·6
South Africa	210 (57–511)	279 (105–672)	1324 (606–2392)	606 (213–1482)	1·1	1·1	3·6	1·4
South Korea	82 (0–423)	18 (0–93)	4 (0–20)	1 (0–5)	0·4	<0·1	<0·1	<0·1
Sri Lanka	121 (60–170)	49 (34–78)	61 (24–106)	25 (9–48)	0·9	0·3	0·4	0·1
Sudan	9445 (3145–21 803)	17 219 (5795–37 976)	31 764 (10 379–65 289)	17 323 (5832–41 746)	32·4	48·4	75·3	34·9
Suriname	10 (5–18)	10 (6–14)	15 (7–21)	3 (1–7)	2·9	2·5	3·3	0·7
Swaziland	82 (14–250)	288 (52–1005)	574 (111–2033)	296 (48–1172)	15·8	49·1	69·2	31·3
Syria	49 (8–246)	18 (6–53)	11 (5–21)	..	0·4	0·2	<0·1	..
Tajikistan	34 (17–63)	29 (15–52)	26 (16–40)	13 (4–27)	0·6	0·4	0·4	0·2
Tanzania	31 175 (16 318–58 545)	68 134 (47 193–99 977)	92 403 (68 119–142 333)	44 430 (22 223–81 574)	93·7	171·8	192·7	81·1
Thailand	5264 (2656–7211)	2324 (1322–3109)	1000 (687–1537)	327 (110–757)	10·7	4·1	1·4	·4
Timor-Leste	930 (129–2559)	771 (89–2243)	626 (65–2009)	310 (28–1115)	122·4	90·9	65·8	34·3
Togo	4117 (2182–7916)	5321 (2712–10 672)	7021 (3853–12 331)	8216 (4501–13 986)	96·3	93·5	99·3	119·9
Turkey	169 (0–912)	32 (0–168)	7 (0–34)	1 (0–8)	0·7	0·1	<0·1	<0·1
Turkmenistan	14 (0–74)	3 (0–18)	1 (0–4)	..	0·7	0·1	<0·1	..
Uganda	15 949 (7678–30 520)	30 919 (18 842–48 070)	65 581 (44 046–91 376)	41 648 (27 162–63 831)	81·6	123·4	203·5	111·0
United Arab Emirates	0 (0–2)	0 (0–2)	..	..	<0·1	<0·1	..	..

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	Number of deaths (95% uncertainty interval)				Cumulative probability of malaria death (per 1000 population)			
	1980	1990	2000	2010	1980	1990	2000	2010
(Continued from previous page)								
Uzbekistan	57 (0–297)	14 (0–76)	4 (0–19)	1 (0–4)	0·5	0·1	<0·1	<0·1
Vanuatu	16 (6–37)	9 (3–21)	7 (2–16)	4 (1–11)	12·7	7·3	4·2	2·2
Venezuela	23 (14–36)	42 (23–57)	29 (18–42)	19 (8–37)	0·2	0·3	0·1	<0·1
Vietnam	22 133 (3823–89 693)	16 707 (2164–76 039)	8972 (1226–40 304)	1108 (92–2428)	57·5	36·2	15·0	1·4
Yemen	2490 (151–6469)	3297 (156–8158)	7027 (412–15 603)	5603 (355–13 461)	24·2	24·2	43·9	29·2
Zambia	6725 (2933–13 651)	16 632 (9404–25 848)	34 859 (22 454–46 446)	18 070 (11 901–25 327)	76·2	148·4	250·9	113·6
Zimbabwe	1561 (887–2821)	2429 (1518–4408)	8810 (4145–17 901)	6055 (3114–11 003)	29·9	34·1	78·8	60·9

··=No malaria transmission.

Table 4: **Country-specific malaria mortality estimates for individuals of all ages**

We calculated detailed country estimates of the number of malaria deaths and cumulative probability of dying from malaria in the absence of other causes of death for children younger than 5 years (table 2), those aged 5 years or older (table 3), and individuals of all ages (table 4) for 1980, 1990, 2000, and 2010. The risk of malaria death in several countries that have scaled up control efforts, such as Zambia, Tanzania, Kenya, and Ethiopia, has decreased between 2000 and 2010 (figures 4 and 5). Despite these reductions, mortality risk in 2010 is highest in western, eastern, and, in particular, central sub-Saharan Africa (figure 5).

Of all global malaria deaths, a very small proportion occurred in the 15 countries with only *P vivax*. In 1980, we estimate 751 malaria deaths in these countries; in 2010, we estimate nine deaths. We estimate a cumulative total during the 30-year period of 5169 deaths from malaria in these countries. These findings do not represent all deaths from *P vivax* because *P vivax* will account for a proportion of deaths in countries with both *P falciparum* and *P vivax*.

In our analysis for India, we include all available sources of data for malaria mortality (see webappendix for an example showing estimates of malaria mortality for women aged 30–34 years). We include data from the Sample Registration Scheme corrected for garbage coding and data from national VA samples included in the National Family Health Survey round one in 1994 and round two in 1998. Both rounds of the National Family Health Survey and the Sample Registration Scheme record high rates of malaria mortality. We also include findings from the Survey of Causes of Death from 1980 to 1990 and the Medical Certification of Causes of Death from 1990 to 2004. These sources suggest lower rates of malaria mortality. On the basis of implausibly high malaria mortality in the National Family Health Survey round two we do not include these data in our analysis. In 2002, we estimate 19 000 (95% uncertainty interval 6000–39 000) malaria deaths in children younger than 5 years and 87 000 (42 000–132 000) malaria deaths in those aged 5 years or older. We estimate 4800 (780–14 000) malaria deaths in children younger than 5 years and 42 000 (11 000–89 000) malaria deaths in those aged 5 years or older for the year 2010.

See Online for webappendix

Although malaria deaths in children account for most malaria deaths, the number of deaths in adults is high (figure 6). Malaria deaths in individuals aged 15–49 years, 50–69 years, and 70 years or older account for 20%, 9%, and 6% of malaria deaths in 2010, respectively. To substantiate our finding of a large number of adult malaria deaths, we examined vital registration data from 1920 to 1980, all the data from 1980 to 2010 included in this study, hospital mortality data provided directly by eight Ministries of Health, and data from other published studies.[48] On the basis of all these sources that cover all age ranges and have more than five malaria deaths for a given year, the median percentage of deaths of individuals older than 15 years is 58% for sub-Saharan Africa, 76% for Asia, and 69% for the Americas (figure 7). With few exceptions, the proportion of malaria deaths in adults is almost always more than 40%. The exceptions are sub-Saharan African countries, most with high malaria transmission. Data from ten Tanzanian hospitals in lower transmission areas in 2002 is an outlier, showing 11% of deaths in adults.[48] As expected, in countries with historically decreasing malaria risk—Guyana, Sri Lanka (including when it was Ceylon), Thailand, and El Salvador—the proportion of deaths in adults increases with time (webappendix).

We reran regressions with only the MAP 2007 *Pf*PR as a covariate using the original VA data and the adjusted VA data for VA misclassification. The coefficient on *Pf*PR is higher with the adjusted VA data for all forms of the regression in sub-Saharan Africa (table 5). A higher coefficient on the *Pf*PR translates into greater estimates of malaria mortality; therefore, our sensitivity analysis suggests that misclassification in VA leads to underestimation of malaria mortality overall.

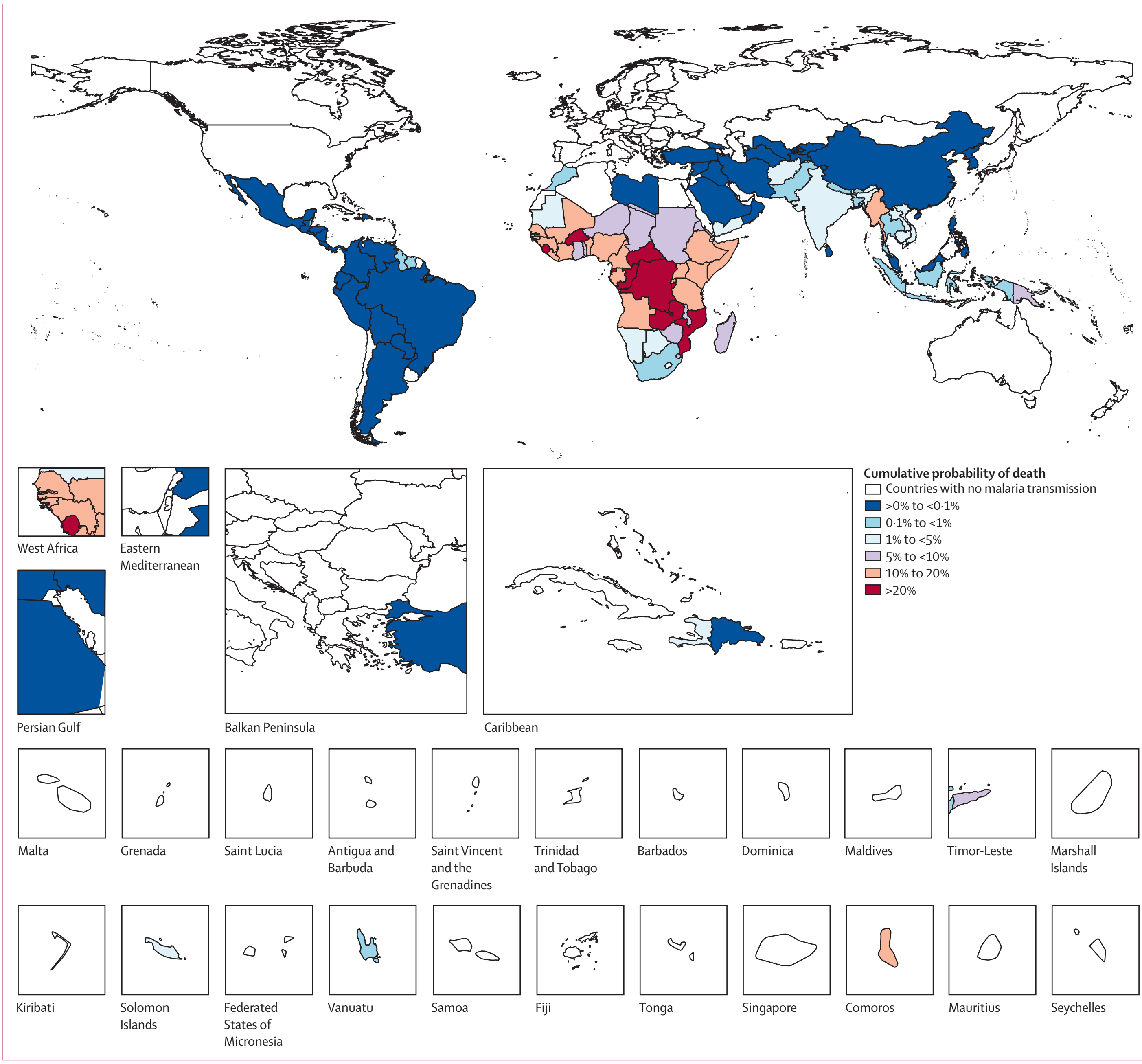

Figure 4: **Cumulative probability of dying from malaria in the absence of all other causes from birth to age 80 years in 2000**

Discussion

Our findings show that malaria is the underlying cause of death for 1·24 million individuals, including 714 000 children younger than 5 years and 524 000 individuals aged 5 years or older in 2010. During the past 5 years, substantial progress has been made in the fight against malaria, with a 31% reduction in global malaria deaths. Our findings show substantially more deaths across all ages and regions than the World Malaria Report 2011[21] assessment for 2010: 1·3 times higher for children younger than 5 years in Africa, 8·1 times higher for those aged 5 years or older in Africa, and 1·8 times higher for individuals of all ages outside of Africa.

When assessed as the proportion of deaths of children younger than 5 years due to malaria in Africa, the difference with previous estimates is even greater (panel). In 2008, we estimate that 24% of child deaths in Africa are due to malaria compared with the 16% reported by Black and colleagues,[49] whose methods were

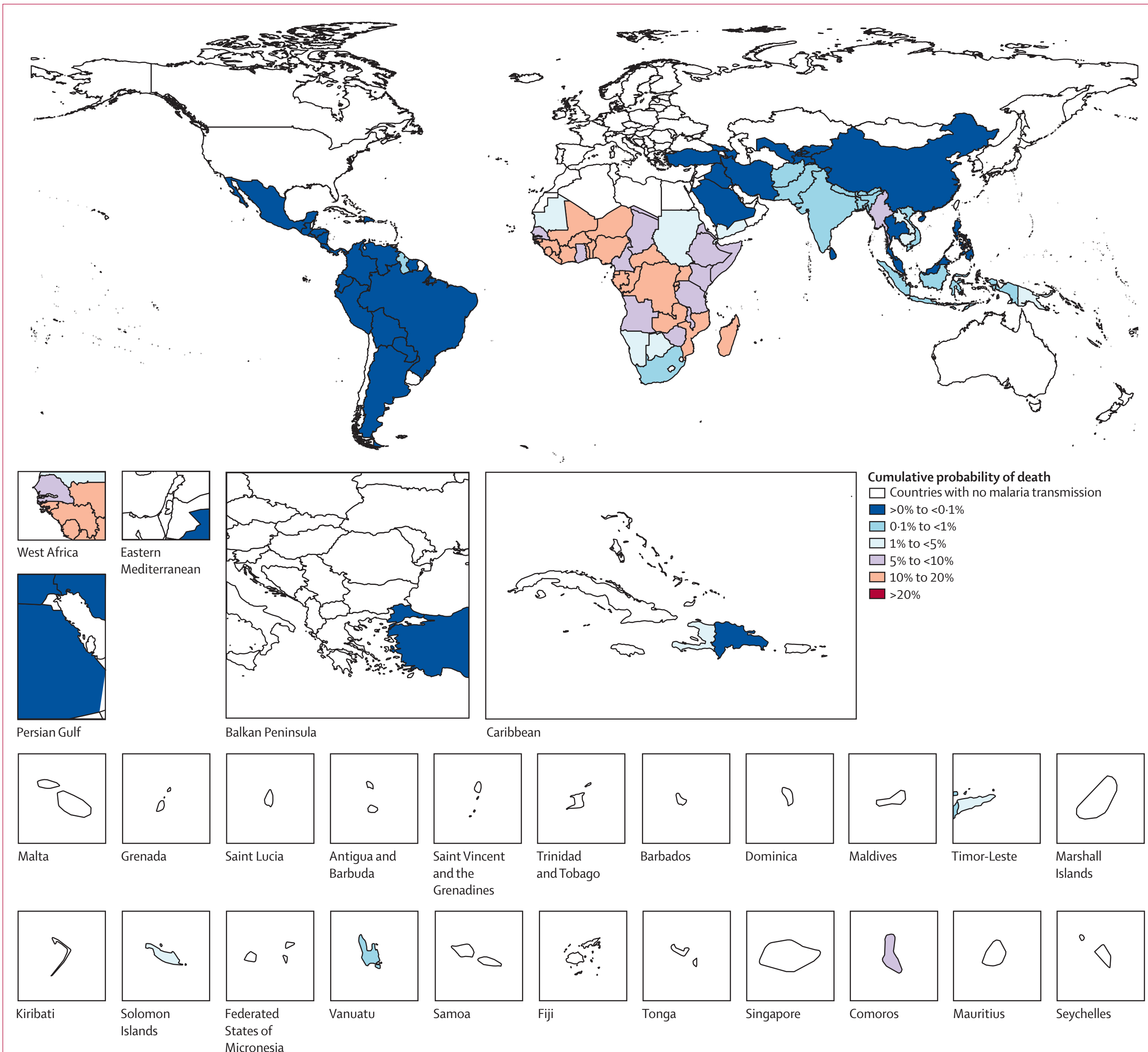

Figure 5: **Cumulative probability of dying from malaria in the absence of all other causes from birth to age 80 years in 2010**

used in deriving the World Malaria Report estimates. This discrepancy is attributable to both the larger numbers of malaria deaths in our analysis and the fact that we use child mortality estimates using a systematic analysis that suggests fewer deaths from all causes than did sources used by Black and colleagues.[27] Furthermore, previous studies have not taken advantage of the MAP *Pf*PR estimates, included the effect of interventions other than vector control, or developed models with rigorous out-of-sample predictive validity. However, much uncertainty exists around our estimates; child mortality due to malaria in sub-Saharan Africa ranges from 415 000 to 1·11 million in 2010.

The important finding of this study is that 433 000 more deaths occurred worldwide in individuals aged 5 years or older in 2010 than was suggested by WHO estimates.[21] Traditional teaching in most medical and public health schools argues that acquired immunity in mesoendemic and hyperendemic areas means that adults have clinical malaria but are not likely to die from it. Inspection of the basic VA, VR, and hospital data, however, clearly shows a substantial percentage of malaria deaths in individuals aged 15 years or older, even in endemic areas such as sub-Saharan Africa.

In addition to the greater numbers of adult malaria deaths, we also estimated 104 000 malaria deaths outside of Africa, despite continuous decreases in malaria mortality through enhanced malaria control in countries such as Malaysia, Thailand, the Philippines, and Brazil.[4,13,14,50,51] For India, the largest contributor to deaths outside of Africa, our estimates are less than those reported by Dhingra and colleagues[22] but are still much higher than those from WHO. One way to put the malaria mortality estimates outside of Africa into context is to divide malaria deaths in 2007 by the MAP *Pf*PR in 2007 multiplied by population size, which gives a rough estimation of the size of malaria mortality compared with a similar measure of malaria prevalence. This number per 1000 population is 1·6 for India, 2·2 for Cambodia, and 3·3 for Burma; in sub-Saharan Africa the mean of this indicator per 1000 population is 8·6. In other words, countries outside of Africa are not outliers in terms of deaths in view of the underlying malaria transmission risk.

There are two factors that could mean that malaria deaths might be higher than estimated in this study. First, our sensitivity analysis of VA misclassification suggests that there would be more malaria deaths if such misclassification were corrected for. Second, in our analysis we have measured only malaria as the underlying cause of death as defined by the ICD. Previous studies[52] show that malaria can exacerbate other causes of death.

Our estimates of malaria mortality trends over time are substantially different than those previously published. The World Malaria Report 2010 shows a continuous decrease in malaria deaths since 2000; WHO revised the trend in World Malaria Report 2011, such that there was a peak in malaria deaths in 2004 with decreases thereafter (figure 1). Outside of Africa, WHO estimates are based on case reports with an assumed case-fatality rate. For African countries, WHO estimates are based on a model of malaria mortality that takes into account only population growth and the effect of vector control—they do not, for example, include the effect of chloroquine resistance, the scale-up of artemisinin-combination treatment, environmental factors such as rainfall, or broader socioeconomic determinants. For sub-Saharan Africa, our estimates show that malaria deaths increased by three times through the 1980s and 1990s to a peak in 2004. Previous studies also show an increase in malaria deaths in this period of two to three times and have noted a temporal association with increasing chloroquine resistance.[53,54] In our final model, first-line antimalarial drug resistance is a prominent covariate and the likely driver of the

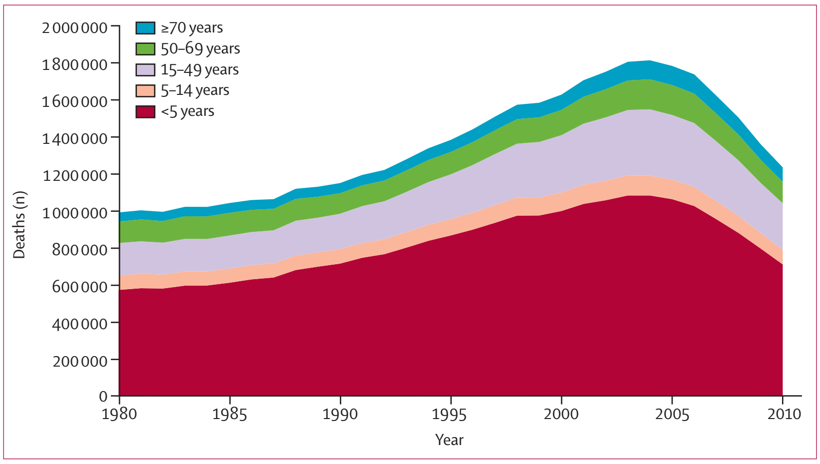

Figure 6: **Malaria deaths by age, 1980 to 2010**

malaria mortality rise in this period. Another possible explanation is the interaction between HIV infection and malaria, with studies suggesting that co-infection might cause many excess malaria cases compared with when HIV infection is absent.[55]

Since the global peak in 2004, there has been a substantial decrease in malaria deaths that is attributable to the rapid, although variable, scale-up of control activities in sub-Saharan Africa. This scale-up has been driven in part by an expansion in health aid targeted towards malaria[3] and suggests that the investments made by major funders such as the Global Fund to Fight AIDS, Tuberculosis and Malaria have rapidly decreased the burden of malaria. However, coverage of insecticide-treated bednets was not a statistically significant predictor of African adult malaria mortality; if bednets are also effective in the reduction of adult mortality, decreases in the past decade might be even more pronounced. Further research on the effect of control strategies, such as insecticide-treated bednets, on adult malaria morbidity and mortality is important. That antimalarial drug resistance led to a growing burden of malaria mortality that was reversed through the scale-up of artemisinin-combination treatment and vector control strategies underscores the importance of addressing the development of both artemisinin and insecticide resistance, which have been identified in several countries.[56,57]

Our finding that malaria mortality has been systematically underestimated has substantial implications for the allocation of health resources. With a substantially larger proportion of malaria deaths of children younger than 5 years in Africa (about 24% of child deaths in 2010), combating malaria should be a central strategy to achieving the fourth Millennium Development Goal. That malaria is a previously unrecognised driver of adult mortality also means that the benefits and cost-effectiveness of malaria control, elimination, and eradication are likely to have been

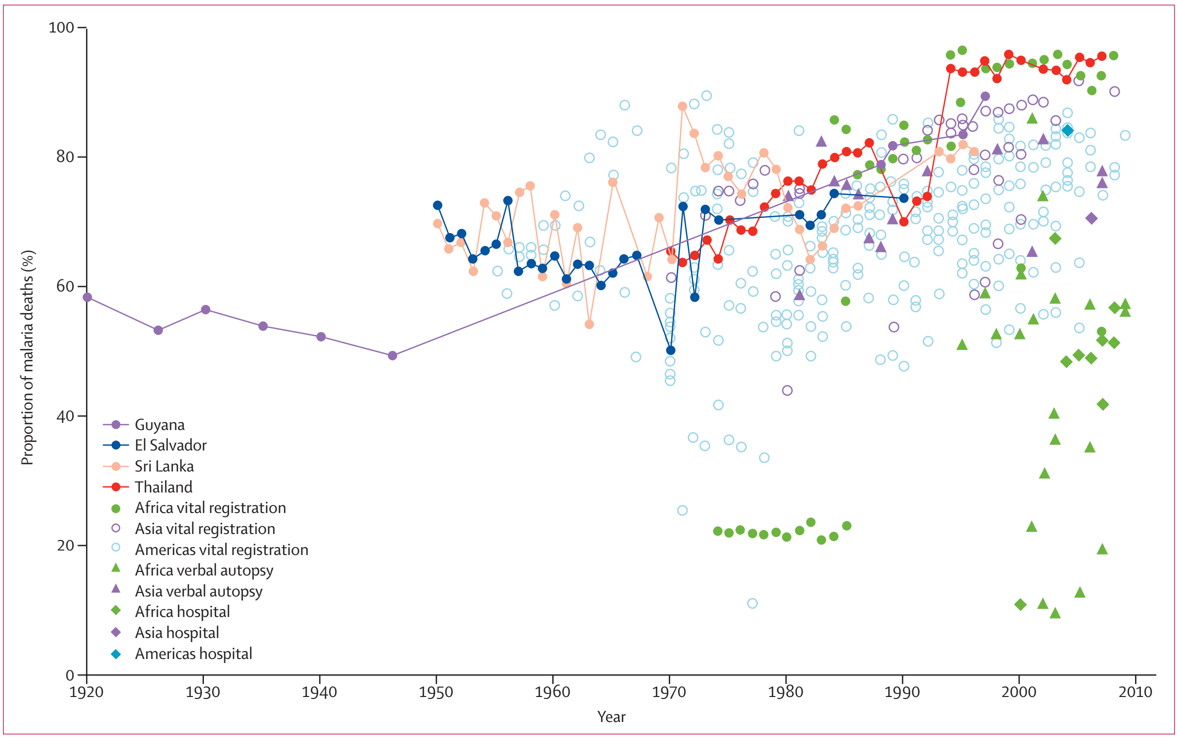

Figure 7: **Proportion of malaria deaths in individuals older than 15 years**

underestimated. Alternatively, more malaria mortality also means that short-term goals—eg, the reduction of malaria deaths to zero by 2015—might be unrealistic. We estimated that if decreases from the peak year of 2004 continue, malaria mortality will decrease to less than 100 000 deaths only after 2020. Our findings also signal a need to shift control strategies to pay more attention to adults—eg, they lend support to the strategy of universal coverage of insecticide-treated bednets among household members rather than focusing on women and children as was the case in the initial distribution campaigns.

The striking reversal of malaria mortality also underscores the dangers posed by the global economic crisis, which has led to a slowdown in the growth of funding for health.[58] The announcement by the Global Fund that round 11 of funding would be cancelled[59] raises enormous doubts as to whether the gains in malaria mortality reduction can be built on or even sustained. From 2003 to 2008, the Global Fund provided 40% of development assistance for health targeted towards malaria.[3] This reduction in resources for malaria control is a real and imminent threat to population health in endemic countries.

Our study is the most systematic assessment to date of malaria mortality but has several limitations. First, data for predictors of malaria mortality over time were restricted. The validity of our estimates could be strengthened substantially with the availability of additional time-series data such as *Pf*PR. Second, the data that underlie the covariates might be sparse or inaccurate. Estimates from Lysenko and Semashko[38] are low-resolution (at a crude geographical level) and based largely on expert opinion. The WHO estimates of populations at risk are similarly low-resolution and are based on potentially inaccurate case reports. Although the MAP estimates are high-resolution and survey-based, for countries outside of Africa the estimates are prone to large uncertainty and potential bias because they are based on older surveys that do not include

	Log (rate) models		Logit (cause fraction) models	
	Observed cause fraction	Corrected cause fraction	Observed cause fraction	Corrected cause fraction
Africa				
Girls younger than 5 years	1·53 (1·40–1·66)	1·72 (1·54–1·90)	1·16 (1·01–1·30)	1·45 (1·21–1·68)
Women and girls aged 5 years or older	0·98 (0·93–1·03)	1·12 (1·06–1·17)	1·00 (0·95–1·04)	1·16 (1·10–1·22)
Boys younger than 5 years	1·41 (1·28–1·54)	1·64 (1·47–1·82)	1·09 (0·95–1·24)	1·38 (1·16–1·61)
Men and boys aged 5 years or older	0·93 (0·88–0·97)	1·07 (1·02–1·13)	0·98 (0·94–1·03)	1·16 (1·10–1·22)
Outside of Africa				
Girls younger than 5 years	0·34 (0·30–0·38)	0·31 (0·27–0·35)	0·34 (0·30–0·37)	0·31 (0·28–0·35)
Women and girls aged 5 years or older	0·26 (0·24–0·28)	0·25 (0·23–0·27)	0·26 (0·25–0·28)	0·25 (0·24–0·27)
Boys younger than 5 years	0·34 (0·30–0·38)	0·31 (0·27–0·35)	0·33 (0·30–0·36)	0·30 (0·27–0·34)
Men and boys aged 5 years or older	0·27 (0·25–0·28)	0·26 (0·24–0·27)	0·27 (0·26–0·29)	0·26 (0·24–0·27)

Table 5: **Verbal autopsy sensitivity analysis for all models**

Panel: Research in context

Systematic review
We systematically searched for all available published and unpublished data on malaria mortality (see Methods section for search strategy). We used published results on malaria endemicity and used a systematic search of the published studies, grey literature, and analysis of survey micro-data to construct variables for first-line drug resistance, insecticide-treated bednet use, and indoor residual spraying. We used out-of-sample predictive validity testing to guide selection of the best models for predicting malaria mortality.

Interpretation
Past efforts to quantify the extent of malaria mortality have led to inconsistent and highly variable results. Estimates from the World Malaria Report 201121 suggest that the burden of malaria mortality is mainly borne by African children. This study, which is based on a systematic analysis of all available data with the latest empirical methods for estimating causes of death, suggests that there are about twice as many deaths than are estimated in the World Malaria Report 2011, with substantially more malaria deaths in adults in Africa and in both adults and children outside of Africa than previously recognised. Estimates of trends over time show that malaria deaths have increased by three times through the 1980s and 1990s, with subsequent declines driven by a rapid scaling-up of control efforts with crucial support from international donors. These findings emphasise the need to increase donor support to tackle malaria if elimination and eradication, as well as broader health and development goals, are to be met.

more recent control measures. The data for first-line drug use and indoor residual spraying are similarly sparse. Third, depending on the subnational population data used, national-level *Pf*PR can change substantially.[60] More accurate estimates of population distribution for Africa have been produced (available from the AfriPop Project), but these data are not available as a time series. Fourth, compared with causes such as maternal death, the data for malaria are sparse and mostly from subnational studies. As a consequence, far greater uncertainty surrounds the number of deaths due to malaria than death from other causes. Better surveillance of malaria mortality is clearly needed. Advances in low-cost, more accurate, and automated VA methods[61–63] suggest a bigger role for VA as an interim solution. For VR, the extent of misclassified deaths to garbage codes such as fever indicate a need to improve registration systems for assigning causes of death according to the ICD.

The scale of the health burden of malaria is far larger than previously thought, particularly the 524 000 deaths in individuals aged 5 years or older. Although malaria causes a larger and more widespread health burden than previously estimated, a rapid scale-up in malaria control with support from donors has reversed the once growing burden of malaria mortality. The present funding crisis, however, is an imminent threat to the gains that have been made. Efforts to combat malaria should continue to be a central focus if health and development goals such as the Millennium Development Goals are to be achieved.

Contributors
CJLM designed the methods and guided all aspects of this report. LCR contributed to methods development, implemented the statistical analysis, and assisted with the review of available studies. SSL guided the analysis of the data, wrote the first draft of the paper, and undertook revisions of the paper. KGA analysed the data and assisted with the review of available studies. KJF contributed to the methodological approach and statistical analysis for mortality data. DH assisted with the production of figures and tables, referencing, and review of available studies. NF analysed data for insecticide-treated bednet and indoor residual spraying coverage. MN mapped and redistributed mortality data. RL interpreted results, provided feedback, and contributed to the final draft of the paper. ADL provided conceptual and technical guidance and contributed to report revisions.

Conflicts of interest
We declare that we have no conflicts of interest.

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For the **AfriPop Project** see http://www.afripop.org/

References

1 United Nations News Service Section. UN envoy stresses malaria deaths can be eradicated, urges world to build on gains. http://www.un.org/apps/news/story.asp?NewsID=38185&Cr=malaria&Cr1 (accessed Aug 3, 2011).
2 Ravishankar N, Gubbins P, Cooley RJ, et al. Financing of global health: tracking development assistance for health from 1990 to 2007. *Lancet* 2009; **373:** 2113–24.
3 Institute for Health Metrics and Evaluation. Financing Global Health 2010: Development assistance and country spending in economic uncertainty. Seattle, WA: IHME, 2010.
4 WHO. World Malaria Report 2010. Geneva: World Health Organization, 2010. http://www.who.int/malaria/world_malaria_report_2010/worldmalariareport2010.pdf (accessed Aug 2, 2011).
5 Flaxman AD, Fullman N, Otten MW Jr, et al. Rapid scaling up of insecticide-treated bed net coverage in Africa and its relationship with development assistance for health: a systematic synthesis of supply, distribution, and household survey data. *PLoS Med* 2010; **7:** e1000328.
6 Strüchler D. How much malaria is there worldwide? *Parasitol Today* 1989; **5:** 39–40.
7 WHO. World malaria situation in 1994. http://www.who.int/malaria/publications/atoz/wer7236-37-38/en/index.html (accessed Aug 2, 2011).
8 WHO. The world health report 1999—making a difference. http://www.who.int/whr/1999/en/index.html (accessed Aug 5, 2011).
9 Snow RW, Guerra CA, Noor AM, Myint HY, Hay SI. The global distribution of clinical episodes of *Plasmodium falciparum* malaria. *Nature* 2005; **434:** 214–17.

10 Korenromp E. Malaria incidence estimates at country level for the year 2004—proposed estimates and draft report. http://www.rbm.who.int/docs/incidence_estimations2.pdf (accessed Aug 2, 2011).

11 Hay SI, Okiro EA, Gething PW, et al. Estimating the global clinical burden of *Plasmodium falciparum* malaria in 2007. *PLoS Med* 2010; **7:** e1000290.

12 WHO. World Malaria Report 2005. http://www.who.int/malaria/publications/atoz/9241593199/en/index.html (accessed Aug 5, 2011).

13 WHO. World Malaria Report 2009. http://www.who.int/malaria/world_malaria_report_2009/en/index.html (accessed Aug 2, 2011).

14 WHO. World Malaria Report 2008. http://www.who.int/malaria/publications/atoz/9789241563697/en/index.html (accessed Aug 2, 2011).

15 WHO. Global Burden of Disease (GBD) 2000 estimates. http://www.who.int/healthinfo/global_burden_disease/estimates_regional_2000/en/index.html (accessed Aug 2, 2011).

16 WHO. Global Burden of Disease (GBD) 2001 estimates. http://www.who.int/healthinfo/global_burden_disease/estimates_regional_2001/en/index.html (accessed Aug 2, 2011).

17 WHO. Global Burden of Disease (GBD) 2002 estimates. http://www.who.int/healthinfo/global_burden_disease/estimates_regional_2002/en/index.html (accessed Aug 2, 2011).

18 WHO. The global burden of disease: 2004 update. http://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/index.html (accessed Aug 2, 2011).

19 Murray CJL, Lopez AD. The Global Burden of Disease: A comprehensive assessment of mortality and disability from diseases, injuries, and risk factors in 1990 and projected to 2020. Harvard School of Public Health.

20 WHO. Global burden of disease (GBD) 2008. http://www.who.int/healthinfo/global_burden_disease/ estimates_regional/en/index.html (accessed Aug 2, 2011).

21 WHO. World Malaria Report 2011. http://apps.who.int/malaria/world_malaria_report_2011/en/index.html (accessed Dec 13, 2011).

22 Dhingra N, Jha P, Sharma VP, et al, and the Million Death Study Collaborators. Adult and child malaria mortality in India: a nationally representative mortality survey. *Lancet* 2010; **376:** 1768–74.

23 Hay SI, Gething PW, Snow RW. India's invisible malaria burden. *Lancet* 2010; **376:** 1716–17.

24 Shah NK, Dhariwal AC, Sonal GS, Gunasekar A, Dye C, Cibulskis R. Malaria-attributed death rates in India. *Lancet* 2011; **377:** 991, author reply 994–95.

25 Hay SI, Guerra CA, Gething PW, et al. A world malaria map: *Plasmodium falciparum* endemicity in 2007. *PLoS Med* 2009; **6:** e1000048.

26 Hogan MC, Foreman KJ, Naghavi M, et al. Maternal mortality for 181 countries, 1980–2008: a systematic analysis of progress towards Millennium Development Goal 5. *Lancet* 2010; **375:** 1609–23.

27 Rajaratnam JK, Marcus JR, Flaxman AD, et al. Neonatal, postneonatal, childhood, and under-5 mortality for 187 countries, 1970–2010: a systematic analysis of progress towards Millennium Development Goal 4. *Lancet* 2010; **375:** 1988–2008.

28 Rajaratnam JK, Marcus JR, Levin-Rector A, et al. Worldwide mortality in men and women aged 15–59 years from 1970 to 2010: a systematic analysis. *Lancet* 2010; **375:** 1704–20.

29 Lim SS, Fullman N, Stokes A, et al. Net benefits: a multicountry analysis of observational data examining associations between insecticide-treated mosquito nets and health outcomes. *PLoS Med* 2011; **8:** e1001091.

30 Lengeler C. Insecticide treated bednets and curtains for malaria control. *Cochrane Database Syst Rev* 1999; 1.

31 Foreman KJ, Lozano R, Lopez AD, Murray CJ. Modeling causes of death: an integrated approach using CODEm. *Popul Health Metr* 2012; **10:** 1.

32 Forouzanfar MH, Foreman KJ, Delossantos AM, et al. Breast and cervical cancer in 187 countries between 1980 and 2010: a systematic analysis. *Lancet* 2011; **378:** 1461–84.

33 Feachem RG, Phillips AA, Hwang J, et al. Shrinking the malaria map: progress and prospects. *Lancet* 2010; **376:** 1566–78.

34 Murray CJL, Rajaratnam JK, Marcus J, Laakso T, Lopez AD. What can we conclude from death registration? Improved methods for evaluating completeness. *PLoS Med* 2010; **7:** e1000262.

35 Korenromp EL, Williams BG, Gouws E, Dye C, Snow RW. Measurement of trends in childhood malaria mortality in Africa: an assessment of progress toward targets based on verbal autopsy. *Lancet Infect Dis* 2003; **3:** 349–58.

36 Rowe AK, Rowe SY, Snow RW, et al. The burden of malaria mortality among African children in the year 2000. *Int J Epidemiol* 2006; **35:** 691–704.

37 Naghavi M, Makela S, Foreman K, O'Brien J, Pourmalek F, Lozano R. Algorithms for enhancing public health utility of national causes-of-death data. *Popul Health Metr* 2010; **8:** 9.

38 Lysenko A, Semashko I. Geography of malaria. A medico-geographic profile of an ancient disease. In: Itogi Nauki: Medicinskaja Geografija. Moscow, USSR: Academy of Sciences, 1968. 25–146.

39 Hay SI, Guerra CA, Tatem AJ, Noor AM, Snow RW. The global distribution and population at risk of malaria: past, present, and future. *Lancet Infect Dis* 2004; **4:** 327–36.

40 Hay SI, Smith DL, Snow RW. Measuring malaria endemicity from intense to interrupted transmission. *Lancet Infect Dis* 2008; **8:** 369–78.

41 Gakidou E, Cowling K, Lozano R, Murray CJL. Increased educational attainment and its effect on child mortality in 175 countries between 1970 and 2009: a systematic analysis. *Lancet* 2010; **376:** 959–74.

42 Ringwald P. Susceptibility of *Plasmodium falciparum* to antimalarial drugs: report on globalmonitoring, 1996–2004. Suiza: World Health Organization, 2005.

43 WHO. Global report on antimalarial efficacy and drug resistance: 2000–2010. http://www.who.int/malaria/publications/atoz/9789241500470/en/ (accessed Aug 2, 2011).

44 Handcock MS, Wallis JR. An approach to statistical spatial-temporal modeling of meteorological fields. *J Am Stat Assoc* 1994; **89:** 368–78.

45 Landagan OZ, Barrios EB. An estimation procedure for a spatial-temporal model. *Stat Probab Lett* 2007; **77:** 401–06.

46 Brus DJ, Voshaar JHO, Knotters M. A comparison of kriging, co-kriging and kriging combined with regression for spatial interpolation of horizon depth with censored observations. *Geoderma* 1995; **67:** 227–46.

47 Lozano R, Lopez AD, Atkinson C, Naghavi M, Flaxman AD, Murray CJ, and the Population Health Metrics Research Consortium (PHMRC). Performance of physician-certified verbal autopsies: multisite validation study using clinical diagnostic gold standards. *Popul Health Metr* 2011; **9:** 32.

48 Reyburn H, Mbatia R, Drakeley C, et al. Association of transmission intensity and age with clinical manifestations and case fatality of severe *Plasmodium falciparum* malaria. *JAMA* 2005; **293:** 1461–70.

49 Black RE, Cousens S, Johnson HL, et al, and the Child Health Epidemiology Reference Group of WHO and UNICEF. Global, regional, and national causes of child mortality in 2008: a systematic analysis. *Lancet* 2010; **375:** 1969–87.

50 Trigg PI, Kondrachine AV. Commentary: malaria control in the 1990s. *Bull World Health Organ* 1998; **76:** 11–16.

51 Barat LM. Four malaria success stories: how malaria burden was successfully reduced in Brazil, Eritrea, India, and Vietnam. *Am J Trop Med Hyg* 2006; **74:** 12–16.

52 Snow RW, Korenromp EL, Gouws E. Pediatric mortality in Africa: *Plasmodium falciparum* malaria as a cause or risk? *Am J Trop Med Hyg* 2004; **71** (suppl)**:** 16–24.

53 Trape JF. The public health impact of chloroquine resistance in Africa. *Am J Trop Med Hyg* 2001; **64** (suppl 1–2)**:** 12–17.

54 Trape JF, Pison G, Spiegel A, Enel C, Rogier C. Combating malaria in Africa. *Trends Parasitol* 2002; **18:** 224–30.

55 Abu-Raddad LJ, Patnaik P, Kublin JG. Dual infection with HIV and malaria fuels the spread of both diseases in sub-Saharan Africa. *Science* 2006; **314:** 1603–06.

56 Dondorp AM, Nosten F, Yi P, et al. Artemisinin resistance in *Plasmodium falciparum* malaria. *N Engl J Med* 2009; **361:** 455–67.

57 Trape J-F, Tall A, Diagne N, et al. Malaria morbidity and pyrethroid resistance after the introduction of insecticide-treated bednets and artemisinin-based combination therapies: a longitudinal study. *Lancet Infect Dis* 2011; **11:** 925–32.

58 Leach-Kemon K, Chou DP, Schneider MT, et al. The global financial crisis has led to a slowdown in growth of funding to improve health in many developing countries. *Health Aff (Millwood)* 2012; **31:** 228–35.

59 The Lancet. The Global Fund and a new modus operandi. *Lancet* 2011; **378:** 1896.

60 Tatem AJ, Campiz N, Gething PW, Snow RW, Linard C. The effects of spatial population dataset choice on estimates of population at risk of disease. *Popul Health Metr* 2011; **9:** 4.

61 Murray CJ, James SL, Birnbaum JK, Freeman MK, Lozano R, Lopez AD, and the Population Health Metrics Research Consortium (PHMRC). Simplified Symptom Pattern Method for verbal autopsy analysis: multisite validation study using clinical diagnostic gold standards. *Popul Health Metr* 2011; **9:** 30.

62 Flaxman AD, Vahdatpour A, Green S, James SL, Murray CJ. Random forests for verbal autopsy analysis: multisite validation study using clinical diagnostic gold standards. *Popul Health Metr* 2011; **9:** 29.

63 James SL, Flaxman AD, Murray CJ, and the Population Health Metrics Research Consortium (PHMRC). Performance of the Tariff Method: validation of a simple additive algorithm for analysis of verbal autopsies. *Popul Health Metr* 2011; **9:** 31.