Supplementary Information

Estimating the potential public health impact of seasonal malaria chemoprevention in African children

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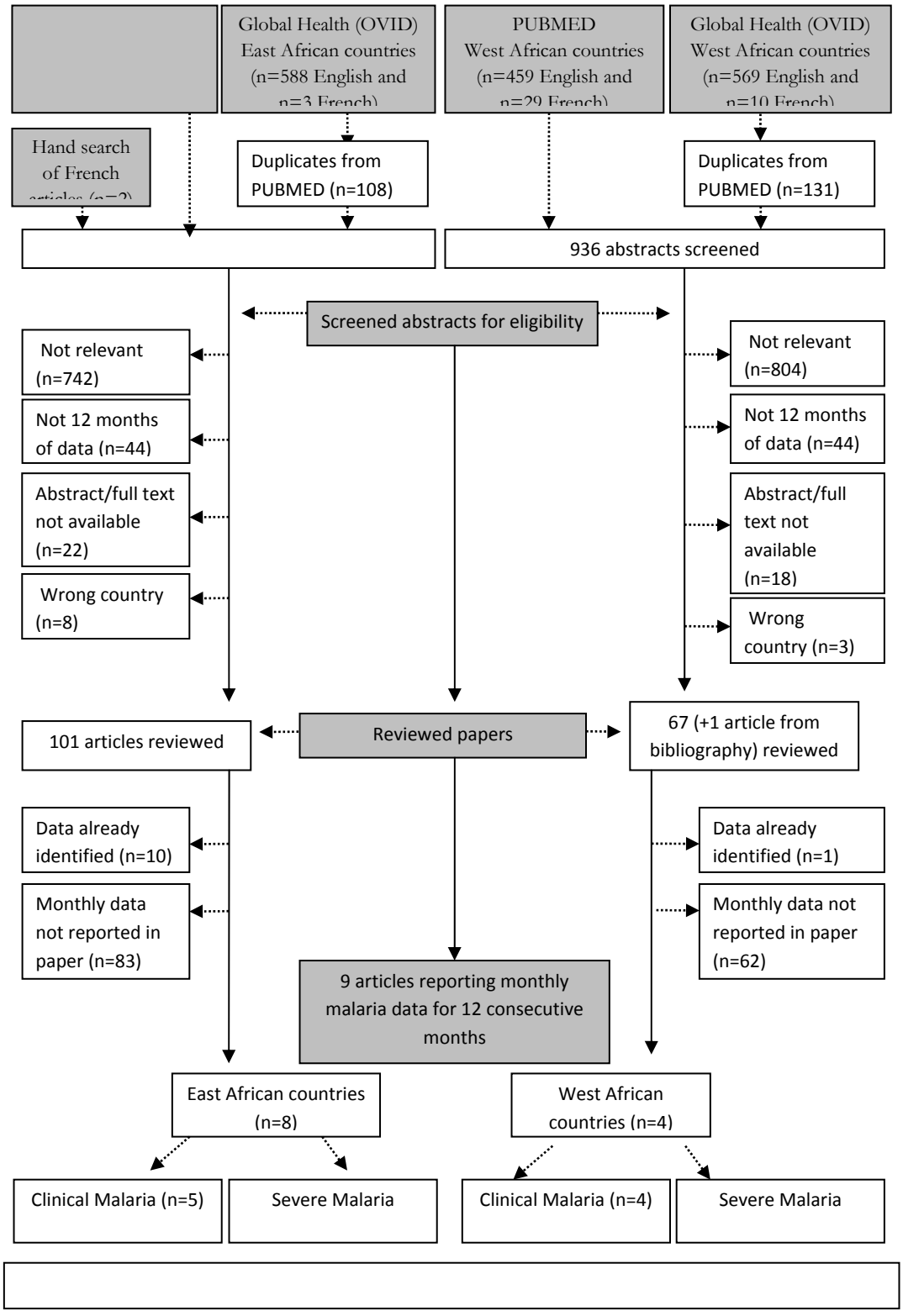
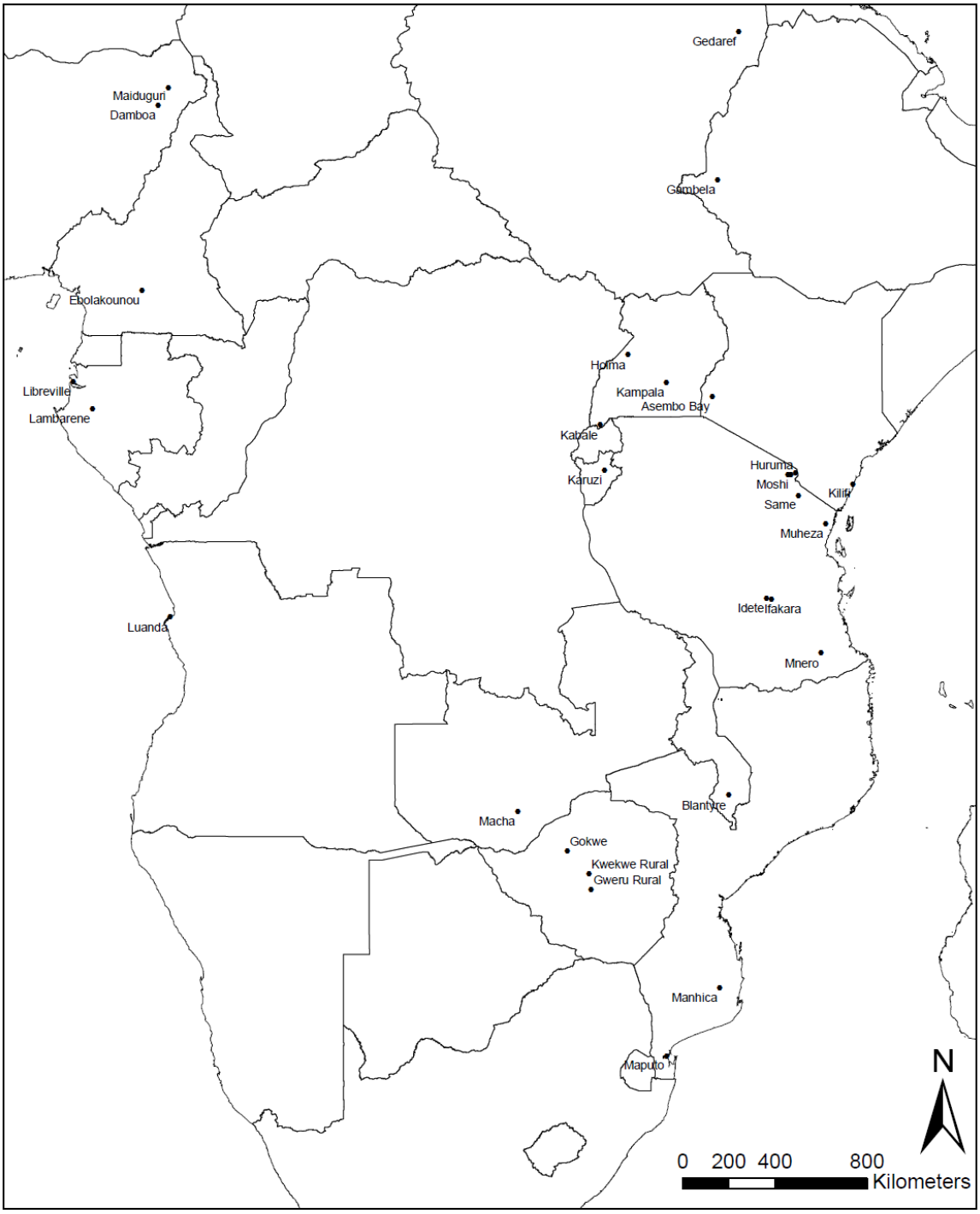
Supplementary Figure S1. Literature review and data abstraction flow chart

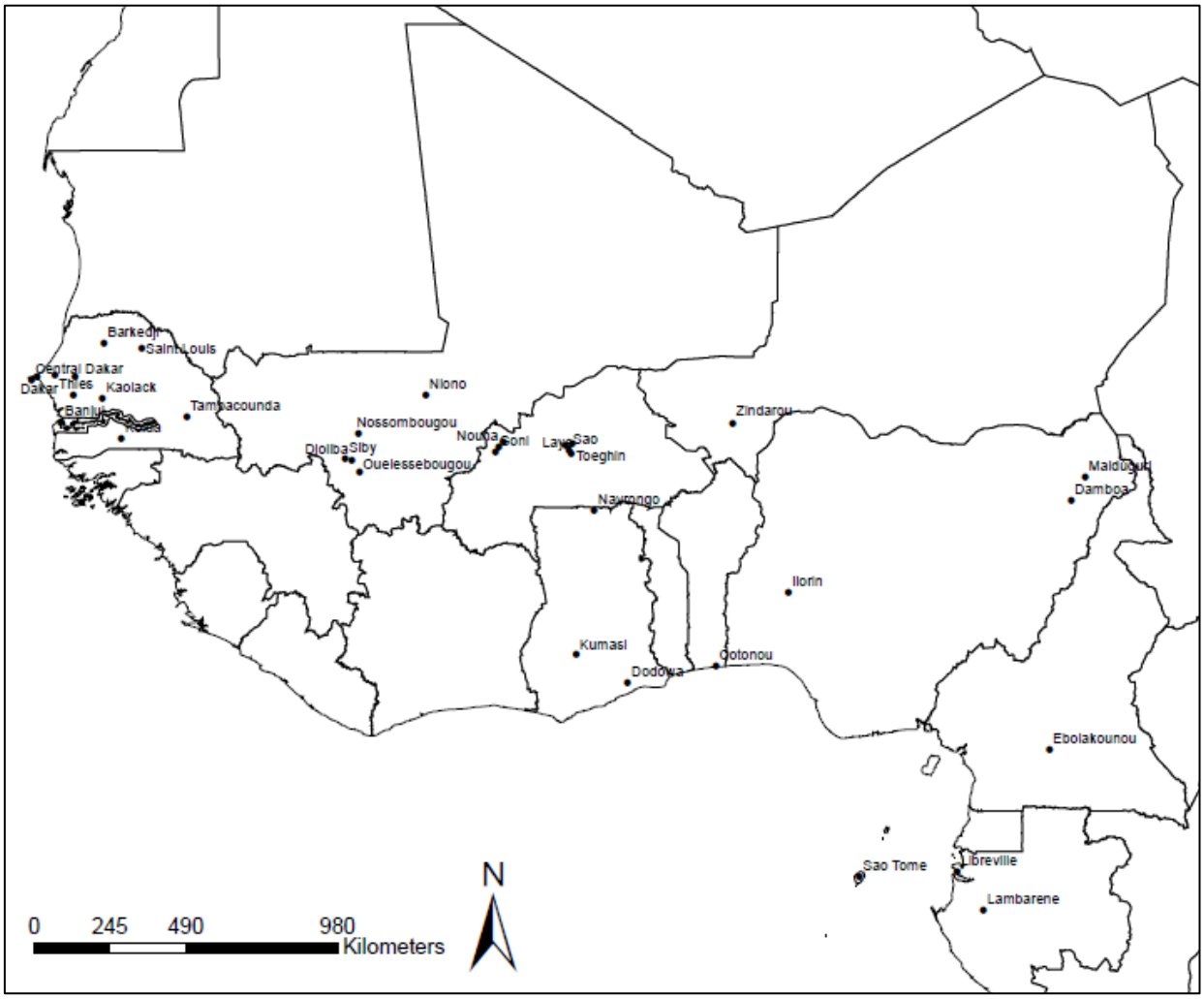


Supplementary Figure S2. Map showing the location of available data points describing the seasonality of the incidence of malaria episodes for East Africa



The locations of sites for which monthly incidence data was available were mapped using ArcGIS version 9.2 (ESRI, CA, USA). Co-ordinates of data points were obtained from the published paper or using the Geographic Names Database maintained by the National Geospatial Intelligence Agency (http://earth-info.nga.mil/gns/html/namefiles.htm) supported by ancillary data from the published paper, where possible.

Supplementary Figure S3. Map showing the location of available data points describing the seasonality of the incidence of malaria episodes for West Africa



The locations of sites for which monthly incidence data was available were mapped using ArcGIS version 9.2 (ESRI, CA, USA). Co-ordinates of data points were obtained from the published paper or using the Geographic Names Database maintained by the National Geospatial Intelligence Agency (http://earth-info.nga.mil/gns/html/namefiles.htm) supported by ancillary data from the published paper, where possible.

Supplementary Table S1. Seasonality assessment of clinical malaria incidence

Site (country)	Method	Reference	Study period	Highest percent of annual incidence in 4 consecutive months*	Comment
West and Central Africa					
Cotonou (Benin)	Review	[33]	Jan to Dec 04	45.2	Bimodal
Bousse District, IPTc sites (Burkina Faso)	Review	Diallo[$]	Dec 08 to Nov 09	**89.1**	
Cisse (Burkina Faso)	Review	[34]	Dec 03 to Nov 04	57.8[ʃ]	
Goni (Burkina Faso)	Review	[34]	Dec 03 to Nov 04	**63.5**	
Nouna (Burkina Faso)	Review	[34]	Dec 03 to Nov 04	57.5[ʃ]	
Ebolakounou & Koundou (Cameroon)	From [12]	[35]	Jun 97 to May 98	58.4	Bimodal
Lambarene (Gabon)	From [12]	[36]	Apr 03 to Mar 05	49.3	
Dodowa (Ghana)	Review	[37]	Sep94 to Aug95	55.3	Bimodal
Navrongo (Ghana)	From [12]	[38]	Oct 00 to Sep 03	**66.8**	
Navrongo (Ghana)	Review	Hodgson[$]	Jan 07 to Dec 09	**78.1 (2007)** **70.6 (2008)** **71.7 (2009)**	
Kalanampala (Mali)	From [12]	[39]	Jan to Dec 97	**80.5**	
Kati Region, IPTc sites (Mali)	Review	Diallo[$]	Dec 08 to Nov 09	**83.6**	
Nonzombougou (Mali)	review	Dicko[$]	Jan to Dec 07	**89.4**	
Tenegue (Mali)	From [12]	[39]	Jan to Dec 97	54.2[ʃ]	
Zindarou (Niger)	Review	Fandeur[$]	Jul 08 to Jun 09	**63.5**	
Barkedji (Senegal)	Review	[40]	Nov 94 to Oct 95	**78.4**	
Dakar region (Senegal)	Review	PNLP	Jan to Dec 08	**65.1**	
Diourbel region (Senegal)	Review	PNLP	Jan to Dec 08	**83.1**	
Fatick region (Senegal)	Review	PNLP	Jan to Dec 08	**61.9**	
Kaolack region (Senegal)	Review	PNLP	Jan to Dec 08	**83.5**	
Kolda region (Senegal)	Review	PNLP	Jan to Dec 08	**77**	
Saint-Louis region (Senegal)	Review	PNLP	Jan to Dec 08	53.1[ʃ]	
Tambacounda region (Senegal)	Review	PNLP	Jan to Dec 08	**80.6**	
Thies region (Senegal)	Review	PNLP	Jan to Dec 08	**60.4**	
East and Southern Africa					
Karuzi (Burundi)	Review	[41]	Jan 97 to Dec 03	<45 (1997-99, 2002-03) **67.4 (2000)** **65.3 (2001)**	Epidemic in 2000-1
Asembo (Kenya)	From [12]	[42]	Jan 03 to Dec 05	49.7	
Manhica (Mozambique)[ʃ]	From [12]	[43]	Jan 97 to Dec 97	43	
Manhica (Mozambique)[ʃ]	From [12]	[43]	Jan 98 to Dec 98	47.9	
Manhica (Mozambique)[ʃ]	From [12]	[44]	Oct 02 to Sep 03	41.8	
Daraweesh (Sudan)	Review	Giha[$]	Aug 98 to Jul 00	**93.1**	
Eastern Sudan	From [12]	[45]	Jan to Dec 97	43.7	
Idete (Tanzania)	From [12]	[46-48]	Aug 93 to Jul 94	41	
Ifakara (Tanzania)	From [12]	[49]	Aug 99 to Jul 01	55.7[ʃ]	
Ifakara (Tanzania)	From [12]	[50]	Jul 00 to Jun 01	44.7	
Kampala (Uganda)	From [12]	[51]	Nov 04 to Oct 05	45.4	Bimodal
Gokwe District (Zimbabwe)	From [12]	[52]	Jan to Dec 2003	58.0[ʃ]	
Gweru District (Zimbabwe)	From [12]	[52]	Jan to Dec 2003	38	
Kwekwe District (Zimbabwe)	From [12]	[52]	Jan to Dec 2003	36.7	

[$] pers. comm. *Sites highlighted in bold indicate sites fulfilling definition B; ʃAdditional sites found to show 'SMC seasonality' if Definition C is used; PNLP: Programme National de Lutte contre le Paludisme

Supplementary Table S2. Seasonality assessment of severe malaria incidence

Site (country)	Method	Reference	Study period	Highest fraction of annual burden in 4 consecutive months*	Comment
West and Central Africa					
Luanda (Angola)	From [12]	[53]	Jan to Dec 01	57.8[∫]	
Lambarene (Gabon)	From [12]	[54]	Jan 01 to Dec 04	39.3	
Libreville (Gabon)	From [12]	[54]	Feb 01 to Jan 05	39.9	
Banjul (Gambia, The)	From [12]	[55]	Jan to Dec 91	**69**	
Banjul (Gambia, The)	From [12]	[56]	Jan 97 to Dec 01	**86.4**	
Banjul (Gambia, The)	From [12]	[54]	Apr 02 to Mar 05	**64.2**	
Kumasi (Ghana)	From [12]	[54]	Feb 01 to Jan 05	50.8[∫]	
Navrongo (Ghana)	Review	[57]	May 03 to Apr 04	**67.3**	
Nonzombougou (Mali)	Review	Dicko[$]	Jan to Dec 07	**90**	
Damboa (Nigeria)	Review	Tunji[$]	Jan 04 to Dec 06	**80.9**	Bimodal
Ilorin (Nigeria)	Review	Mokuolu[$]	Dec 09 to Nov 10	47.4	
Maiduguri (Nigeria)	From [12]	[58]	Jan 95 to Dec 96	**61.1**	
Sao Tome & Principe	Review	[59]	Jan to Dec 2009	52.6	
Dakar (Senegal)	From [12]	[60]	Oct 91 to Sep 92	46.2	
East and Southern Africa					
Gambella (Ethiopia)	Review	[61]	Jun 97 to May 98	**61.2**	Bimodal
Kilifi (Kenya)	From [12]	[62]	Jan to Dec 91	48.2	Bimodal
Kilifi (Kenya)	From [12]	[54]	Jul 01 to Jun 05	41.2	Bimodal
Blantyre (Malawi)	From [12]	[54]	Apr 01 to Mar 05	47.3	
Manhica (Mozambique)	Review	[63]	Jun 03 to May 05	43.2	
Maputo (Mozambique)	From [12]	[64]	May 95 to Apr 97	**74.6**	
Huruma (Tanzania)	From [12]	[65]	Feb 02 to Jan 03	58.7[∫]	Bimodal
Ifakara (Tanzania)	From [12]	[66]	Jan to Dec 1995/2000	43.2	
Kibosho (Tanzania)	From [12]	[65]	Feb 02 to Jan 03	50.5[∫]	
Mnero (Tanzania)	From [12]	[65]	Feb 02 to Jan 03	46.5	
Moshi (Tanzania)	From [12]	[65]	Feb 02 to Jan 03	44.9	
Same (Tanzania)	From [12]	[65]	Feb 02 to Jan 03	55.5[∫]	
Teule (Tanzania)	From [12]	[65]	Feb 02 to Jan 03	43.2	
Kabale (Uganda)	Review	[67]	Mar 02 to Feb 03	48.2	Bimodal
Kabale (Uganda)	Review	[68]	Jan 97 to Dec 98	35.6	Bimodal
Hoima (Uganda)	Review	[68]	Jan 97 to Dec 98	35.2	Bimodal
Macha (Zambia)	From [12]	[69]	Jan 03 to Dec 04	76.4	

[$] pers. comm. *Sites highlighted in bold indicate sites fulfilling definition B; ∫Additional sites found to show 'SMC seasonality' if Definition C is used.

Supplementary Table S3. Populations mapped by >60% of annual rainfall in 3 months

	Total population[$]	Population in SMC area[^]	Percent in SMC zone	Under 5 population in SMC area[#]	Percent urban
Benin	8,812,518	557,092	6%	92,422	24%
Burkina Faso	15,708,964	13,854,376	88%	2,710,747	45%
Cameroon	19,126,809	2,950,626	15%	460,947	45%
Chad	10,912,155	7,134,093	65%	1,279,072	31%
Gambia	1,852,882	1,852,882	100%	291,403	68%
Ghana	24,501,245	177,859	1%	24,934	60%
Guinea	10,574,798	5,995,674	57%	986,348	44%
Guinea-Bissau	1,562,554	1,560,770	100%	259,868	47%
Mali	13,117,059	12,387,872	94%	2,146,942	33%
Mauritania	3,597,585	3,403,999	95%	492,252	39%
Niger	14,436,029	14,376,419	100%	3,095,243	39%
Nigeria	145,248,683	37,671,263	26%	6,135,519	52%
Senegal	13,481,010	13,472,934	100%	2,235,833	60%
Sierra Leone	6,629,124	2,563,964	39%	430,567	69%
Sudan	42,415,970	32,765,822	77%	4,490,228	46%
Western Sahara	434,628	52,568	12%	5,477	95%
TOTAL SAHEL	**332,412,013**	**150,778,213**		**25,137,802**	
Angola	13,421,810	766,379	6%	130,875	44%
Botswana	1,890,943	254,314	13%	29,119	22%
D. R Congo	71,412,940	1,871,914	3%	335,466	86%
Djibouti	525,782	21,708	4%	2,683	3%
Egypt	84,731,710	17,352,928	20%	1,983,787	95%
Eritrea	5,333,163	4,926,333	92%	800,923	54%
Ethiopia	81,845,206	23,420,878	29%	3,808,703	50%
Kenya	39,835,135	331,710	1%	55,837	59%
Malawi	14,825,033	14,582,132	98%	2,490,628	42%
Mozambique	22,526,159	13,858,847	62%	2,286,710	23%
Namibia	2,126,549	1,930,604	91%	245,669	47%
Tanzania	42,861,827	9,074,545	21%	1,614,361	32%
Zambia	12,393,193	11,235,159	91%	2,007,835	40%
Zimbabwe	12,276,732	8,099,518	66%	1,109,067	47%
TOTAL OTHER	**406,006,182**	**107,726,969**	27%	**16,901,663**	
TOTAL AFRICA	**738,418,195**	**258,505,182**		**42,039,465**	

$ LandScan population estimate adjusted to 2010 using population growth projections from the UN World Population Prospects (WPP) 2008. ^ Estimated from LandScan populations in areas mapped by seasonality in rainfall (>60% of annual total rainfall occurs in 3 months), also adjusted to 2010 using UN WPP projections. # Estimated using percentage aged 0-4 in UN WPP 2008, using estimates for 2010. % urban are estimated from population density threshold as described in the text.

Supplementary Table S4. Populations at risk in seasonal areas defined by the MARA seasonality map

Country	Total Population[$]	Population in SMC zone[^]	% in SMC zone	Under 5 population in SMC zone[#]	% low risk	% high risk	% urban
Benin	9,211,741	756,914	8%	125,572	0%	100%	42%
Burkina Faso	16,286,706	15,135,571	93%	2,961,426	0%	100%	26%
Cameroon	19,958,351	6,694,266	34%	1,045,778	19%	74%	58%
CAR	4,505,945	129,623	3%	19,057	0%	100%	39%
Chad	11,506,130	10,777,985	94%	1,932,385	9%	86%	28%
Gambia	1,750,732	1,750,732	100%	275,338	0%	100%	58%
Ghana	24,332,755	1,664,040	7%	233,282	2%	98%	51%
Guinea	10,323,755	1,033,949	10%	170,095	1%	99%	35%
Guinea-Bissau	1,647,380	1,139,857	69%	189,786	0%	100%	30%
Mali	13,323,104	11,911,186	89%	2,064,328	8%	90%	36%
Mauritania	3,365,675	1,307,914	39%	189,137	23%	41%	41%
Niger	15,891,482	15,296,510	96%	3,293,339	8%	89%	17%
Nigeria	158,258,917	56,407,741	36%	9,187,129	1%	99%	50%
Senegal	12,860,717	12,852,136	100%	2,132,812	3%	97%	42%
Sudan	43,192,438	25,490,857	59%	3,493,267	44%	56%	40%
Togo	6,780,030	406,175	6%	58,091	0%	100%	43%
Sahel zone	353,195,858	162,755,457		27,370,822			
Angola*	18,992,707	8,289,268	44%	1,415,558	41%	46%	59%
Botswana	1,977,569	520,285	26%	59,573	23%	13%	61%
Burundi*	8,518,862	1,207,773	14%	171,673	42%	21%	11%
DRC*	67,827,495	3,764,450	6%	674,627	6%	85%	35%
Eritrea	5,223,994	3,187,056	61%	518,152	72%	16%	22%
Ethiopia	84,975,606	28,205,256	33%	4,586,739	22%	14%	17%
Kenya	40,862,900	9,257,222	23%	1,558,268	26%	21%	22%
Malawi	15,691,784	13,283,756	85%	2,268,866	19%	77%	20%
Mozambique	23,405,670	19,068,144	81%	3,146,244	4%	96%	38%
Namibia	2,212,037	1,295,042	59%	164,794	59%	8%	38%
Rwanda*	10,277,212	1,022,822	10%	173,440	41%	7%	19%
South Africa*	50,492,408	9,145,237	18%	933,729	11%	15%	62%
Swaziland*	1,201,904	835,792	70%	111,946	14%	69%	21%
Uganda*	33,796,461	1,865,625	6%	361,651	16%	73%	13%
Tanzania	45,039,573	16,600,395	37%	2,953,210	17%	75%	26%
Zambia	13,257,269	11,051,238	83%	1,974,967	12%	83%	36%
Zimbabwe	12,644,041	6,123,000	48%	838,422	42%	54%	38%
Rest of Africa	436,397,492	134,722,362		21,911,858			
Total	789,593,350	297,477,819		49,282,680			

$ Estimate from the UN World Population Prospects (WPP) 2008, using estimates for 2010. ^ % of MARA populations in areas with 1-6 months suitable for malaria transmission, applied to total population in 2010. # Estimated using percentage aged 0-4 in UN WPP 2008, using estimates for 2010. % low risk and % high risk are estimated from the MARA suitability index: 0.25-0.75, low; >0.75, high; as in the World Malaria Report 2008. % urban are estimated from UN World Urbanisation Prospects 2009.

Supplementary Table S5. Search terms used in literature review

Pubmed	Global Health
("Malaria, Falciparum"[Mesh] AND ("Seasons"[Mesh] OR month OR "Incidence"[Mesh] OR "Epidemiology"[Mesh] OR "Cohort Studies"[Mesh] OR "Morbidity"[Mesh]))	malaria, seasons, month, incidence, epidemiology, cohort studies, morbidity
AND	AND
(Angola OR Cameroon OR (Central African Republic) OR Chad OR Congo OR (Democratic Republic of the Congo) OR (Equatorial Guinea) OR Gabon OR (Sao Tome and Principe) OR Benin OR (Burkina Faso) OR (Cape Verde) OR (Cote d'Ivoire) OR (Ivory Coast) OR Gambia OR Ghana OR Guinea OR (Guinea-Bissau) OR Liberia OR Mali OR Mauritania OR Niger OR Nigeria OR Senegal OR (Sierra Leone) OR Togo OR Algeria OR Egypt OR Libya OR Morocco OR Sudan OR Tunisia OR (Sahrawi Arab Democratic Republic))	(Angola OR Cameroon OR Central African Republic OR Chad OR Congo OR Democratic Republic of the Congo OR Equatorial Guinea OR Gabon OR SaoTome and Principe OR Benin OR Burkina Faso OR Cape Verde OR Coted'Ivoire OR Ivory Coast OR Gambia OR Ghana OR Guinea OR Guinea-Bissau OR Liberia OR Mali OR Mauritania OR Niger OR Nigeria OR Senegal OR Sierra Leone OR Togo OR Algeria OR Egypt OR Libya OR Morocco OR Sudan OR Tunisia OR Sahrawi Arab Democratic Republic).mp. [mp=abstract, title,original title, broad terms, heading words]
AND	AND
(Burundi OR Comoros OR Djibouti OR Eritrea OR Ethiopia OR Kenya OR Madagascar OR Malawi OR Mauritius OR Mozambique OR Rwanda OR Seychelles OR Somalia OR Tanzania OR Uganda OR Zambia OR Botswana OR Lesotho OR Zimbabwe OR Namibia OR South Africa OR Swaziland)	(Burundi OR Comoros OR Djibouti OR Eritrea OR Ethiopia OR Kenya orMadagascar OR Malawi OR Mauritius OR Mozambique OR Rwanda OR Seychellesor Somalia OR Tanzania OR Uganda OR Zambia OR Botswana OR Lesotho OR Zimbabwe OR Namibia OR South Africa OR Swaziland).mp. [mp=abstract,title, original title, broad terms, heading words]

Supplementary Methods

Defining the epidemiological situations suitable for SMC

A series of literature reviews were undertaken to identify studies reporting the incidence of uncomplicated malaria and/or admissions with malaria by month for 12 consecutive months. Several sources of data were used:

- published monthly malaria incidence data from a series of systematic literature reviews conducted in 2005 [12]
- routine data from Senegal
- an additional literature review carried out in November/December 2010 in order to identify additional studies that were not included in the earlier review.

For the independent literature review, both the PubMed and Global Health (OVID) online abstracting databases were searched by two investigators. The search was limited to English and French and to articles published after the year 2000. MeSH terms were used where possible (e.g. PubMed). Studies were retained if they provided incidence data for clinical malaria or severe malaria by month for a minimum period of 12 consecutive months, and if diagnosis of malaria was parasitologically confirmed using microscopy or a rapid diagnostic test. Studies were excluded if they were conducted in countries other than those included in the search criteria (see Supplementary Table S2) and the abstract or full text of the article was not available for screening. In addition, citation searches of selected articles were also made and key investigators were contacted for additional or unpublished data. Relevant monthly data from studies were extracted into a Stata database. If data related to an intervention study, only the control/placebo group was abstracted.

Estimating the population under five years of age at risk in SMC areas

The total population within each first administrative unit was calculated using the LandScan™ estimates of population for 2007 (http://www.ornl.gov/sci/landscan/). These data are synthetic estimates of populations produced by models incorporating available census data and other predictors of populations (e.g. night lights). Whilst they provide an indication of populations, in some parts of Africa there is uncertainty in these and other synthetic datasets that must be borne in mind [70].

The population living in the area identified as suitable for SMC based on seasonality in rainfall and, if appropriate, lower thresholds of malaria endemicity was then calculated within each first administrative unit. Population estimates were adjusted for growth since 2007 by scaling up by the change in total country population from the UN WPP data [23]. The percentage living in urban areas within the SMC zones was estimated. The total population in SMC areas (and in urban areas within the SMC areas) was then summed across administrative units for each country. The number of children under 5 years of age was estimated by applying the national percentage of children aged 0-4 years from UN World Population Prospects (WPP) 2008, using the estimates for 2010 [23].

The datasets used in this analysis were available at varying resolution, and we therefore went through a number of aggregation stages. The LandScan population estimates are available as a high resolution dataset with 1/120 degree resolution (approx. 1 km^2 at the equator). At this resolution each pixel was classified as urban or rural, using a definition of >386 individuals per km^2 as urban [24]. This dataset was then aggregated to a resolution of 1/24 degree (approx 5 km^2 at the equator), to match each pixel to the malaria endemicity status [71]. The rainfall data are available at 0.1 degree

resolution, however, here we used a reduced grid of 0.2 degree resolution to classify locations as suitable for SMC based on malaria endemicity and rainfall seasonality. As the estimates of the percentage of children and population growth were available at country level only, we aggregated the populations by administrative unit and in a last step applied the population growth rate and estimated the number of children.

To provide an alternative comparison with the LandScan™ population estimates in areas determined by rainfall and Malaria Atlas Project estimates of malaria endemicity, population estimates from the Mapping Malaria Risk in Africa (MARA) data were extracted [13]. Populations living in areas defined as 'epidemic and strongly seasonal, 1-3 months transmission', or 'endemic and seasonal, 4-6 months transmission' were used. Although the MARA categorisation of '4-6 months suitable for malaria transmission' suggests a longer period of transmission than potentially suitable for SMC, the geographical areas mapped by the areas fitting this definition overlap very closely with those identified as suitable for SMC using the methods based on seasonality in rainfall described previously. The percentage of the total population living in these two seasonality categories were applied to the total country population estimates using the UN WPP projections for 2010 [23]. The proportion of individuals living in urban areas were extracted from the UN World Urbanization Prospects 2009, using estimates for 2010 [72]. As for the previous method, the number of children under 5 years of age was estimated by using the percentage of children aged 0-4 in the UN World Population Prospects (WPP) 2008, using the estimates for 2010 [23].

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