

MALARIA INCIDENCE ESTIMATES AT COUNTRY LEVEL FOR THE YEAR 2004 – PROPOSED ESTIMATES AND DRAFT REPORT -

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ABBREVIATIONS

AFRO = WHO region sub-Saharan Africa
API = annual parasite index = malaria infection incidence rate.
CFR = case fatality rate
CHERG = Child Health Epidemiology Reference Group
CHW = community health worker
CI = confidence interval
DALY = Disability-adjusted Life Year (lost)
DRC = Democratic Republic of the Congo
d.f. = degrees of freedom
DHS = Demographic and Health Survey
EIR = entomological inoculation rate
EMRO = WHO region Middle-East and North Africa
EURO = WHO region Europe
GDP = Gross Domestic Product
HIS = (routine) health information system
IPT = intermittent preventive therapy
IRS = indoor residual spraying
ITN = insecticide-treated mosquito net
LSHTM = London School of Hygiene & Tropical Medicine
MDG = Millennium Development Goals
MICS = Multiple Indicator Cluster Survey

PAHO/AMRO = WHO region Americas

P. falciparum/vivax = Plasmodium *falciparum/vivax*

PNG = Papua New Guinea

Pppa = per person per annum

RBM = Roll Back Malaria

RR = relative risk

SEARO = WHO region South East Asia

WHO/EIP = World Health Organization, Evidence & Information for Policy cluster

WPRO = WHO region Western Pacific.

SUMMARY

An estimation of the annual incidence of acute malaria episodes at country-level is proposed, to be used as the Millennium Development Goal (MDG) indicator malaria 'prevalence' and as the basis of malaria incidence numbers for the Global Burden of Disease by WHO/EIP. The estimation was based on populations at risk of malaria transmission in each country, multiplied with a fixed incidence rate for each given category of malaria endemicity, age group and separately for urban and rural areas, and reduced by an estimated local impact of ITNs and IRS based on national ITN and IRS coverage. Furthermore, for countries outside of Africa, incidence was constrained to be consistent with a case reporting completeness in the national health information system of between 1% and 100%.

Across 107 malaria-endemic countries, estimated incidence in 2004 totalled 402 million (range 350-500 million) cases, of which around 57% in AFRO and 30% in SEARO. This includes an estimated 311 million (range 270-400 million) cases of *falciparum* malaria, of which around 72% in AFRO and 19% in SEARO. These numbers is around 6-fold higher than cases globally recorded in national health information systems, or around 17-fold higher for non-African countries.

Country-specific incidence estimates, however, are for most countries very imprecise, because the national (historic) impacts of IRS and ITNs are not known, malaria endemicity distributions of countries were estimated very crudely, research studies used to infer basic incidence rates by endemicity may not have been generalizable, and the influence of urban residence was uncertain.

REQUIREMENTS

The following requirements were identified for the incidence estimations:

- The estimates must be an intuitively understandable unit of acute disease. Given that malaria infection, if untreated, can persist a long time after an episode of acute disease, and that malaria infections in immune individuals can pass entirely without illness, the incidence of acute episodes of malarial illness is preferable above the prevalence of infection. The estimates do not need to include indirect (comorbidity) effects or the possible sequelae of acute episodes. A simple statistical processing of data from HIS or research studies is preferable above complicated transmission models.
- The estimates must be useful:
 1. as the Millennium Development Goal (MDG) indicator malaria 'prevalence' (which denotes the morbidity site of the malaria burden) for all malarious countries;

2. for estimates of malaria morbidity in the Global Burden of Disease by WHO/EIP, by 5-year age group. If the unit is incidence rather than prevalence, it can subsequently be converted into DALYs by applying a certain average duration per episode.
- The estimation method should allow for regular (e.g. every two years) updating, to enable tracking of time trends in burden, of the impact of RBM, and of the progress toward the MDG of 'having halted by 2015 and begun to reverse the incidence of malaria'.
 - Estimates are to be made at the country level, for all countries with malaria. Ideally, the estimations should be replicable by the countries' statistical offices or national malaria control programmes themselves.

METHODS

Routine HIS data either on reported cases, or on case-fatality rates in conjunction with mortality data or estimates were judged to be not good enough to form the basis for the incidence estimations. As the basis instead is proposed to use an existing map of malaria transmission risk, in various endemicities (Background paper II and ¹), combined with an estimated fixed incidence rate for each endemicity category. The same basic incidence rates are applied for all countries, but country incidences are thereafter downward adjusted to account for the local impact of malaria prevention, according to the country-specific coverage of vector control measures.

Basic incidence rates

Table 1 summarizes the assumed basic incidence rates by world region, level of malaria endemicity, age group, on which the local impact of ITN and IRS was subsequently imposed at country level.

For the AFRO region excepting Southern Africa (see below), the basic incidence rate was estimated by CHERG/LSHTM for children under-five, based on 22 high-quality longitudinal studies of populations not benefiting from malaria prevention (Background paper I). In brief, studies began in 1980 or later, and malaria was defined as fever and malaria parasitemia on blood slide. For studies that analyzed only subperiods of a year, usually the high-transmission season, the incidence rate was converted to a year-round rate by assuming zero incidence for the months of the year which had not been studied. For studies that included only a sub-age group among the under-fives, incidence rates were converted to an overall under-five rate by applying the age pattern in malaria incidence found in five studies that reported fever incidence in 1-year age groups ^{2, 3, 4, 5, 6}. Twenty-one studies were from high-intensity transmission areas (defined as parasite prevalence $\geq 25\%$ or MARA climate suitability index ≥ 0.75), and one from a low-intensity transmission area (parasite prevalence $< 25\%$ and MARA climate suitability index between 0 and 0.75). For the high-transmission areas, in multivariate regression, incidence was higher in rural than in urban areas, and higher in areas with good access to safe water compared to poor access to safe water. No causal explanation was given for the latter association, and therefore we did not use this finding. In view of considerable differences in the proportion of urban population between the AFRO countries (from 6% in Rwanda to 65% in Congo), the urban-rural difference in malaria incidence was considered important. We therefore applied the estimated rates of 1.04 episodes per child per year for urban high-endemic areas and 0.60 for rural high-endemic areas. For low transmission areas, the one available study reported a rate of 0.991 pppa and this we applied for to all (urban and rural) low-transmission areas of all middle African countries.

For older age groups, existing rate estimates from Snow *et al.* ⁷ were used. For areas of high transmission intensity (defined as a MARA index of ≥ 0.75), estimated rates were 0.59 pppa for 5-14 years old 0.117 pppa for ≥ 15 years old. For low transmission intensity areas (defined as a MARA index of > 0 but < 0.75),

rates were 0.182 pppa for 5-14 years old and 0.091 pppa for >15+ years old. No urban/rural distinction was made.

For the Southern African countries Botswana, Namibia, South Africa, Swaziland and Zimbabwe, the above described approach of applying fixed incidence rates to all areas that are climatically ‘at risk’ would grossly overestimate actual malaria incidence, since large-scale and effective vector control has considerably reduced the areas of actual malaria transmission in this region^{8,9}. Because malaria case notifications are of reasonable completeness and quality in these countries⁹, we instead used the national malaria case notification rates averaged over the years 2001-2003. No adjustment for ITN or IRS coverage was applied to these rates as the impact of ITNs and IRS should already be reflected in the malaria case burden presenting to the health system.

Outside of AFRO, for populations at hyper-endemic and meso-endemic risk, basic incidence rates were estimated from an analysis of 40 community-based longitudinal studies of the incidence of malaria episodes (defined as fever symptoms + parasitemia) (Annex 1). In brief, available data were not comprehensive and representative enough to infer precise incidence rates, but they revealed as general patterns that incidence was higher in hyper-endemic than in meso-endemic areas (except possibly in adults), that incidence declined with age, at least in hyper-endemic areas, and that incidence was lower in urban than in rural areas. Starting from the two rate estimates that appeared to be most representative – 1.09 pppa for children in hyper-endemic rural settings and 0.45 for children in meso-endemic rural settings – corresponding rates for other age groups and urban settings were derived using a mixture of results from this regression model and from the analyses for AFRO described above. A ratio urban-to-rural of 0.3 was applied for all age groups in both endemicity categories.

For non-AFRO areas at hypo-endemic (including epidemic) risk, no longitudinal community-based incidence data were available. For epidemic areas in Africa, the average incidence rate has previously been estimated at 0.061 pppa, for all age groups, based on an estimated incidence of 0.976 per person during epidemics and an estimated frequency of epidemics for 3 months every 3 to 5 years¹⁰. We applied this rate to areas of hypo-endemic risk outside of AFRO, thus ignoring actual interannual variation in malaria incidence in countries due to epidemics.

For non-AFRO areas of holo-endemic risk, the only available four studies were from Papua New Guinea, and for children under-5. Since the pooled incidence rates for under-fives (0.96 pppa) was very similar to that in African high-endemic rural areas (see above), the AFRO rates were applied for all age groups.

Table 1. Assumed basic incidence rate, for the absence of malaria control through ITNs and IRS, by world region, endemicity category and age group.

<i>Region</i>	<i>Malaria endemicity</i>	<i>Age</i>	<i>Incidence rate (pppa)</i>		<i>Source</i>	
			<i>rural</i>	<i>urban</i>		
AFRO - Middle Africa	High endemic	Under-5	1.91	0.60	Estimates from community-based longitudinal studies (¹¹ and Background paper I).	
	Low endemic			0.50		
	High endemic	5-14 years		0.59		Estimates from community-based longitudinal studies ⁷ .
	Low endemic			0.18		
	High endemic	≥15 years		0.11		
	Low endemic			0.091		
Southern Africa	National	All ages	Country-specific, 4-		Passive case detection ⁹ + assuming that	

Region	Malaria endemicity	Age	Incidence rate (pppa)		Source
			rural	urban	
			fold the country-specific case rate reported in HIS.		HIS capture one-fourth of actual malaria cases in each country.
Outside of AFRO/sub-Saharan Africa	Holo-endemic		As Middle Africa		Similarity rate from 4 community-based longitudinal studies in under-5s in PNG and middle African under-5 estimate.
	Hyper-endemic	Under-5	1.09	0.33	Estimates from community-based longitudinal studies, see Annex 1.
		5-14 years	0.33	0.10	
		≥15 years	0.06	0.02	
	Meso-endemic	Under-5	0.45	0.14	
		5-14 years	0.45	0.14	
		≥15 years	0.30	0.09	
	Hypo-endemic areas	All ages		0.061	Estimate for African areas at epidemic risk ¹⁰ .

Influence of preventive measures

The basic incidence estimates based on research studies (Annex 1 and Background paper I) were, as per the reviews' eligibility criteria, for populations not subject to malaria preventive measures. To account for the impact of ITN and IRS in countries, the incidence rates of Table 1 were downward adjusted for each country with an estimated local impact of ITN or IRS. Local impact was defined as a fixed efficacy multiplied with the national intervention coverage. ITN coverage was derived from national household surveys (Annex 2). For some WPRO countries, ITN coverage was taken from reports by WPRO, which denote the proportion of the population at risk that was covered with ITN programmes.

Few data were available on IRS coverage, but reports of proportions of risk population covered by IRS from SEARO and WPRO were used. For 22 countries, IRS coverage could be estimated based on volumes of insecticides used for malaria vector control, assuming a specific application rate for each insecticide and average sprayable area per house (Annex 2). A further forty countries had IRS programmes in place but no coverage estimate could be made. For 7 of these for which the incidence estimate without accounting for IRS impact was more than 100 times larger than the case notification rate (mainly in EURO), we assumed IRS coverage to be 40%; for the remaining 33 countries assumed IRS coverage was 0%.

For countries with less than 100% of the population at risk, national-level coverage estimates were converted to coverage estimates for the population at risk by assuming that vector control was concentrated in households at risk.

Based on a recent Cochrane review¹², ITNs were assumed to reduce malaria incidence by 50% in stable endemic areas (applied to all risk areas in AFRO), and in areas of lower endemicity (applied to all countries outside AFRO), by 62% for *P.falciparum* and by 52% for *P.vivax*. The average coverage in these trials, defined as proportion of person-nights protected, was 60%. For extrapolation to countries, which all had less than 60% coverage, we calculated the impact of ITNs by assuming ITN impact to fall linearly with falling coverage. Lacking consensus on whether IRS is less or more efficacious than ITNs¹³, IRS was assumed to be equally efficacious as ITNs. Studies in the Solomon islands¹⁴, in a highland area of Kenya¹⁵, in Madagascar¹⁶ and in Pakistan¹⁷ found that IRS to be more effective than ITNs, but in

other studies in KwaZulu Natal (South Africa)^{18,19}, on the Solomon islands²⁰ and in Western India²¹ suggested the opposite.

In contrast to ITN and IRS, the possible impact of antimalarial treatment on malaria incidence was not considered, for two main reasons. First, most treatment strategies used in countries are expected to reduce mortality and disease but not transmission or incidence - except perhaps for artemisinin-based combination treatment if implemented at high coverage. Second, the coverages of prompt and effective antimalarial treatment at national levels is generally not known²².

Populations at risk

For AFRO, malaria risk was defined according to climatic suitability, as per the Mapping Malaria Risk in Africa (MARA) project estimate for the year 2002²³. In brief, long-term climate data was used to define the probability of malaria transmission, in terms of a "climate suitability index", ranging from 0 (unsuitable) to 1 (very suitable), at a resolution of 5x5 km². To allow extrapolation of the malaria incidence rates in African under-fives (Background paper I) to countries, areas with a MARA index greater than 0.75 were considered to be at high transmission risk, and areas with a MARA index greater than 0 but below 0.75 at low transmission risk.

Outside AFRO, an existing global map of malaria risk was used and updated, in which risk was stratified into 4 categories: holo-endemic, hyper-endemic, meso-endemic and hypo-endemic¹. Endemicity as used in this map (originally produced by Lysenko¹) is defined by the prevalence of parasitemia (of any species that affect humans) in children aged 2-10 years, with hypoendemic denoting <10% parasite prevalence, mesoendemic 11-50%, hyperendemic 51-75%, and holoendemic a prevalence among children aged 1 year of over 75%. Local endemicities according to available parasite prevalence surveys, which covered a small and discontinuous part of the world, were then extrapolated to the rest of the world, using expert opinion and global maps of temperature and rainfall²⁴. To reflect changes in endemicity since the 1950s and 1960s, when the Lysenko map was made, the outer boundaries of malaria risk was constraint by overlaying a WHO map of malaria risk for the year 2003²⁵. For the purpose of deriving country-level population distributions in these endemicity categories, the resulting map was overlaid with maps of population distribution, for the year 2004²⁶.

For 32 non-AFRO countries, a part of the population (median 12.4%) was left undefined because the original Lysenko map did not describe the endemicity level but there still is malaria according to the WHO 2002 map²⁵; for these, we redistributed the undetermined population equally over the categories 'no risk' and 'hypo-endemic risk'. For the Solomon Islands and Vanuatu, which were left undefined on the Lysenko map, we assumed 99% and 96%, respectively (as reported by WPRO), at risk and a distribution over endemicity categories as in PNG (Table 2).

Triangulation based on notified cases

For countries outside sub-Saharan, the risk-based incidence estimates were triangulated against case notification rates. Case notification rates were derived from reports to RBM averaged over the most recent three years (mostly 2000-2002 or 2001-2003). Reporting completeness (for years with a report made) was constrained to be between 1% and 100% in all non-AFRO countries. In other words, if the incidence estimate would imply a reporting completeness of below 1% or over 100%, that estimate was replaced by the number of reported cases multiplied with a factor 100 or 1.0, respectively. This adjustment may be seen as compensating for the impact of IRS or ITN in countries where coverage of these interventions was not known so assumed to be zero, or as a correction for a possible underestimate or overestimate of population at risk.

For AFRO, no constraints were placed on reporting completeness, for three reasons. First, in AFRO countries malaria diagnosis is often done presumptively without slide confirmation, so that overdiagnosis and consequent overreporting is conceivable. Second, in countries with laboratory confirmation of clinical diagnoses but high endemicity, overdiagnosis may still be possible since parasitemia may be asymptomatic and concurring with non-malarial fevers. Third, the HIS may function so poorly in some AFRO countries that a reporting completeness of below 1% is also conceivable.

Falciparum incidence

Based on the overall estimated incidence, the incidence of *falciparum* malaria was estimated for each country by applying the proportion of *falciparum* cases among cases reported in the national HIS in the year(s) **2002-4**. For sub-Saharan African countries that did not report cases by species, all malaria was assumed to be due to *Plasmodium falciparum*. The proportion of *falciparum* among diagnosed cases may be an overestimate of the true proportion *falciparum* among all incident cases in countries where laboratory confirmation is not done routinely and for example limited to the more severe, hospitalized cases.

RESULTS

Regional and global incidence estimate and distribution

Estimated incidence rates at country level for all age groups combined range from 0 to 0.48 malaria episodes per person per year (Table 2, Figures 1 and 2). Incidence rates were highest in AFRO, then in SEARO and EMRO (Figure 2b). A global total of 402 million cases were estimated for 2004, of which about 57% in AFRO and 30% in SEARO (Figure 2a). Of those cases, 311 million were attributed to *falciparum* malaria, of which 72% in AFRO and 19% in SEARO.

Within AFRO, most cases were estimated to occur in Nigeria, DRC, Tanzania, Uganda and Ethiopia (Figure 3a). The highest incidence rates were estimated for Niger, Burkina Faso, Guinea-Bissau, Guinea and Chad (0.48-0.53 pppa), but incidence rates were very high for many other AFRO countries (e.g. over 0.3 pppa for 27 countries, Figure 3b). Ethiopia had a lower estimated incidence rate (0.15 pppa) but many cases due to its large population size. The relative similarity in estimated incidence rates across AFRO countries reflects that many of them have close to 100% endemic risk, and coverage and impact of ITNs negligibly low.

Outside of AFRO, countries with most estimated cases include India, Indonesia, Pakistan, Myanmar, Bangladesh, Sudan and Viet Nam (Figure 3c). This ranking in part reflected the large population sizes of these countries. Countries with highest estimated incidence rates included Lao PDR, Myanmar, Cambodia, Solomon Islands, Honduras, Nicaragua, Suriname, Yemen, and Sudan (Figure 3d).

Big, malarious countries outside of Africa

For India, the estimate was 83 million cases, which would be consistent with an HIS reporting completeness of 2.5%. This estimate was based on an assumed 23% of the national population living at hypo-endemic risk, 41% at meso-endemic risk and 27% at hyper-endemic risk. The estimated ITN and IRS coverage among populations at risk in India were 20% and 40%, respectively; without the impact of ITN and IRS the estimate for India would have been 100 million cases higher.

For Indonesia, the assumed 23% of the national population living at hypo-endemic risk, 41% at meso-endemic risk and 27% at hyper-endemic risk would be consistent with a risk-based estimate of 19.2 million, 77 times higher than the case notification rate. No data were available on IRS coverage, which in

the risk-based approach was assumed zero, and may have contributed to an unrealistically high initial estimate.

23% of Myanmar's population was assumed to live at hypo-endemic risk and 65% at hyper-endemic risk. At negligible or unknown IRS and ITN coverage, this corresponded to an incidence estimate of 8.6 million, of which the HIS reporting completeness would have capture 2%.

Viet Nam was estimated to have around 5 million cases of which the HIS recorded an estimated 1%. ITN and IRS coverage were known to be around 17% and 19%, respectively.

The estimate for Pakistan, 10 million cases, was based on an assumed reporting completeness of 1%. IRS coverage has been estimated at 3.8%, but ITN coverage was unknown, which may have contributed to an overestimation by the risk-based approach. Alternatively, the assumed populations at risk (34% hypo-endemic, 42% meso-endemic and 6% hyper-endemic) may have been overestimates.

Age distributions

Across the 6 world regions, around 35% of cases were estimated to occur in children under-five, 36% in children aged 5-14 years, and 28% in adults over age 15 years (Figure 4a). In all world regions, the incidence rate declined with age (Figure 4b), but this decline was strongest in AFRO, as expected because of the relatively high endemicity (Figure 4c).

For AFRO, the estimated proportion of cases in under-fives was 44%, in comparison to 37% in age-specific HIS data from 22 countries. For SEARO, the estimated proportion of cases in under-fives was 24%, in comparison to a mean 10% in age-specific HIS data from 7 countries.

Coverage and impact of ITN and IRS

The coverage of ITN and IRS was known for 52 and 38 countries, respectively (Annex 2). In addition, IRS coverage was set at 40% in 7 countries where IRS is routinely used but no coverage estimate was available (Table 2). ITN coverage in populations at risk pooled across countries ranged from 0.13% to 73%, with a median of 3%. IRS coverage among populations at risk ranged from 0% to 40%, and if including the assumed 40% coverage for 7 countries, the median coverage in all countries with data would be 13%.

At these levels of coverage, ITN and IRS together were estimated to have prevented a minimum of 151 million additional malaria infections in the countries with a risk-based estimate; this is a minimum estimate of global prevention impact, because it does not include the impact in countries with HIS-based incidence estimates (for which the impact was included implicitly). Around 100 million cases were estimated to be prevented in India annually.

Reporting completeness

Of the 107 evaluated countries, for 9 (including five in Southern Africa) incidence could not be estimated because their population at actual risk was zero or undefined. Instead, incidence was estimated based on the HIS case notification rate, by assuming the median reporting completeness of countries with a risk-based incidence estimate in that WHO region. The imputed reporting completeness was 24% for AFRO (applied to the 5 Southern African countries, Algeria and Cape Verde), 11% for the EMRO country Egypt, and 9% for Uzbekistan in EURO.

Of the remaining countries, in AFRO the incidence estimate was consistent with a reporting completeness of over 100% for Burundi, Sao Tome & Principe and Tanzania, and this was left as such. Outside of

AFRO, for 9 countries the incidence estimate would be consistent with a reporting completeness of <1% (between 0.009% and 0.96%) and for these the estimate was replaced by 100* the notified cases to meet the constraint of $\geq 1\%$ reporting completeness. For 4 non-AFRO countries, the initial incidence estimate would be consistent with a reporting completeness of >100% (between 105% and 521%) and these were replaced by the notified cases to meet the constraint of $\leq 100\%$ reporting completeness.

With these corrections, the overall reporting completeness pooled across all countries would be 16% - in which overreporting in some countries compensated for underreporting in others. For non-AFRO countries, the overall reporting completeness would be 6%. This is lower than for AFRO because AFRO includes three countries with estimated reporting completenesses above 100% (Table 2). It must be noted that these estimates of reporting completeness refer to years for which the countries did report case numbers – if we would account for years with no reports, reporting completeness would be (even) lower.

Figure 5 shows the reporting completeness based on incidence estimates for selected countries, in comparison to earlier independent estimates of reporting completeness, mainly from SEARO and WPRO. For all fourteen countries, the currently estimated reporting completeness is lower than that estimated before. This may reflect that earlier completeness estimates were presumably based on the number of health facilities and districts reporting and/or the number of months for which cases were reported, and did not take into account cases missed because they did not access the health system at all.

SENSITIVITY ANALYSES

The estimation relied on a great number assumptions and sub-estimations, many of which were uncertain. In order to grasp the magnitude of the resulting uncertainty in the estimates, we re-estimated malaria incidence in a number of alternative scenarios which each differed in one parameter (Table 3). The chosen scenarios reflect that the largest quantitative uncertainties at regional and global levels were thought to lie in:

- proportion of non-AFRO national populations in different endemicity categories
- basic incidence rates
- for the 9 countries for which the incidence estimate was constrained to give a reporting completeness of at least 1%, the validity of this assumption.
- proportion of national populations that are urban
- IRS coverage and impact for the 40 countries with no survey-based coverage data available but IRS programmes in place.

In a first scenario (1a), for all non-AFRO countries, the estimates based on fixed incidence rates multiplied with populations at risk was replaced by 10 times the cases notified, i.e., assuming a fixed reporting completeness of 10%. The total number of cases would then be smaller (340 million) than under 'default' (402 million). For many individual countries, the number of estimated cases would either increase or decrease considerably, reflecting that the reporting completeness consistent with the default estimates varied widely between much less than 10% and much more than 10%. If we believe that a 10% reporting completeness is for all countries more likely than 1% or 100%, 'increased' country estimates in this scenario may be explained by epidemics or exceptional upsurges in malaria that occurred in recent years and would not be typical for the average level of endemicity in the particular country. 'Decreases' might in turn relate to a sudden large impact of improved malaria control if (preventive) measures were recently implemented at large scale but not yet reflected in survey-based coverage estimates.

Scenario 1b illustrated how much incidence estimates will increase if reporting completeness in non-AFRO countries was constrained at a maximum of 33% instead of 100%. Thirty-three per cent has earlier been proposed as a reasonable maximum completeness for these countries²⁷, and this would reflect that, even with complete reporting within the formal health system, there are always malaria cases that do not reach the health system or get treated in the informal sector or in private clinics which do not report. Assuming a maximum completeness of 33% increased the incidence estimate for the 4 countries, but since these were mostly low-malaria countries, so that the global incidence changed only slightly, from 402 to xxx million.

If, conversely, the risk-based incidence estimation was taken literally without any constraints on HIS reporting completeness (scenario 1c), the total number of estimated cases would become an impressive 899 million, of which much more (79%, compared to 43% under default) outside of AFRO. This increase reflects that the default incidence estimate would for many countries, and especially those with much malaria, be consistent with a reporting completeness of below 1%.

The estimated distributions of non-AFRO populations over the different malaria endemicity categories were not always in line with countries' own statement on malaria risk (Annex 3). If for each non-AFRO country, the minimum of the risk proportion between the default estimation and the country's own report was taken, the global total cases decreased to 307 million (scenario 2a). Conversely, if the maximum risk estimate was taken, the total cases would be slightly higher than default, namely yyy million (scenario 2b). Importantly, however, this range does not reflect the full uncertainty associated with estimated populations at risk, since the estimated endemicities may be wrong also for countries without own estimates, and scenarios 2a+b still applied the distribution over endemicity categories from the global Lysenko-based map on the countries' own estimate of total population at risk.

Scenarios 3 through 7 explored the sensitivity of estimates to the assumed basic incidence rates, in turn for under-fives in AFRO, over-fives in AFRO, and by level of endemicity outside of AFRO. We halved and doubled the assumed rates; this magnitude of variation was chosen considering the coefficients of variation (COV, i.e. standard error divided by point estimate) of the estimated rates¹. These must be considered as minimum indications of the true uncertainty, since they reflect only the uncertainty within the regression models and not the probable biases due to non-representativeness of the included research sites. Incidence estimates were most sensitive to the basic incidence rate for African over-fives: doubling and halving this rate shifted the global total cases to >484 million and >286 million, respectively (scenario 4). Second most critical was the basic incidence rate for African under-fives (scenario 3: range >336 to >423 million). In contrast, the basic incidence rate for hypo-endemic areas outside of Africa was not critical at global scale (scenario 5), because these areas contribute for only a very small part of total global cases; rates for meso-endemic and hyper-endemic areas outside of Africa were roughly equally important (scenarios 6 and 7: range ...-... million). The influence of varying the basic rates outside of AFRO was limited by the continued constraint of reporting completeness between 1% and 100% - due to which for many non-AFRO countries estimates were ultimately derived from case notifications and not from basic incidence rates (see column Remarks in Table 3).

Scenario 8a accounted for a lower incidence of malaria in urban areas^{28, 29} for the age and endemicity categories for which this distinction was not yet made under default: middle African under-fives in low-transmission areas, middle African over-fives, and all age groups at hypo-endemic risk outside of Africa. Urban rates were assumed to be 0.30-fold times the default rate, similarly to the urban-rural ratio

¹ For outside of AFRO, incidence rates derived from the analysis of research studies (Annex 1) had COV's of between 30% and 85%. For under-fives in AFRO, COV's were around 25%?

estimated for other age/endemicity categories (Table 1) and the default rate was applied to rural areas, since most relevant research studies came from rural areas^{7, 10} and Background paper 1). With 48% of the population of all malarious countries defined as urban (32% of AFRO and 51% of SEARO), the total incidence in this scenario was 321 million, without much shift in the distribution over world regions. Scenarios 8a and 8b illustrate how critical the assumed proportions of urban populations in the countries are: with double or half the default urban proportion (from UNPD), global incidence would change to XXX or YYY million, respectively.

Scenario 9 included an impact of untreated bed nets in addition to ITNs, at half the efficacy of ITNs, in line with data from a trial and two observational studies^{30, 31, 32}. This reduced the estimated incidence somewhat, to ZZZ million, without much change in the inter-regional distribution.

Scenario 10 concerned the IRS coverage in the 40 countries where IRS was used but no coverage estimate was available. If for 33 such countries (in addition to 7 others under default), IRS coverage was assumed to be 40%, the global incidence estimate would be ZZZ million. Conversely, if for the 7 countries the assumption of 40% coverage was dropped, estimated malaria incidence would be ZZZ million.

In scenario 11, the estimates for Somalia, Sudan and Djibouti, under default based on the basic incidence rates for outside AFRO (Table 1) was instead derived from the assumptions for middle Africa, since these countries lie on the fringe of the African area of stable malaria. Estimated cases increased by 1.8-fold in Sudan and by 4-fold for Djibouti. For Somalia, ... Estimates at regional and global scale were not changed.

UNCERTAINTY BOUNDS ON COUNTRY ESTIMATES

The sensitivity analyses showed that at regional and global levels, the largest uncertainties lie in:

- the validity of our constraintment of estimated reporting completeness at a minimum of 1% (applied for 9 non-AFRO countries).
- the basic incidence rates for middle Africa, especially for age groups over 5 years
- proportion of national populations in different endemicity categories
- proportions of national populations that are urban.

Several scenarios more than halved or more than doubled the incidence estimates for many individual countries (Table 3). Although our synthesis of methods and components in these estimations make it impossible to derive exact confidence intervals around country estimations, we can therefore safely conclude that all country estimates have an uncertainty bound around them of at least the value of the point estimate itself.

For some countries, the estimate was probably more certain than for others. Notably, a risk-based estimate may be considered more credible if it is consistent with a HIS reporting completeness of between 1% and 100%. Conversely, the following factors may make country estimates relatively more uncertain:

- if estimated proportion-at-risk based on the Lysenko map was very different from that reported by the country itself or regional office (Annex 3);
- if most of the population is divided over hypo-endemic risk and no risk, which were difficult to distinguish in the endemicity mapping (Background paper II);
- at the fringe between AFRO and EMRO;
- with considerable, but unquantified IRS coverage;

- small (island) countries or countries with very low endemicity, for which no risk-based estimate could be made.

The relative level of certainty of country estimates according to these criteria is indicated in the last column of Table 2. The majority of countries meet at least one of the 'uncertainty criteria'.

HOW TO UPDATE THE ESTIMATES FOR A NEXT MDG REPORTING ROUND?

The input parameters that will lead to updates in incidence estimates depend on the estimation method. For countries with a risk-based estimate, trends in national-level ITN or IRS coverage and in the proportion of the population that is urban will lead to updates in estimated incidence rates. Trends in the proportion of the population that is at risk of malaria transmission would change the estimated incidence rate and number, although changes in endemicity may in the short term be unlikely. With updates of populations at risk, extreme care would have to be taken not to spuriously conclude upon time trends if the update represents a changed risk definition or method rather than a true time trend.

For countries with incidence estimated based on an assumed 1% or 100% reporting completeness, the basis for updating is not obvious. Because HIS reporting completeness may change over time, the trend in case notifications may not be valid. For the short term, it is proposed to instead apply the trend in national-level ITN or IRS coverage, in the proportion of population that is urban and in the population at risk, just as for countries with a risk-based estimate. If, e.g. over a longer period, the case notification rate shows a consistent and large upward or downward trend for any such country which cannot be explained from data on ITN and IRS coverage, urbanicity and population at risk, application of that trend to the incidence estimate may be considered, although the preferred method is to get the appropriate inputs for risk-based estimates for all countries.

For all countries, irrespective of the estimation method, population growth will lead to updated estimates of absolute numbers of incident cases. Updates in *falciparum* incidence will follow from the update in overall estimated cases and the trend in proportion of HIS cases that is recorded as *falciparum*.

DISCUSSION

Based on national populations at risk, fixed 'basic' incidence rates for different malaria endemicity categories and national coverages with ITN and IRS, we estimated the annual incidence of acute malaria episodes for 107 malarious countries. Country incidences are consistent with a global total of 40 million malaria cases in 2004, of which 57% in AFRO and 30% in SEARO. These include an estimated 311 million cases of *falciparum* malaria, of which 72% in AFRO and 19% in SEARO. Striking outcomes include:

- Only 57% of malaria episodes, and 70% of *falciparum* episodes, were estimated to occur in AFRO (Figure 2). In comparison, for 2001 EIP/WHO estimated a global total of 396 million cases (range 300-500, all species combined³³), of which 86% in AFRO³⁴.
- For non-African countries especially in WPRO and SEARO, we estimated considerably coverage of actual malaria cases in the national HIS than those countries or the regional office themselves estimate (Figure 4).

- A positive correlation was found between the estimated incidence rate and the proportion of *falciparum* cases among malaria cases reported in the HIS (Figure 6). The existence of such a relationship is generally accepted; it arises because *P. falciparum* flourishes and overwhelms *P. vivax* where transmission conditions are most intense and advantageous to the parasites, whereas under harsher conditions (including successful malaria control), *P. falciparum* fades before the more robust *P. vivax*²⁷. Importantly, the correlation with the proportion of *falciparum* cases was much more pronounced for the estimated incidence (Figure 6b) than for the case notification rate from HIS (Figure 6a). This finding might be seen as support for the usefulness of the estimates to replace the case notifications, as MDG indicator etc..
- A positive correlation was found between the estimated incidence rate and the proportion of cases in the under-5 age group cases reported in the HIS (Figure 7). The existence of such a relationship is plausible, because at higher endemicity proportionally more cases occur in young children. The correlation between incidence rate and proportion of cases in under-5s was stronger for incidence estimates (all species or *falciparum* specifically, Figure 7b+c) than for the case notification rate from HIS (Figure 7a). This finding might be seen as support for the usefulness of the estimates to replace the case notifications, as MDG indicator etc..
- If we compare the estimated global malaria incidence (402 million) with estimates of the global mortality (directly) attributed to malaria (0.7 to 3 million deaths annually³⁵), a case fatality rate (CFR) of between 0.2% and 0.75% results. For AFRO, the CFR corresponding to our incidence estimate would be 0.40% (900,000 deaths¹⁰ out of 226 million cases or 221 million *falciparum* cases), consistent with previous CFR estimates³⁶. Outside AFRO, the CFR corresponding to the incidence estimates is between 0.06% and 0.09% for all species combined (100-150,000 deaths **Reference** out of 172 million cases), and 0.12% to 0.17% (100-150,000 deaths out of 86 million cases) for *falciparum* malaria assuming that all malaria deaths are attributable to *falciparum* episodes. These non-AFRO CFRs are in the (lower) range of previous estimates, such as, for *falciparum* malaria in non-AFRO endemic countries, 0.01-0.3%²⁷ or 'up to 1%'³⁶.

Advantages and limitations

Advantages of the proposed method include, first, that it can be updated with data from countries (Table 4), that the estimation is relatively simple and transparent and that it can be performed, updated and checked within one spreadsheet. However, the country incidence estimates are very imprecise. Specific major limitations are:

1. The 'model' is not one single homogeneous method. First, the basic incidence rates for different world regions, endemicities and age groups were based on slightly different methods (Table 1), and for endemic areas outside AFRO, are mere guesstimates since available research studies probably grossly oversampled high-transmission areas. Second, for many countries the risk-based estimate was so much higher than the case notifications (over 100 times higher) that we replaced it by 100 times the case notification rate, which is a very crude and arbitrary estimate.
2. The country estimates depend critically on the assumed national populations living at different endemicities, and these were known only very imprecisely. Risk estimates were in part based on the malaria situation in the 1950s and 1960s, or historic expert opinion on this, and that situation was especially in South-East Asia much worse than now. Specific limitations of the risk distributions and possible solutions are discussed in Background paper II and in the next section point (a).

3. We may have underestimated the impact of control measures, and thereby overestimated malaria incidence, for certain countries. In particular, the impact of IRS may be larger than we allowed for, first, if the long-term impact of IRS in low-to-moderate endemic areas would be greater than that derived from short-term ITN efficacy. Second, data on IRS coverage were scarce and coverage was assumed to be 0 for countries without data. Third, the incidence estimates did not take into account the transmission reduction potentially accomplished by artemisinin-based combination therapy in selected countries. In Thailand, large-scale implementation of artemisinin-based combination therapy has been shown to reduce disease incidence by a significant amount^{37, 38}. Also the impact of environmental management³⁹ was not accounted for, apart from possible long-term effects that would have translated into a smaller population at risk. It is of note that also for ITNs true efficacy might be larger than we assumed, because existing efficacy estimates are based on short-duration intervention trials¹² in areas where high coverage in the longer term might lead to a reduction in transmission. However, given the low current coverage of ITNs (Table 2) this is unlikely to make substantial difference to the estimates for 2004.
4. The impact of urban environment in reducing malaria incidence was not taken into account for all age groups and endemicities in middle Africa, specifically not for children under-five in low endemic areas, and for those aged over 5 years at all endemicities. This resulted in a seeming inconsistency that the assumed incidence rate in urban middle Africa was higher for under-5s in areas at low endemicity (0.911 pppa) compared to high endemicity (0.60 pppa, Table 1). Furthermore, the use of proportions of national populations that are urban as available from the United Nations Population Division (UNPD) may be questioned. These are based on definitions from the countries themselves, which vary between countries and may be based on administrative units, size and population density, functional characteristics (e.g. majority of economic activity non-agricultural) or no definition whatsoever⁴⁰. The large differences in proportions urban, e.g. between 6% in Rwanda and 65% in Congo, may in part reflect differences in definitions rather than true differences in urbanicity, which would invalidate the estimated malaria incidence differences between these countries. Probably not all of the UNDP-denoted 'urban' population is truly as urban as the population in urban research studies (Annex I and Background paper I), in which case we may have underestimated incidence.
5. The approach of applying fixed average incidence rates does by definition not reflect annual fluctuations in malaria burden, in particular epidemics, as occur especially in hypo-endemic areas.
6. The estimation is not a formal statistical approach, and does not provide confidence intervals or ranges.

POSSIBLE IMPROVEMENTS AND NEXT STEPS

- a) Improve country endemicity distributions using population distribution databases at 1 km² resolution (instead of current 5x5 km²) and by urban-rural division, reflecting the local impact of altitude, and updated information from WHO/RBM on the boundaries of stable transmission in specific countries with large spatial heterogeneity in malaria transmission. Do in-depth analysis for specific countries with ambiguities and much malaria (India, China, Mexico, Colombia, Venezuela, Malaysia...). Explore the use of case notification data to 'validate' population endemicity distributions:
 - For countries where the age distribution (under 5 years versus over 5 years) in notified cases is recorded, this might be used to estimate, or confirm, the intensity of transmission.
 - The mid-point of the parasite prevalence levels that define the different endemicity categories should not exceed the slide positivity rate in HIS data at administrative 1 (i.e. provincial)

level?

- b) Add IRS coverage estimates based on country data forthcoming from WHOPEPES.
- c) Triangulate or cross-validate estimates by comparing the estimated reporting completeness with independent estimates of reporting completeness, where available. Reporting completeness could be independently estimated as the proportion of districts reporting and/or months of the year with complete reporting. Several countries, including China, have already done their own surveys to assess completeness.

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Table 2. Country estimations of malaria incidence (pppa).

Country	% urban	Population at risk of malaria transmission		Case notification rate (pppa)	% falciparum among notified cases	ITN coverage ^{&&} (in population at risk)	IRS coverage	Estimates		Cases	Relative certainty of estimate [%]
		Low risk	High risk					Reporting completeness	Incidence rate		
Algeria	58%			1.4E-05	61%			24%*	0.00001	1,880	Very uncertain
Angola	34%	53%	46%	0.12	100%	2.3%	0.2%	35%	0.33	4,683,567	
Benin	42%	0%	100%	0.12	100%	7.4%		27%	0.43	2,957,739	
Botswana	49%	26%	13%	0.019	100%		68% ^{&}	24%*	0.02	140,706	Very uncertain
Burkina Faso	17%	0%	100%	0.10	100%	12.4% ^{SS}		20%	0.50	6,713,298	
Burundi	9%	64%	21%	0.40	100%	1.5%		176%	0.23	1,617,538	
Cameroon	49%	24%	74%	0.056	100%	1.4%		17%	0.34	5,577,081	
Cape Verde	62%			0.00016			**	24%*	0.00016	324	Very uncertain
Central African Republic	41%	0.1%	99.9%	0.033	100%	1.5%		8%	0.43	1,692,141	
Chad	24%	14%	86%	0.049	100%	0.6%		10%	0.48	4,237,526	
Comoros	33%	50%	50%	0.011	95%	9.3%	**	4%	0.29	229,872	
Congo	65%	0%	100%	0.004	100%		**	1%	0.42	1,604,461	
Côte d'Ivoire	44%	0%	100%	0.062	100%	1.1%		15%	0.41	6,948,136	
DRC	30%	10%	85%	0.017	100%	0.7%		4%	0.45	24,533,262	
Equatorial Guinea	48%	2%	97%	0.039	100%	0.7%		9%	0.43	218,160	
Eritrea	19%	83%	16%	0.023	57%	63%	10%	25%	0.09	397,169	
Ethiopia	16%	50%	14%	0.006	57%		11.3%	4%	0.15	10,802,430	
Gabon	81%	0%	96%	0.060	100%	1.9%		19%	0.32	431,554	
Gambia	31%	0%	100%	0.20	100%	14.7%		52%		567,334	

Country	% urban	Population at risk of malaria transmission		Case notification rate (pppa)	% falciparum among notified cases	ITN coverage ^{&&} (in population at risk)	IRS coverage	Estimates		Cases	Relative certainty of estimate [%]
		Low risk	High risk					Reporting completeness	Incidence rate		
Ghana	36%	2%	98%	0.16	100%	3.5%		40%	0.39		
Guinea	28%	1%	99%	0.105	100%	0.5% ^{SS}		22%	0.40	8,545,020	
Guinea-Bissau	32%	0%	100%	0.15	100%	7.4%		32%	0.48	4,127,792	
Kenya	33%	57%	21%	0.0035	100%	5.5%	1.1%	2%	0.48	736,670	
Liberia	45%	0%	100%	0.25	100%		0% ^{&}	53%	0.18	5,805,201	
Madagascar	30%	36%	60%	0.12	100%	0.2%	4%	34%	0.47	1,646,761	
Malawi	15%	22%	77%	0.28	100%	2.5%		62%	0.35	6,183,112	
Mali	30%	10%	90%	0.009	100%	8.6%		2%	0.45	5,523,708	
Mauritania	58%	59%	41%	0.082	100%			30%	0.46	6,176,816	
Mozambique	32%	4%	96%	0.15	100%	3.5% ^{SS}	13%	39%	0.28	827,983	
Namibia	31%	76%	8%	0.27	100%		84% ^{&}	24%*	0.39	7,546,147	Very uncertain
Niger	21%	11%	89%	0.058	100%	1.0%		11%	0.27	2,230,989	
Nigeria	44%	1%	99%	0.020	100%	1.2%		5%	0.53	6,539,322	
Rwanda	6%	60%	7%	0.12	100%	9.7%	1.3%	84%	0.44	55,623,433	
Sao Tome & Principe	47%	85%	15%	0.30	95%	22.8%		174%	0.14	1,159,660	
Senegal	47%	3%	97%	0.12	100%	1.7%	6.5%	30%	0.17	28,203	
Sierra Leone	37%	0.1%	99.9%	0.077	100%	2%		17%	0.39	4,025,657	
South Africa	57%	27%	15%	0.00042	100%		95%	24%*	0.47	2,414,767	Very uncertain
Swaziland	26%	27%	69%	0.022	100%	0.3%	100%	24%*	0.0004	78,185	
										100,235	Very uncertain

Country	% urban	Population at risk of malaria transmission		Case notification rate (pppa)	% falciparum among notified cases	ITN coverage ^{&&} (in population at risk)	IRS coverage	Estimates		Cases	Relative certainty of estimate [%]
		Low risk	High risk					Reporting completeness	Incidence rate		
Togo	33%	0%	100%	0.091	100%	2%		20%	0.02		
Uganda	14%	20%	73%	0.15	100%	0.2%	0.2%	33%	0.45	2,274,346	
Tanzania	32%	21%	75%	0.41	100%	2%		106%	0.47	12,452,208	
Zambia	40%	16%	83%	0.20	100%	6.6%	1.9%	50%	0.38	14,485,589	
Zimbabwe	35%	45%	54%	0.074	100%	1.3%	54%	24%*	0.39	4,297,893	Very uncertain
AFRO	32%	20%	65%	0.078	93%			24%	0.33	226,183,873	

Country	% urban	Population at risk of malaria transmission, by endemicity				Case notification rate (pppa)	% falciparum among notified cases	ITN coverage ^{&&} (population at risk)	IRS coverage	Estimates		Cases	Relative certainty of estimate [%]	
		Hypo-	Meso-	Hyper-	Holo-					Reporting completeness	Incidence rate			
Afghanistan	23%	14%	5%	27%	0%	0.0223	12%	0.8%	**	24%	0.09	2,311,536	Very uncertain	
Djibouti	84%	81%	7%	0%	0%	0.0069	98%			8%	0.09	60,636		
Egypt	42%		3%	0%	0%	3.0E-07	98%			11%	0.00000	3	1,844	Very uncertain
Iran (Islamic Republic of)	67%		3%	13%	2%	0.0003	20%		**	1% ^{\$}	0.03	1,977,287	Very uncertain	
Iraq	67%		4%	7%	16%	0%	3.4E-05		**	1% ^{\$}	0.0034	87,641	Very uncertain	
Morocco	57%		0%	2%	0%	2.6E-06	0%		**	1% ^{\$}	0.0003	8,119	Very uncertain	
Oman	78%	1.0%	0%	0.04%	0%	0.0002	40%		**	30%	0.0008	2,333		
Pakistan	34%	34%	42%	6%	0%	0.0007	36%			3.8%	1% ^{\$}	0.06	9,989,265	Very uncertain
Saudi Arabia	88%		3%	13%	0.9%	0%	0.0002	72%	**	17%	0.001	26,754	Very uncertain	
Somalia	28%	43%	4%	39%	0%	0.0012	90%	0.4%		1% ^{\$}	0.10	1,067,966	Very uncertain	
Sudan	36%	37%	39%	12%	0%	0.1236	95%	0.5%	2.4%	85%	0.15	5,008,821		
Syrian Arab Republic	50%		0.5%	0.1%	19%	0%	2.9E-06		**	1% ^{\$}	0.0003	5,312	Very uncertain	
Yemen	26%		8%	1.1%	47%	0%	0.0297	97%		0.7%	22%	0.14	2,851,558	
EMRO	46%	16%	19%	8%	0%	0.011	46%			11%	0.05	23,399,073		

Country	% urban	Population at risk of malaria transmission, by endemicity				Case notification rate (pppa)	% falciparum among notified cases	ITN coverage ^{&&} (population at risk)	IRS coverage	Estimates			Cases	Relative certainty of estimate [%]
		Hypo-	Meso-	Hyper-	Holo-					Reporting completeness	Incidence rate			
Armenia	64%	23%	0%	6%	0%	1.7E-05	0%		40% [£]	1% ^{\$}	0.0017	5,288	Very uncertain	
Azerbaijan	50%	2%	0.3%	15%	0%	8.2E-05	0%	8.2%	40% [£]	46%	0.0002	1,502		
Georgia	52%	0.2%	0%	4%	0%	7.9E-05	1%		**	11%	0.0007	20,202	Very uncertain	
Kyrgyzstan	34%	0.1%	0.1%	0%	0%	2.1E-04	0%			65%	0.0003	1,695		
Tajikistan	25%	4%	0%	13%	0%	2.0E-03	5%	8.3%	40% [£]	12%	0.02	104,968	Very uncertain	
Turkey	66%	7%	3%	2%	0%	1.6E-04	0%		40% [£]	2%	0.01	582,370	Very uncertain	
Turkmenistan	45%	0%	0%	5%	0%	3.5E-06	0%		40% [£]	1% ^{\$}	0.0004	1,748	Very uncertain	
Uzbekistan	37%					1.9E-09	0%		40% [£]	9%	0.0000	1	Very uncertain	
EURO	64%	2%	0.9%	1.4%	0%	0.00009	0.3%			9%	0.0048	717,774		
Argentina	90%	3%	4%	0%	0%	7.8E-06	0%		**	1% ^{\$}	0.0008	30,135	Very uncertain	
Belize	48%	83%	0%	4%	0%	0.0048	0%		40% [£]	13%	0.04	9,701	Very uncertain	
Bolivia	63%	5%	32%	2%	0%	0.0024	5%		**	3%	0.07	631,443	Very uncertain	
Brazil	83%	3%	7%	2%	0%	0.0026	23%		**	20%	0.01	2,380,992	Very uncertain	
Colombia	76%	5%	6%	19%	0%	0.0040	46%	9.3%	**	13%	0.03	1,337,309	Very uncertain	
Costa Rica	61%	0%	0%	19%	0%	3.6E-04	0.2%		**	1.5% ^{\$}	0.02	99,003	Very uncertain	
Dominican Republic	59%	0%	94%	0%	0%	1.4E-04	100%		**	1% ^{\$}	0.01	123,680	Very uncertain	
Ecuador	62%	1.4%	55%	0%	0%	0.0078	23%		**	7%	0.11	1,448,498	Very uncertain	
El Salvador	60%	0%	0%	93%	0%	6.5E-05	0%		**	1% ^{\$}	0.01	43,115	Very uncertain	
French Guiana	75%	0%	5%	0%	0%	0.022	83%			100% ⁺	0.02	4,026	Very uncertain	
Guatemala	46%	1.2%	0.05%	50%	0%	0.0036	5%	2.3%	**	4%	0.10	1,238,845	Very uncertain	
Guyana	38%	0.02%	22%	15%	0%	0.0320	48%	21.9%	**	51%	0.06	48,365	Very uncertain	
Haiti	37%	0%	94%	0%	0%	0.0012	100%			1% ^{\$}	0.12	977,246	Very uncertain	
Honduras	46%					0.0039	4%		(space sprayi ng)					
		0%	0%	86%	0%					2%	0.16	1,142,700	Very uncertain	
Mexico	75%	9%	4%	6%	0%	5.5E-05	0.4%		**	12% ^{\$}	0.0005	48,050	Very uncertain	
Nicaragua	57%	1%	0%	90%	0%	0.0027	13%		**	1.8%	0.15	857,410	Very uncertain	
Panama	57%	0.2%	3%	0.7%	0%	0.0008	15%		**	11%	0.01	23,984	Very uncertain	
Paraguay	57%	0%	20%	0%	0%	7.4E-04	0%			2%	0.04	256,570		
Peru	74%	9%	47%	0%	0%	0.0029	19%		**	12%	0.02	657,134	Very uncertain	
Suriname	76%	0.2%	6%	0.7%	0%	0.034	76%	38.9%		12% [*]	0.28	123,190	Very uncertain	
Venezuela	88%	3%	6%	5%	0%	0.0012	9%		**	8%	0.01	376,989	Very uncertain	
PAHO	76%	4%	12%	9%	0%	0.0020	18%			12%	0.02	11,858,384		
Bangladesh	24%	23%	2%	66%	0%	3.9E-04	74%			1% ^{\$}	0.04	5,837,568	Very uncertain	
Bhutan	9%	34%	0%	2%	0%	0.0025	44%			19%	0.02	37,376		
DPR Korea	61%	1.1%	0%	0%	0%	0.0034	0%			100% ⁺	0.003	78,002	Very uncertain	

Country	% urban	Population at risk of malaria transmission, by endemicity				Case notification rate (pppa)	% falciparum among notified cases	ITN coverage ^{&&} (population at risk)	IRS coverage	Estimates			Relative certainty of estimate [%]
		Hypo-	Meso-	Hyper-	Holo-					Reporting completeness	Incidence rate	Cases	
India	28%	23%	41%	27%	0%	0.0019	49%	20% ^{££}	40% ⁺⁺	2.5%	0.08	82,864,215	Very uncertain
Indonesia	46%	17%	25%	34%	0.15%	0.0011	32%	0.1%	**	1.3% ^{\$}	0.09	19,200,504	Very uncertain
Myanmar	29%	23%	0%	65%	0%	0.0032	82%		0.81% ^{##}	2%	0.17	8,620,746	
Nepal	15%	4%	0%	64%	0%	3.7E-04	4%		**	1% ^{\$}	0.04	951,910	Very uncertain
Sri Lanka	21%	42%	0%	35%	0%	0.0057	12%		20%	33%	0.02	333,335	
Thailand	32%	29%	45%	23%	0%	0.0010	51%		21% ^{##}	2% ^{\$}	0.05	3,237,574	
Timor-Leste	8%	87%	0%	0%	0%	0.055	55%			100% ⁺	0.06	45,438	Very uncertain
SEARO	51%	22%	32%	32%	0%	0.0017	48%			4%	0.07	121,206,667	
Cambodia	19%	20%	48%	20%	0%	0.0040	89%	22% [#]	**	2%	0.17	2,441,406	Very uncertain
China	39%	27%	19%	6%	0%	1.9E-05	23%	65% ^{&&}	20%	1.1%	0.002	2,377,657	Very uncertain
Lao PDR	21%	0%	28%	63%	0%	0.0055	97%	15.9%	**	3%	0.20	1,178,664	Very uncertain
Malaysia	64%	6%	70%	11%	0%	4.3E-04	64%		13%	1.1%	0.04	992,943	Very uncertain
Papua New Guinea	13%	11%	0%	24%	17%	0.0149	82%		0.23% ⁵	42%	0.04	214,680	
Philippines	61%	53%	7%	2%	0%	4.7E-04	62%	5.5% [#]	9% ⁵	1.3%	0.04	2,915,485	
Republic of Korea	80%	0.5%	0%	0%	0%	6.0E-05	0%		0%	19%	0.00	15,256	
Solomon Islands	16%	27%	0%	58%	41%	0.16	67%	68% [#]	7.4% ⁶	100% ⁺	0.16	79,608	Very uncertain
Vanuatu	23%	26%	0%	56%	40%	0.0466	51%	73% [#]	**	47%	0.10	21,489	Very uncertain
Viet Nam	26%	24%	9%	60%	0%	8.0E-04	77%	17%	19%	1.3%	0.06	4,957,443	
WPRO	40%	27%	18%	9%	0.1%	0.00029	32%			1.8%	0.01	15,194,631	

&& Unless otherwise indicated, based on reported child usage in national-level household survey (DHS or MICS), conducted between 1999 and 2003. If less than 100% of the national population is at malaria risk, survey data were converted into coverage estimates for the population at risk by assuming that all ITNs are concentrated in households at risk (Annex 2).

^{££} Based on reported child usage in a Netmark, Omnibus or RBM baseline household survey conducted in several districts in a country (but not national), in 2000 or 2001.

[#] From WPRO country profile (web, Jan. 2004), unknown definition, for the population at malaria risk.

^{##} From RBM/SEAR/WPR/IC/WP99 report (1999) for 1996, for the population at malaria risk.

⁵ From WPRO country profile (web, 1998), for the population at malaria risk.

⁶ From WPRO country profile (web, 2000) (for the population at malaria risk??).

[&] For the population at malaria risk⁴¹.

* Assumed reporting completeness, based on the weighted mean reporting completeness in the WHO region to which this country belongs, in the absence of a malaria incidence estimate based on transmission risk.

⁺ The HIS reporting completeness consistent with a risk-based incidence estimate would be >100%, therefore reporting completeness was taken as 100% and the incidence rate calculated from that and the case notification rate.

[§] The HIS reporting completeness consistent with a risk-based incidence estimate would be <1%, therefore reporting completeness was taken as 1.0% and the incidence rate calculated from that and the case notification rate.

[£] Assumption in the absence of quantitative data, when IRS coverage was >0 according to ⁴².

** IRS coverage >0 according to ⁴², but assumed to be 0 in the absence of quantitative coverage data.

^{££} Based on KAP survey, Dr. Ravi Kumar p.c. February 2004.

⁺⁺ Dr. Ravi Kumar p.c. February 2004: 68 million people in India protected by IRS \approx between 14% of overall risk population and 92% of high-risk population.

[%] Relative level of uncertainty according to criteria discussed in section 'Uncertainty bounds on country estimates' in main text.

^{&&} Assumption in the absence of quantitative data.

Table 3. Alternative scenarios of estimated malaria incident cases in all malarious countries of the world in 2004 (all species). Numbers in brackets show estimate for *falciparum* malaria only.

Scenario	Estimated global cases	% in AFRO	% in SEAR	Countries for which the estimate is more than doubled ²	Countries for which the estimate is more than halved ²	Countries for which the estimate increases by >5 million cases ²	Countries for which the estimate decreases by >5 million cases ²	Comments
Default	402 million (311 million)	57% (72%)	30% (19%)	n.a.	n.a.	n.a.	n.a.	See Table 2.
1a. Outside AFRO: notified cases times 10 instead of estimation from basic incidence rates by endemicity, populations at different endemicities and ITN+IRS impact.				Egypt, Libya, Oman, Sudan, Tunisia, UAE, Kazakhstan, Kyrgystan, Uzbekistan, French Guyana, Suriname, Bhutan, DPR Korea, E.Timor, Solomon Islands, Vanuatu	36 non-AFRO countries	Sudan	Pakistan, Bangladesh, India, Indonesia, Myanmar, Thailand, Viet Nam	Overall non-AFRO reporting completeness (by definition) of 10%, compared to 6.2% under default.
1b. Outside AFRO: constrain reporting completeness between 1% and 33%.				Egypt, Libya, Sudan, Tunisia, UAE, Kazakhstan, Uzbekistan, French Guyana, Suriname, DPR Korea, E.Timor, Solomon I.	-	Sudan	-	
1c. Outside AFRO: no constraints on reporting completeness in HIS.				Iraq, Morocco, Pakistan, Syria, Armenia, Azerbaijan, Turkmenistan, Argentina, Dominican Republic, El Salvador, Haiti, Mexico, Bangladesh, Nepal, China, Malaysia	French Guyana, Suriname, DPR Korea	Pakistan, Bangladesh, Indonesia, China	-	Estimated reporting completeness now ranges from 0.0007% (in Syria) to 521% (in DPR Korea) instead of from 1% to 100%. In this scenario, 22 countries would have a reporting completeness of below 1%; the overall completeness outside AFRO would be 4.3% .
2a. National populations at risk outside AFRO: <i>minimum</i> between ²⁶ and countries' own report, for 19 countries.				-	Cambodia, China, Malaysia, Philippines, Viet Nam	-	-	Distribution of risk population over endemicity categories still done according to ²⁶ and Background paper II. For AFRO, stick to MARA.
2b. National populations at risk outside AFRO: <i>maximum</i> between ²⁶ and countries' own				French Guyana, Venezuela, DPR Korea, R.Korea	-	DPR Korea	-	

² Compared to default. Countries for which, in the absence of a risk-based estimate, the 'default' estimate had been defined as 100% * the case notifications (Algeria, Botswana, Namibia, South Africa, Swaziland, Zimbabwe, Cape Verde, Seychelles, Egypt, Libya, Tunisia, United Arab Emirates, Kazakhstan and Uzbekistan) were excluded from these lists.

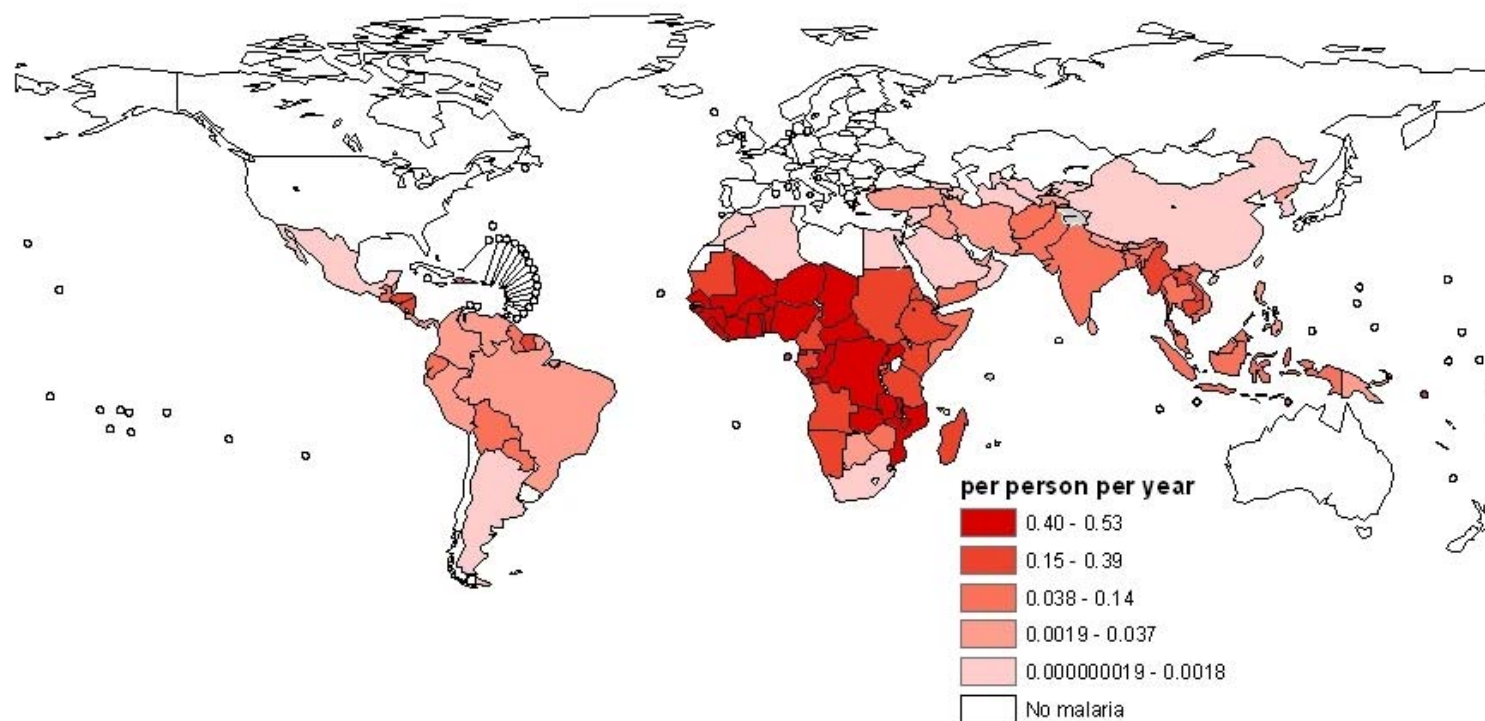
<i>Scenario</i>	<i>Estimated global cases</i>	<i>% in AFRO</i>	<i>% in SEAR O</i>	<i>Countries for which the estimate is more than doubled²</i>	<i>Countries for which the estimate is more than halved²</i>	<i>Countries for which the estimate increases by >5 million cases²</i>	<i>Countries for which the estimate decreases by >5 million cases²</i>	<i>Comments</i>
report, for 22 countries.								
3a. Basic incidence rate: double for under-5s in Africa (& holo-endemic areas outside Africa)				-	-	DRC, Ethiopia, Nigeria, Tanzania	-	All-age incidence rates in middle African countries increase by 37-60%.
3b. Basic incidence rate: halve for under-5s in AFRO (& holo-endemic areas outside AFRO)				-	-	-	Nigeria	All-age incidence rates in middle African countries decrease by 19-28%.
4a. Basic incidence rate: double for over-5s in AFRO (& holo-endemic areas outside AFRO)				-	-	DRC, Ethiopia, Nigeria, Tanzania	-	All-age incidence rates in middle African countries increase by 43-69%.
4b. Basic incidence rate: halve for over-5s in AFRO (& holo-endemic areas outside AFRO)				-	-	-	DRC, Nigeria	All-age incidence rates in middle African countries decrease by 20-35%.
5a. Basic incidence rate: double for hypo-endemic areas outside AFRO				-	-	-	-	For 22 countries (the same as under default), risk-based estimate replaced by case notifications / 1%; for 4 instead of 5 countries (E. Timor no longer), risk-based estimate replaced by case notifications / 100%.
5b. Basic incidence rate: halve for hypo-endemic areas outside AFRO				-	-	-	-	For 21 instead of 22 countries (Iran no longer), risk-based estimate replaced by case notifications / 1%; for 5 countries (the same as under default), risk-based estimate replaced by case notifications / 100%.
6a. Basic incidence rate: double for meso-endemic areas outside AFRO				-	-	India	-	For 24 instead of 22 countries, risk-based estimate replaced by case notifications / 1%; for 5 countries (the same as under default), risk-based estimate replaced by case notifications / 100%.
6b. Basic incidence rate: half for meso-endemic areas outside AFRO				-	-	-	India	For 18 instead of 22 countries, risk-based estimate replaced by case notifications / 1%; for 6 instead of 5 countries (Kyrgyzstan in addition), risk-based estimate replaced by case

<i>Scenario</i>	<i>Estimated global cases</i>	<i>% in AFRO</i>	<i>% in SEAR O</i>	<i>Countries for which the estimate is more than doubled²</i>	<i>Countries for which the estimate is more than halved²</i>	<i>Countries for which the estimate increases by >5 million cases²</i>	<i>Countries for which the estimate decreases by >5 million cases²</i>	<i>Comments</i>
								notifications / 100%.
7a. Basic incidence rate: double for hyper-endemic areas outside AFRO				-	-	India, Myanmar	-	For 27 instead of 22 countries, risk-based estimate replaced by case notifications / 1%; for 5 countries (the same as under default), risk-based estimate replaced by case notifications / 100%.
7b. Basic incidence rate: half for hyper-endemic areas outside AFRO				-	-	-	India	For 18 instead of 22 countries, risk-based estimate replaced by case notifications / 1%; for 5 countries (the same as under default), risk-based estimate replaced by case notifications / 100%.
8a. Add a reduction in incidence in urban areas for the age/endemicity categories for which no urban/rural distinction was yet made, at 0.30 times the default overall rate, which in this scenario becomes the rural rate.				-	R. Korea	-	Nigeria	32% of AFRO, 51% of SEARO and 48% of total populations in malarious countries are urban. Impact is much restricted by the constraint to maintain HIS reporting completeness between 1-100%.
8c. Halve urban population for all countries.				-	-	India	-	
8b. Double urban population for all countries.				-	Georgia	-	India, Indonesia	
9. Add an impact of untreated mosquito nets, at half the efficacy compared to ITNs.				-	-	-	-	For Indonesia, this brings the estimated reporting completeness to (just) above 1%.
10a. IRS coverage: drop the assumed 40% coverage for 7 countries that use IRS but have no quantitative coverage data.				-	-	-	-	This concerns Armenia, Azerbaijan, Tajikistan, Turkey, Turkmenistan, Uzbekistan and Belize.
10b. Add an 40% assumed IRS coverage for 33 more countries				-	Cambodia	-	Indonesia	Estimated reporting completeness for Vanuatu

<i>Scenario</i>	<i>Estimated global cases</i>	<i>% in AFRO</i>	<i>% in SEAR O</i>	<i>Countries for which the estimate is more than doubled²</i>	<i>Countries for which the estimate is more than halved²</i>	<i>Countries for which the estimate increases by >5 million cases²</i>	<i>Countries for which the estimate decreases by >5 million cases²</i>	<i>Comments</i>
that use IRS but have no quantitative coverage data.								changes from (<)1% to 45%.
11. Somalia, Sudan and Djibouti: AFRO instead of outside-AFRO basic rates and ITN efficacy.				Sudan: 9.7 million instead of 5.3 million cases; reporting completeness 44% instead of 80%. Djibouti: 177,520 instead of 43,113 cases; reporting completeness 2.8% instead of 11%. Somalia: Estimated reporting completeness ??? instead of 1.2%.				

Figure 1. Estimated malaria incidence rates (per person per year) in countries, for 2004. (a) All species; (b) *falciparum* malaria. Dashed (green) areas indicate countries for which no estimate was made. (a)

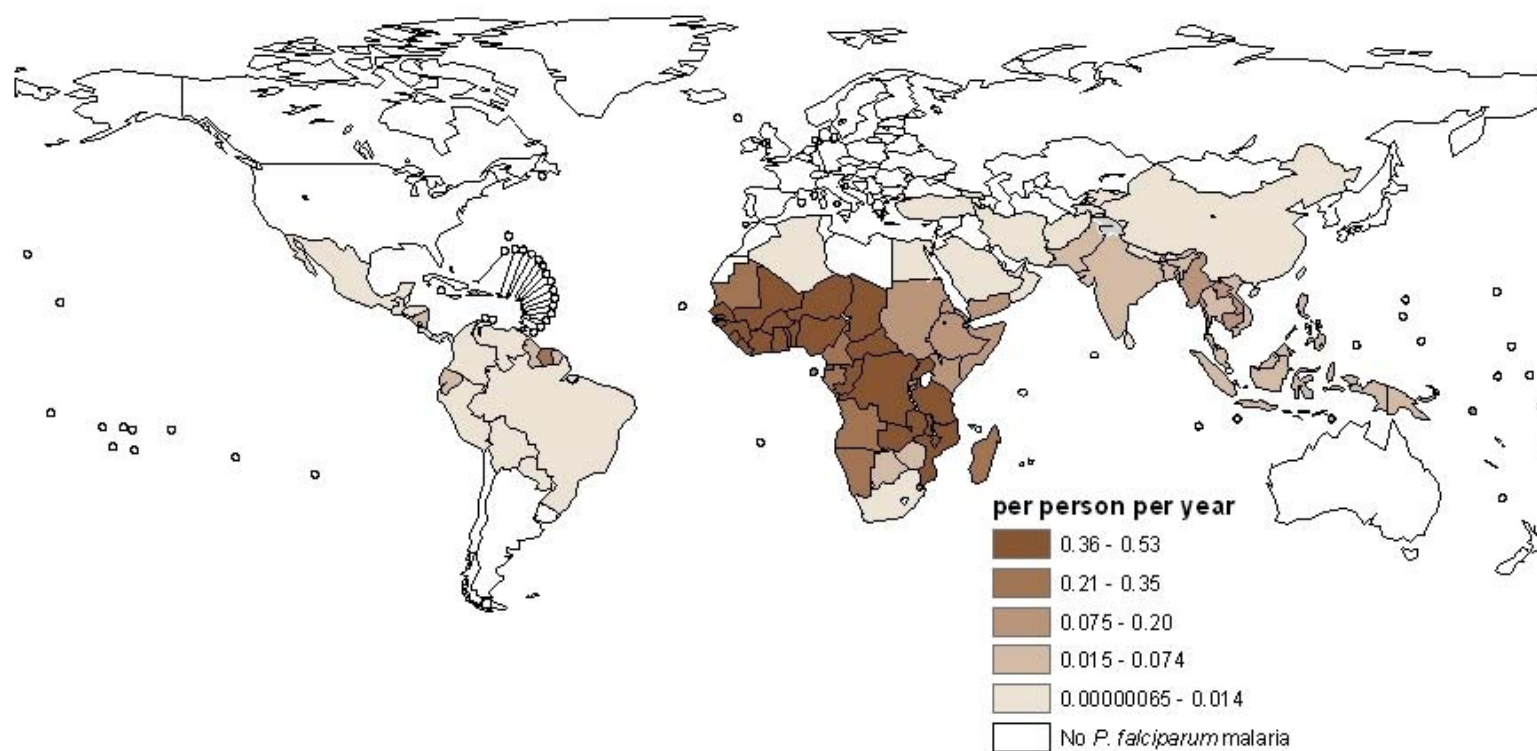
Estimates of malaria incidence, 2004



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Estimates of *P. falciparum* malaria incidence, 2004



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.
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(b)

Figure 2. Regional totals of estimated malaria incidence in 2004, by world region and *Plasmodium* species. (a) Number of incident cases; b) Incidence rate, per person per year.

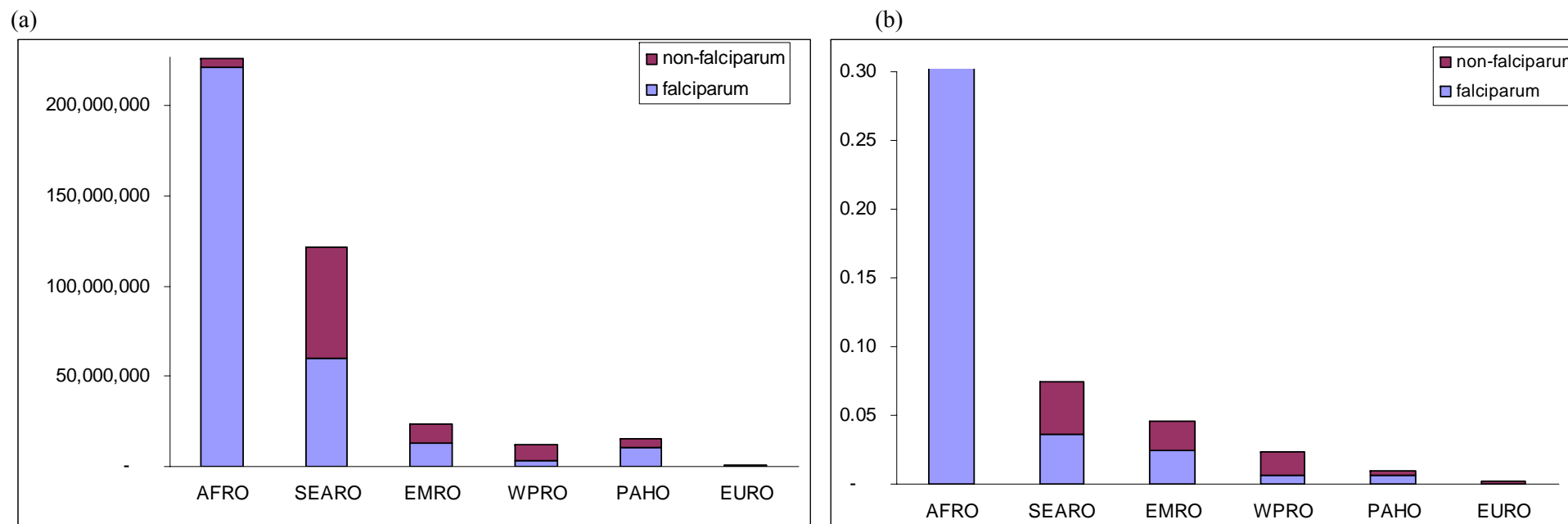
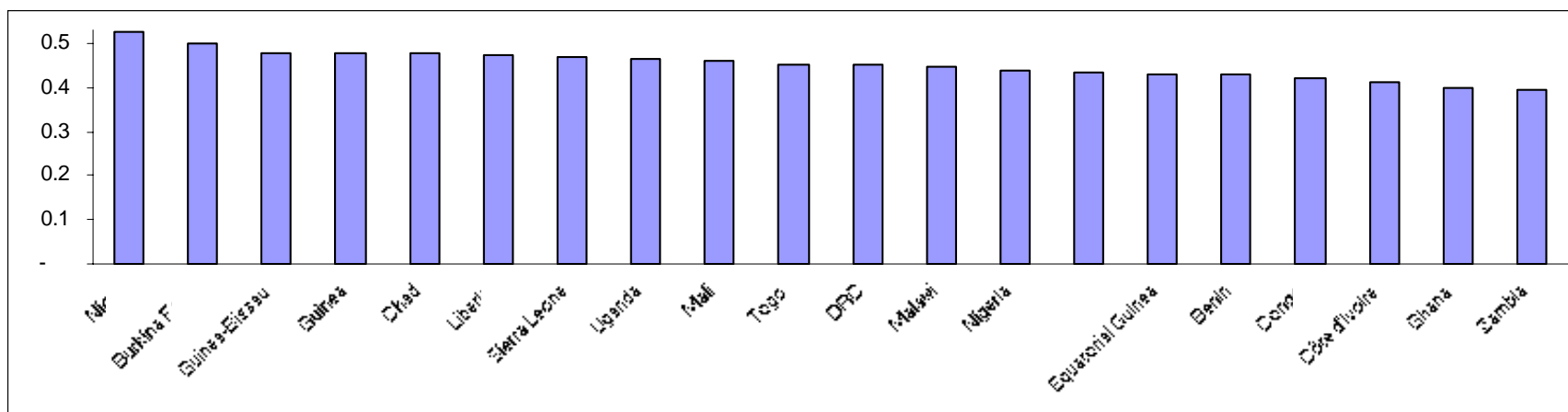
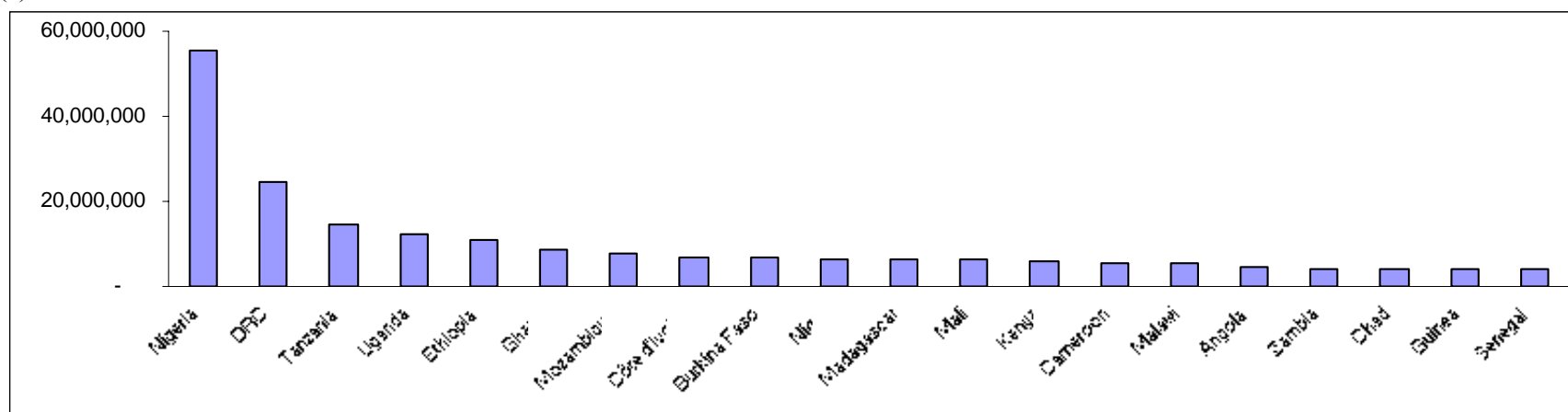


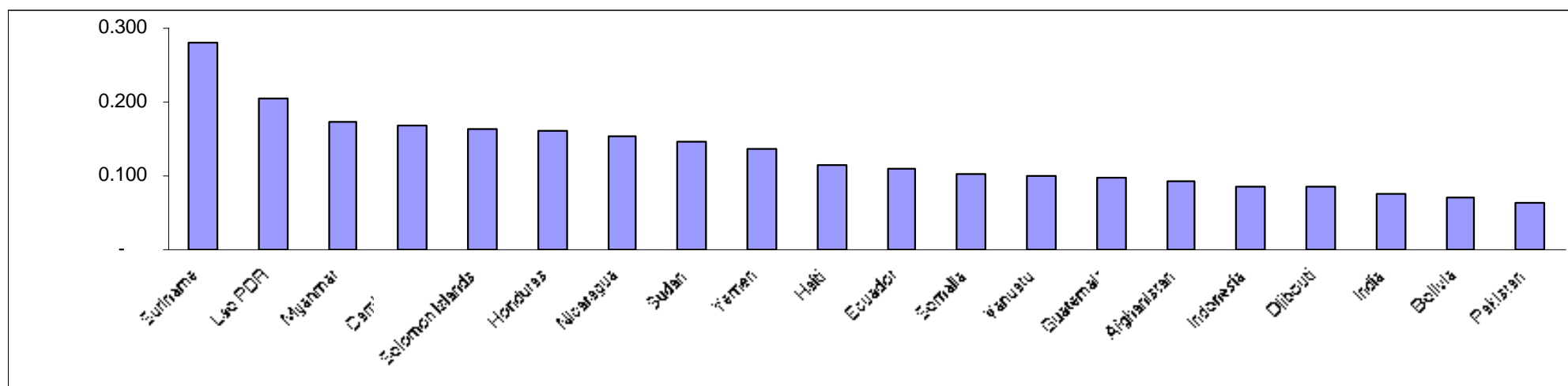
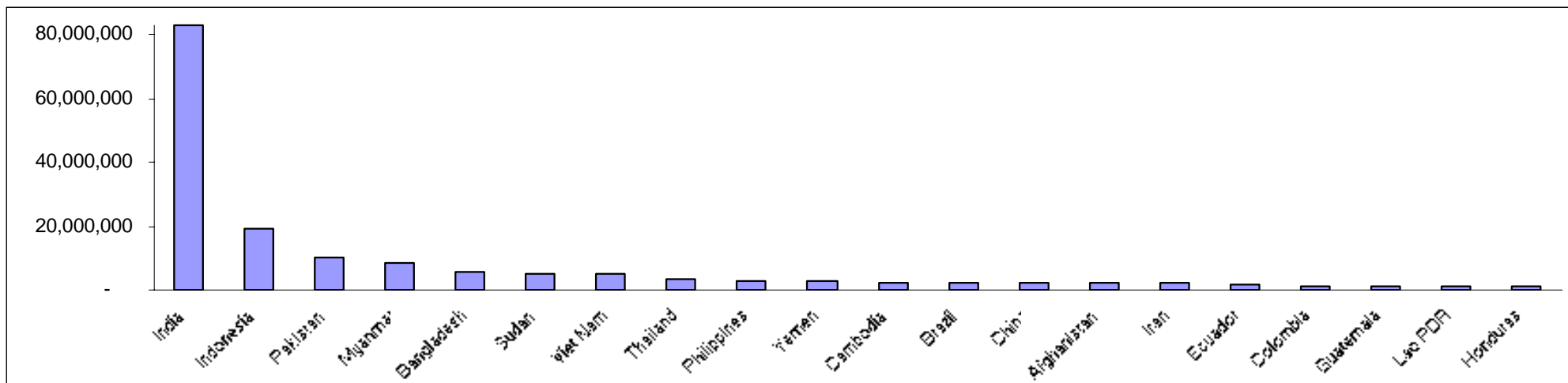
Figure 3. Ranking of countries by estimated malaria incidence in 2004, all species combined. (a) 20 AFRO countries with most estimated cases; (b) 20 AFRO countries with highest estimated incidence rate (per person per annum); (c) 20 non-AFRO countries with most estimated cases; (b) 20 non-AFRO countries with highest estimated incidence rate (per person per annum). CAR = Central African republic, DRC = Democratic Republic of the Congo.

(a)



(b)

(c)



(d)

Figure 4. Regional totals of estimated malaria incidence in 2004, by age group. (a) Numbers of incident cases; (b) incidence rate, per person per year; (c) age distribution in cases.

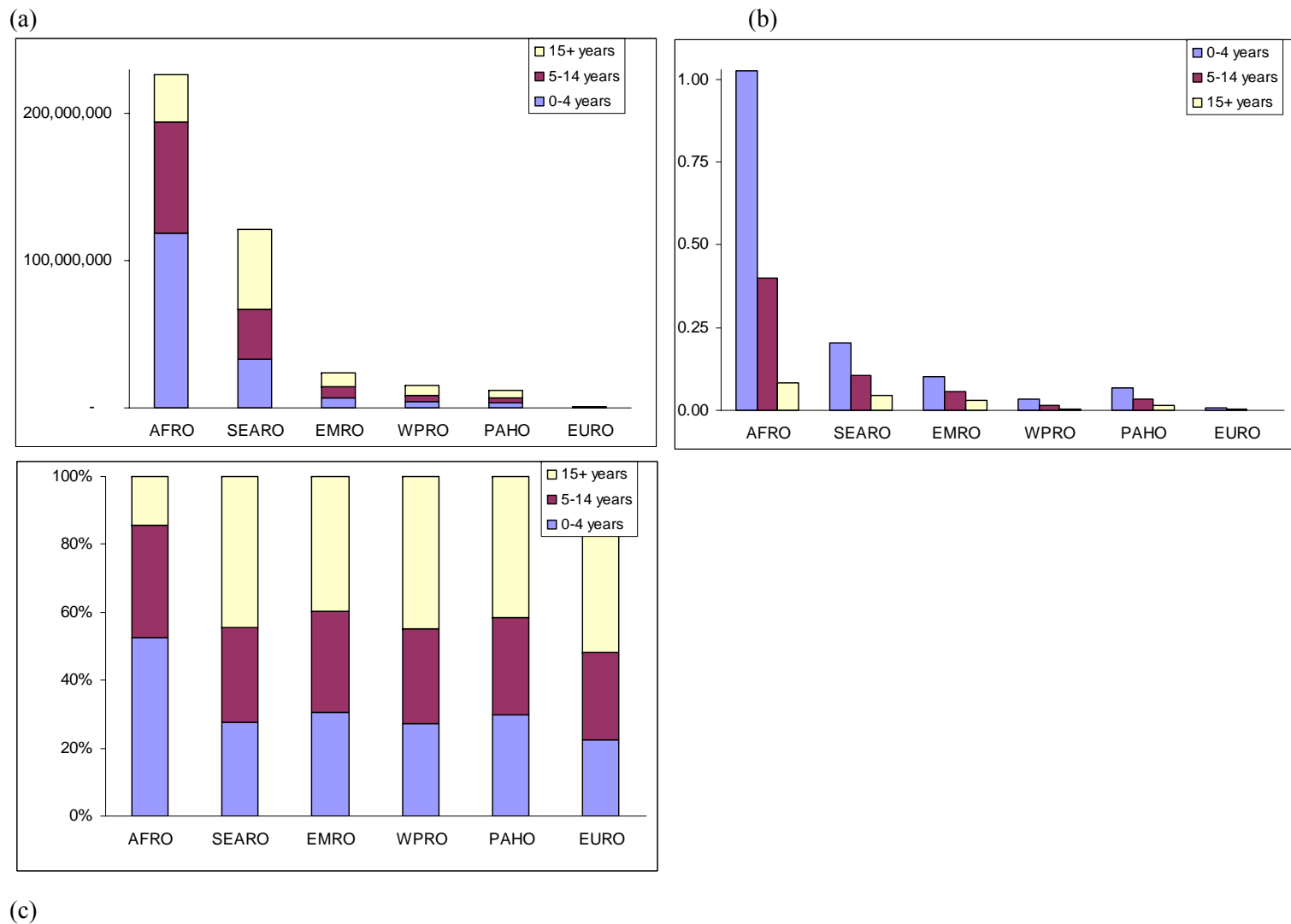


Figure 5. Proportion of malaria cases captured in national Health Information Systems, according to the incidence estimation based on risk mapping (dark red bars, in comparison to country's or region's own estimates of HIS reporting completeness (light blue bars). Error bars indicate minimum and maximum completeness estimate by the country or region.

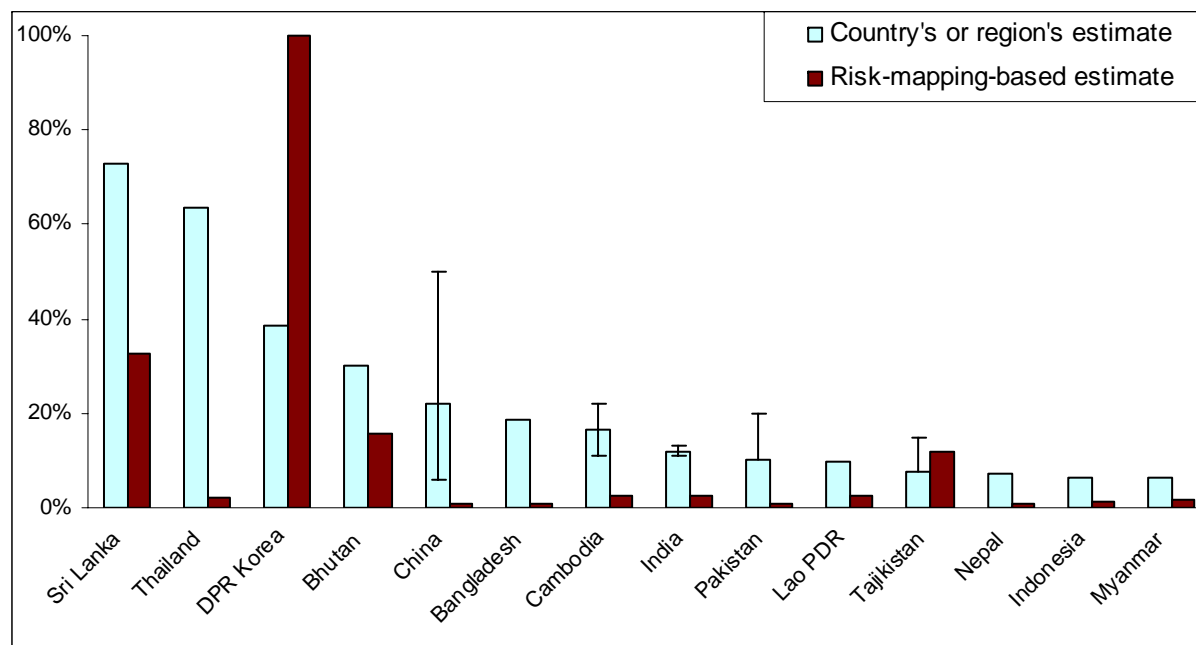
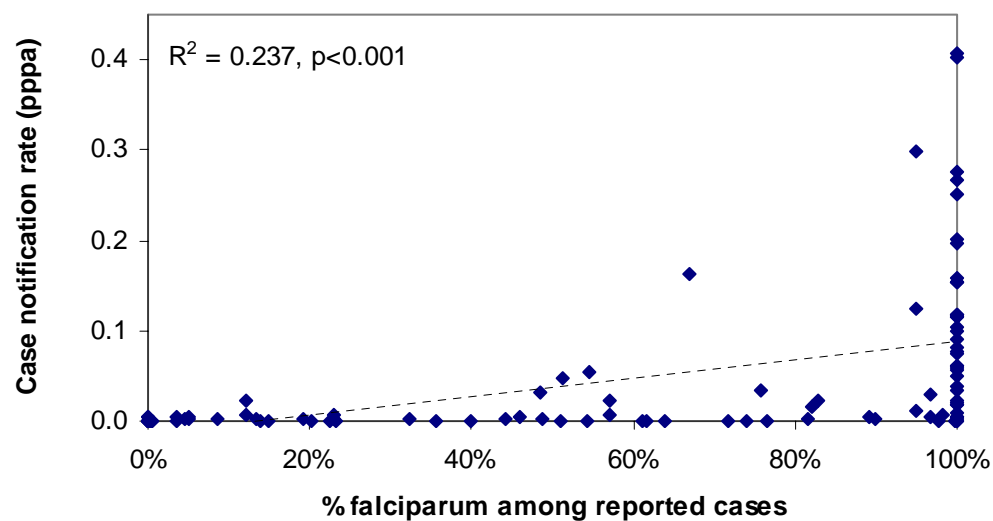
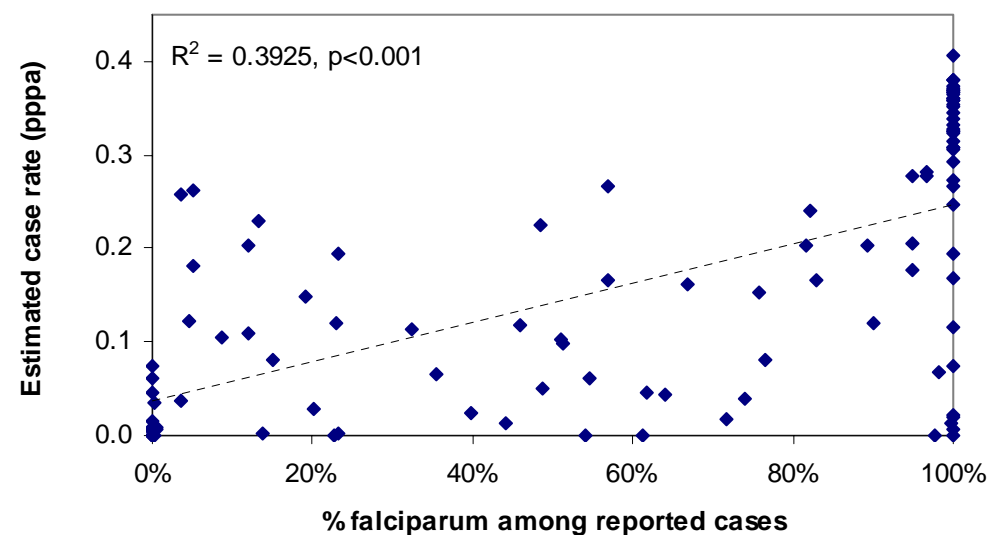


Figure 6. Country level (a) malaria case notification rate, (b) estimated malaria incidence rate and (c) estimated *falciparum* incidence rate, as a function of the proportion *falciparum* among reported (outpatient) cases. Compared to the case notification rate, the estimated incidence shows a stronger positive correlation with proportion *falciparum* among cases. Dots denote country data; dashed lines denote the correlation, for which statistics are given in the upper left corner of each diagram. Evaluation for 107 malarious countries throughout the world.

(a)



(b)



(c)

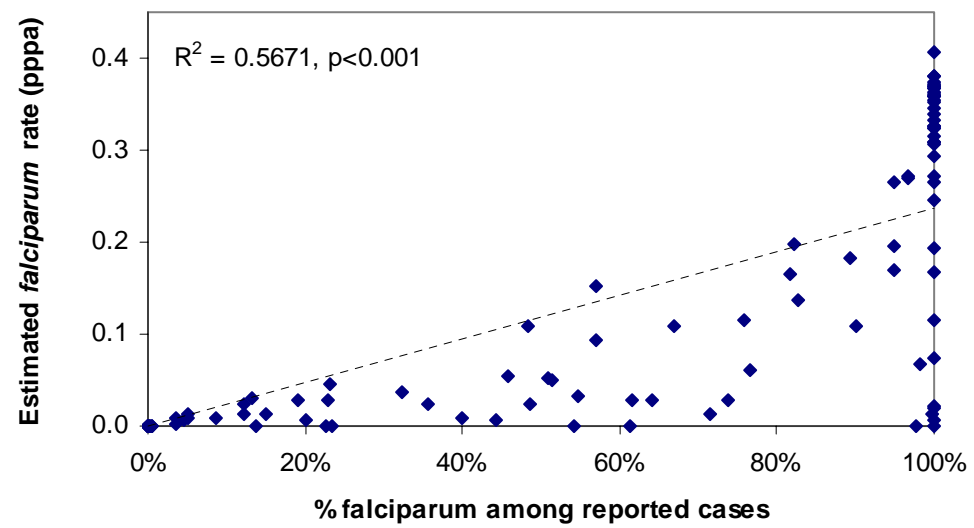
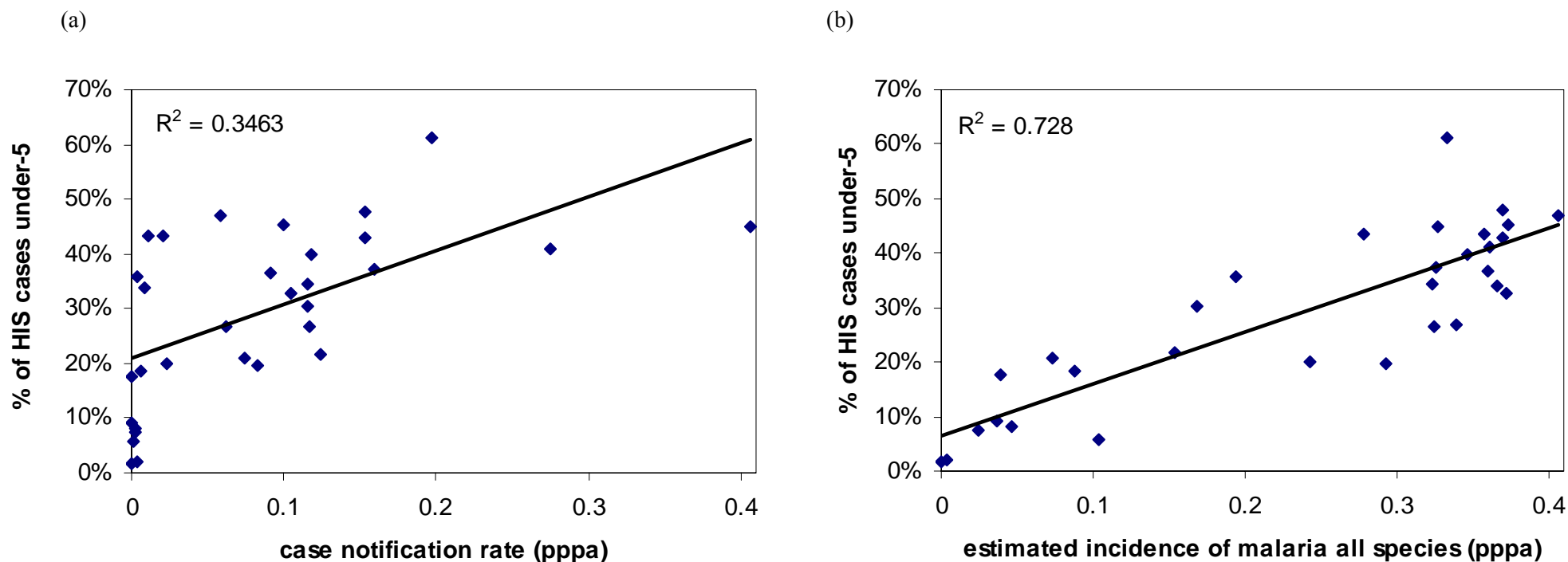


Figure 7. Proportion of HIS-recorded malaria cases that is in children under-5, as a function of (a) malaria case notification rate, (b) estimated malaria incidence rate and (c) estimated *falciparum* incidence rate. Compared to the case notification rate, the estimated incidence (all species or *falciparum* specifically) shows a stronger positive correlation with proportion of cases in under-5s. Dots denote country data; dashed lines denote the correlation, for which statistics are given in the upper left corner of each diagram. Evaluation for 22 AFRO countries and 9 non-AFRO countries with age-specific HIS data available.



(c)

