THE LANCET

Supplementary webappendix

This webappendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Dhingra N, Jha P, Sharma VP, et al, for the Million Death Study Collaborators. Adult and child malaria mortality in India: a nationally representative mortality survey. *Lancet* 2010; published online October 21. DOI:10.1016/S0140-6736(10)60831-8.

METHODS

Definition of states

High-malaria states were defined as those with more than double the national death rate: Orissa, Chhattisgarh, Jharkhand and the Northeastern states (including Assam), as shown in Figure S1.

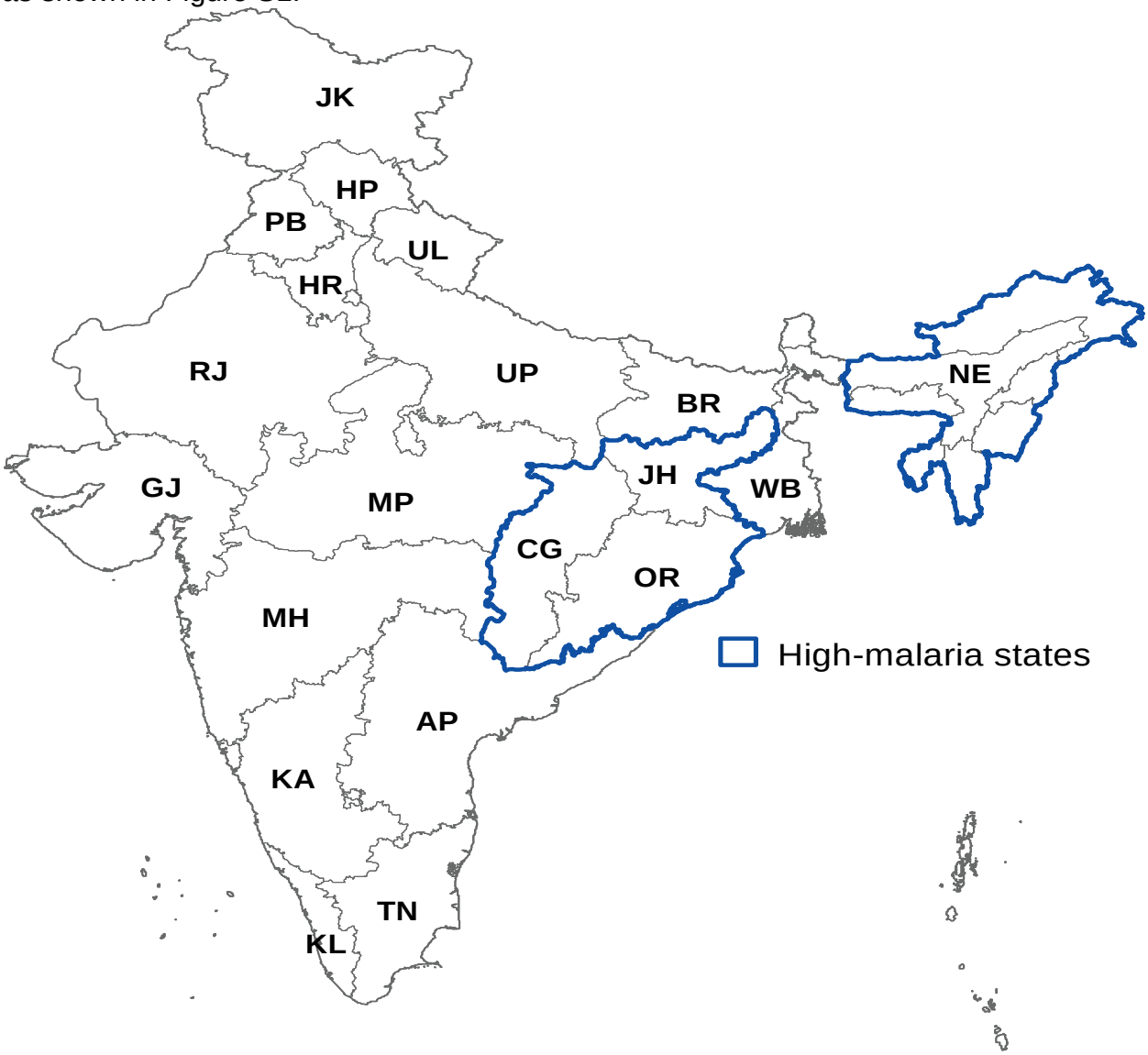

Figure S1 – **High-malaria states**: OR, Orissa; JH, Jharkhand; CG, Chhattisgarh; NE, Assam and the Northeastern states. **Low-malaria states**: JK, Jammu and Kashmir; HP, Himachal Pradesh; PB, Punjab; UL, Uttaranchal; HR, Haryana; RJ, Rajasthan; UP, Uttar Pradesh; BR, Bihar; WB, West Bengal; MP, Madhya Pradesh; GJ, Gujarat; MH, Maharashtra; AP, Andhra Pradesh; KA, Karnataka; KL, Kerala; TN, Tamil Nadu.

Verbal autopsy methods

Causes of death were determined using the "RHIME" or **R**epresentative, **R**e-sampled, **R**outine **H**ousehold **I**nterview of **M**ortality with **M**edical **E**valuation method (Table S1).[1-3] This is an enhanced form of "verbal autopsy".[4] About 800 SRS non-medical field staff reporting to the Registrar General of India (RGI), plus another 60 such staff reporting to the Centre for Global Health Research (CGHR) academic partners in each state, were trained an average of three times on how to collect from a relative or close associate of the deceased the symptoms, signs and key circumstances leading to death using a two-page structured form with a brief narrative in local language. The field workers were instructed not to assign a cause of death, but only to collect the major symptoms and a narrative of the events leading to death. The methods, quality control checks, validation results and comparisons of double coding by physicians have been published.[1,2,5-9] Field workers knew that a random sample of about 5% of the units would be re-surveyed by an independent team as a check on fieldwork quality, completeness and accuracy. All study materials (field forms, field manuals, physician coding manuals, etc) are freely available at www.cghr.org/project.htm.

Table S1: Million Death Study methods overview

Design of field forms	Combined open/closed format. Structured questions plus symptom list plus open-ended narrative.
Form layout	One-page, double-sided, scannable forms. Four age-specific forms (neonatal, child, adult, maternal). Forms available in either English or Hindi, with narrative usually written in local language.
Interviewers	Non-medical Registrar General of India surveyors (mostly male) with knowledge of local language(s), trained in RHIME.
Interview technique	One-on-one interviews during 30-45 minute home visits.
Respondents	Family members or other informants (usually neighbours or close associates of the deceased).
Recall period	Mean 2 years for deaths in 2001-3 monitored in 2003-5.
Data quality	Random resample of 5% of deaths to encourage and monitor completeness of fieldwork. Re-checking of completeness of field work at state RGI offices. Refresher training prior to field work.
Derivation of diagnosis	Internet-based web application provided central medical review of cause by two independent physicians using modified RHIME reports (Physician Reports), with anonymous reconciliation attempted if they disagreed, then adjudication of persisting disagreements by a third expert physician.
Mortality classification	International Classification of Diseases (ICD-10) 3-character coding; B50-B54 was malaria.[10]

The RHIME method was introduced into the ongoing Sample Registration System (SRS) half-yearly monitoring of fact of death in some states from December 2002. Subsequently, a special survey was conducted during 2004-2005 of all deaths recorded by the SRS for calendar years 2001-2003 (except those already covered). Due to out-migration and change in households, informants could not be found for 12% of deaths.

Central physician coding of causes of death

The assignment of causes involved medical evaluation by two of 130 independent trained physicians who examined the field reports using a web-based system developed specifically for this study [5]. Reports were assigned randomly to physicians based only on the language of the narrative. Thus, physicians in one state could code records in another state, increasing comparability across states. If the two physicians did not agree to three-character coding according to the *International Classification of Diseases, tenth revision (ICD-10)*,[10] their forms were re-assigned to each other automatically (and anonymously) for reconciliation. Minor exemptions were made for specific codes within overall categories (such as malaria, B50-B54). Continuing disagreements were referred to a senior third physician who adjudicated the final ICD-10 code. We relied on central diagnosis by a trained panel of physician coders rather than opinion-based algorithms, as previous studies have found that the former yields consistently higher sensitivity for most causes of deaths.[11] Physician coders were trained (for at least 3 days) to screen all relevant information provided, noting all of the positive and negative evidence,[3] and their first 50 records were checked by senior physicians. For each death, physician coders recorded an underlying cause of death in words; the corresponding ICD-10 code, selected from an automated menu with built-in age and consistency checks; and the key words used to guide and support their decision.

Malaria definitions

For all deaths with fever as a key symptom, field staff were instructed to record whether it (1) was high or low grade; (2) lasted more than 30 days; (3) was continuous with no normal temperature, intermittent (on and off), or occasional; (4) rose every day; (5) involved repeated attacks with shivering (chills or shaking); (6) was associated with sweating, muscle pain, diarrhoea, cough, headache, chest pain, jaundice, burning sensation while passing urine, neck stiffness, irritation by light or sound, fits, confusion, drowsiness, coma, rash or blisters. (The complete symptom list is at http://www.cghr.org/symptomlist%20june%2020.pdf).

The physician coders' training, and their written guidelines,[3] instructed them to use their best medical judgement as to whether death was from malaria, but advised to exclude malaria if there was evidence of respiratory infection, burning during urination, rash, blisters, heatstroke or another major diagnosis, eg, tuberculosis. They were advised to consider whether there was blood-test positivity for malaria parasites and whether there was acute onset of fever with shivering. In addition, they were advised that at least one of jaundice, vomiting, breathlessness, decreased urine output, headache, convulsions or unconsciousness should be required. In practice, the main characteristic of the deaths assigned to malaria (based on keywords recorded by the coder) was fever with chills or shaking (Supplementary table S2). Separate guidelines were issued for other diseases, such as typhoid fever and meningitis.

RESULTS

Age, gender and temporal distribution of malaria-attributed deaths

A total of 4690 deaths had at least one coder assign a code of malaria (ICD-10 codes B50-B54). Of these, a final code of malaria was eventually assigned to 3657 deaths at all ages and 2685 deaths at ages 0-69. Below age 70, the code most likely to be revised to malaria was fever of unknown origin (Table S3). Table S4 provides the male and female results separately and the age-specific numbers for both sexes when both coders immediately assigned malaria or if any coder did so. Figure S2 provides the national age-specific malaria deaths rates for the high-and low-malaria states estimated from the present study. To examine seasonality, we plotted monthly totals of malaria-attributable deaths before age 70 (Figure S3). To avoid date preference for January 1, 2001 (the start of the MDS survey), deaths in that month are excluded from this Figure. Table S5 compares the age patterns for malaria deaths based on about 300 urban hospitals (not-representative of India) in 2002 with that from self-reports by households from the nationally-representative survey in 1998-9. In both, the age patterns are similar to that observed in our study. Table S6 provides the details of study deaths and estimated state totals for Orissa. Table S7 shows the distribution of Infection-attributed deaths at ages 0-69, by state, with the rural fever deaths that were not at a health facility subdivided by the disease to which the coders eventually assigned them.

Table S2: Percentages of keywords recorded by physician coder for deaths at ages 15-59 eventually assigned to malaria (B50-B54), to fever of unknown origin (R50), or to other infectious diseases (rest of A and B)

Keyword	Malaria, n=1207	Fever of unknown origin, n=663	Other infectious diseases, n=7869
Any fever	99	97	63
Shivering (Chills/shaking)	80	17	4
Body ache/headache	39	19	6
High fever	35	29	8
Sweat	29	5	3
Blood test positive for malaria	19	0	0
Vomiting	18	7	16
Intermittent fever	16	11	3
Coma/delirium	15	8	3
Weight loss	8	13	26
Weakness	8	19	19
Cough/breathing	6	13	53
Diarrhoea	3	4	20

The tabulation is restricted to ages 15-59, but results were similar for ages 0-69.

Similarly, our unpublished sub-study of 1360 death records abstracted from 6 rural hospitals in Karnataka, Maharashtra, and Orissa found that fever was a reasonable good predictor of medically-certified malaria deaths in these hospitals. Among malaria deaths fever was present or absent in 336 and 12 cases, respectively; among other infectious causes of death, fever was present or absent in 272 and 727 cases, respectively; sensitivity 97%, specificity 73%, positive predictive value 55%, negative predictive value 98%.

Table S3: Causes other than malaria initially assigned by one coder to deaths at ages 0-69 years where the eventual assignment was to malaria (B50-B54)

Initial assignment of underlying cause of death	ICD-10 codes	Diagnoses	Percent
None (malaria initially assigned as the cause by both coders)	B50-B54	1735	65
Fever of unknown origin	R50	289	11
Acute respiratory infection	J09-J22	112	4
Other infectious disease	Other A+B codes	88	3
Meningitis or encephalitis	A81, A83-A89, G00-G09	74	3
Diarrhoea (except Typhoid)	A02-A09	60	2
Typhoid	A01	58	2
Unspecified cause	R95-R99	54	2
Tuberculosis	A15-A19, B90	25	1
Other	All other	190	7
Total		**2685**	100

Table S4: Numbers of malaria-attributed deaths in the present study, by age and gender

	Male			Female			Both sexes			
Age range in years or months (m)	All deaths	Finally adjudicated as malaria[a]	2 coders immediate-ly agreed [b]	All deaths	Finally adjudicated as malaria[a]	2 coders immediately agreed [b]	All deaths	Finally adjudicated as malaria	2 coders immediately agreed	One coder diagnosed malaria initially
<1 m	6069	2	2	4823	2	1	10 892	4	3	5
1-59 m	5624	262	158	6636	325	196	12 260	587	354	834
5-14	1921	153	106	1955	196	134	3876	349	240	444
15-29	4727	198	129	4358	190	132	9085	388	261	481
30-44	6817	171	120	4046	148	108	10 863	319	228	402
45-59	11 725	269	186	6399	231	159	18 124	500	345	635
60-69	12 117	260	149	9017	278	155	21 134	538	304	710
Subtotal: ages 0-69	**49 000**	**1315**	**850**	**37 234**	**1370**	**885**	**86 234**	**2685**	**1735**	**3551**
70+	18 718	477	198	17 339	495	189	36 057	972	387	1179

[a] Deaths where the eventual ICD-10 code was malaria (ICD-10 B50-B54).
[b] Malaria was assigned as the cause by both coders, so no subsequent reconciliation or adjudication was required

Table S5: Malaria-attributed deaths (and malaria as % of all deaths) by age and sex in other Indian populations

	All ages	0-4	5-14	15-24	25-34	35-44	45-54	55-64	65-69	70+
Medically certified causes of death in selected urban hospitals, 2002 [12]										
Male	**3268(1.0%)**	338 (0.8)	347 (3.1)	467 (2.3)	479 (1.6)	508 (1.3)	494 (1.0)	365 (0.7)	101 (0.4)	169 (0.3)
Female	**2193(1.1%)**	315 (1.0)	294 (3.8)	359 (2.0)	345 (1.7)	258 (1.5)	260 (1.3)	180 (0.8)	60 (0.4)	122 (0.3)
Deaths self-reported by households in the Second National Family Health Survey (NFHS-2), 1998-99 [13]										
Male	**156 (2.4%)**	23 (3.0)	29 (4.7)	18 (4.5)	13 (3.6)	14 (3.6)	11 (2.1)	9 (1.1)	9 (2.3)	24 (1.8)
Female	**134 (2.6%)**	19 (2.7)	33 (5.7)	17 (3.9)	12 (4.2)	8 (3.3)	6 (1.8)	12 (2.0)	8 (2.4)	12 (0.9)

Table S6. Orissa only: malaria-attributed deaths in the present study and estimated state-wide totals, by age

Age range in years or months (m)	Study deaths, 2001-2003 Malaria / all coded deaths Numbers	Proportion	Details of the malaria deaths Died in a health facility	Rural area	Two coders immediately agreed	Orissa state-wide deaths, 2005 Estimated malaria mortality Deaths (1000s)	Rate per 100 000	Period risk, %
<1 m ‡	2 / 763	0·0%	0	2	1	0	360	1·72
1-59 m	175 / 749	23·7%	21	169	139	13		
5-14	80 / 235	34·2%	13	71	69	5	66	0·66
15-29	104 / 570	17·8%	38	85	85	5	50	0·75
30-44	113 / 657	17·4%	33	100	90	7	81	1·22
45-59	171 / 1048	16·5%	35	137	140	10	199	2·98
60-69	178 / 1233	14·6%	14	159	140	10	521	5·21
Ages 0-69 (lower/upper bounds)*	**823 / 5255** (664, 898)	**16·2%** (12·8, 17·2)	**154**	**723**	**664**	**51** (39, 55)	**126** (102, 137)	**12·54** (9·96, 13·64)
70 +	239 / 2061	11·6%	8	213	144	13	1114	-

* Based on initial coding.

Table S7. Infection-attributed deaths at ages 0-69, by state, with the rural fever deaths that were not at a health facility subdivided by the disease to which the coders eventually assigned them

	Deaths attributed to an infectious disease in the study, 2001-03				Estimated infectious disease deaths with fever (thousands) in the whole country, 2005		Of the rural deaths with fever not at a heath facility, percentages eventually assigned by coders to:					
	Total, urban or rural	Total with fever	Rural with fever	Rural with fever, not at facility	Total with fever	Rural with fever, not at facility	TB	Diarr-hoea	Malaria	Pneu-monia	Other specified infection	Fever of unknown origin
Malarial states												
North-East states	2808	2206	2014	1795	104	82	14	18	**20**	19	24	4
Orissa	2392	1821	1613	1388	108	74	15	13	**43**	14	12	2
Madhya Pradesh	2322	1821	1712	1557	180	133	14	16	**12**	32	17	8
Chhattisgarh	731	575	531	481	54	37	21	11	**22**	28	11	8
Jharkhand	772	558	520	503	69	60	14	15	**21**	25	16	9
Other states												
Uttar Pradesh	5391	3940	3537	3264	529	387	16	18	**4**	31	24	7
Bihar	3247	2101	2014	1925	186	160	13	15	**8**	38	21	6
Rajasthan	2114	1593	1501	1385	129	99	13	14	**7**	43	16	7
Gujarat	1493	1215	1097	968	89	55	25	17	**8**	19	20	11
Maharashtra	959	769	572	488	98	45	23	16	**12**	20	25	4
Karnataka	1201	735	680	551	49	28	16	18	**5**	12	33	16
Haryana	948	728	581	516	35	21	18	24	**6**	25	22	7
West Bengal	1183	722	614	501	54	29	24	9	**6**	29	22	10
Andhra Pradesh	899	533	472	423	74	50	23	20	**20**	6	23	8
Tamil Nadu	879	533	448	389	47	27	30	15	**3**	12	20	20
Jammu+Kashmir	321	249	205	161	10	5	10	9	**0**	61	14	5
Punjab	364	205	172	147	17	10	15	16	**2**	23	26	19
Kerala	249	129	109	37	5	0.5	23	9	**9**	27	27	9
Delhi	177	111	20	11	9	0.2	0	0	**0**	0	50	25
All other states	752	526	469	348	30	20	30	16	**4**	30	8	9
All INDIA	**29 202**	**21 070**	**18 881**	**16 838**	**1877**	**1312**	**17**	**16**	**11**	**28**	**20**	**7**

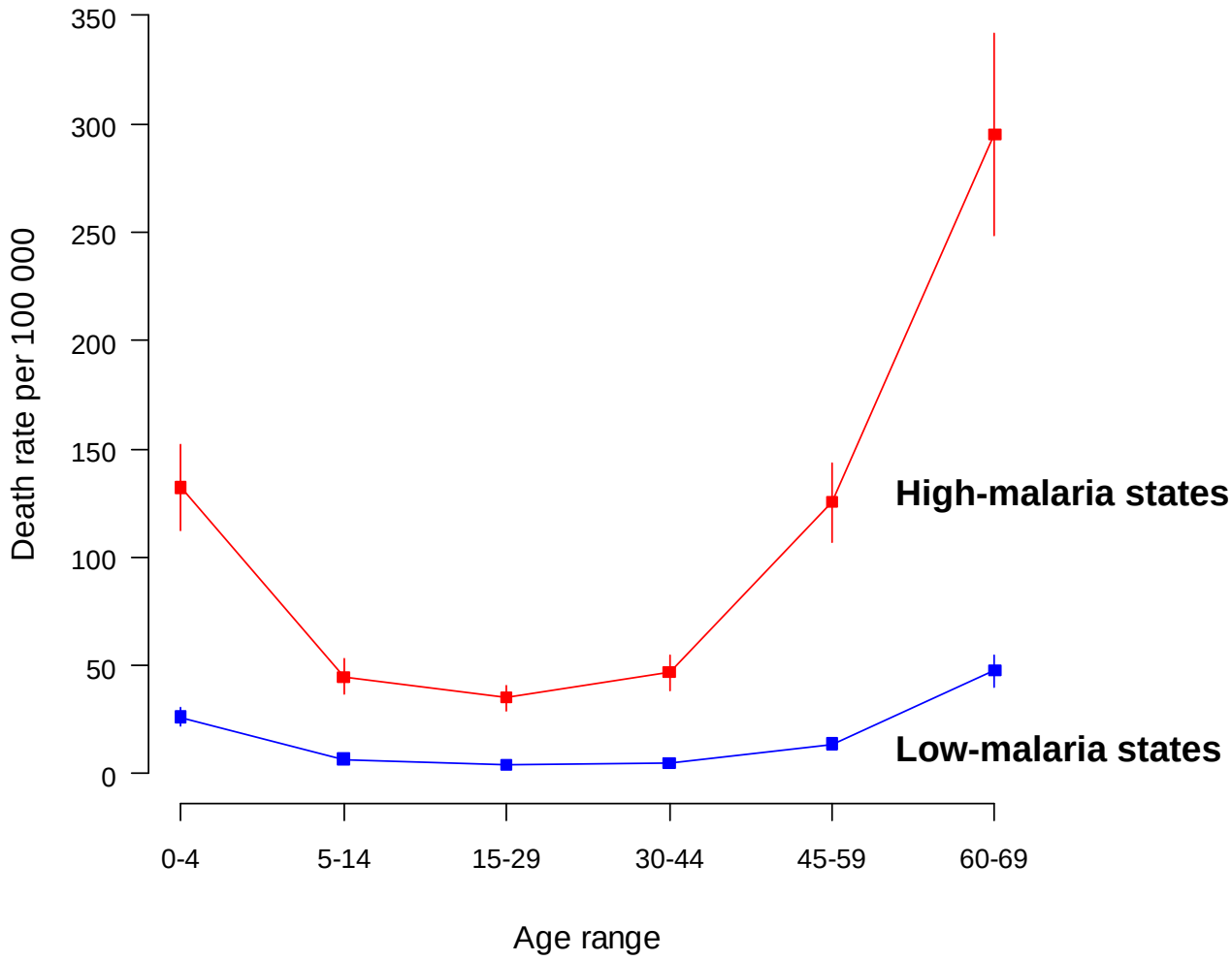

Figure S2: India 2005: age-specific malaria death rates by region. Rates are age-standardised within age-classes shown based on the United Nations population estimates for each 5-year age group in India in 2005. Vertical bars indicate 99% CIs.

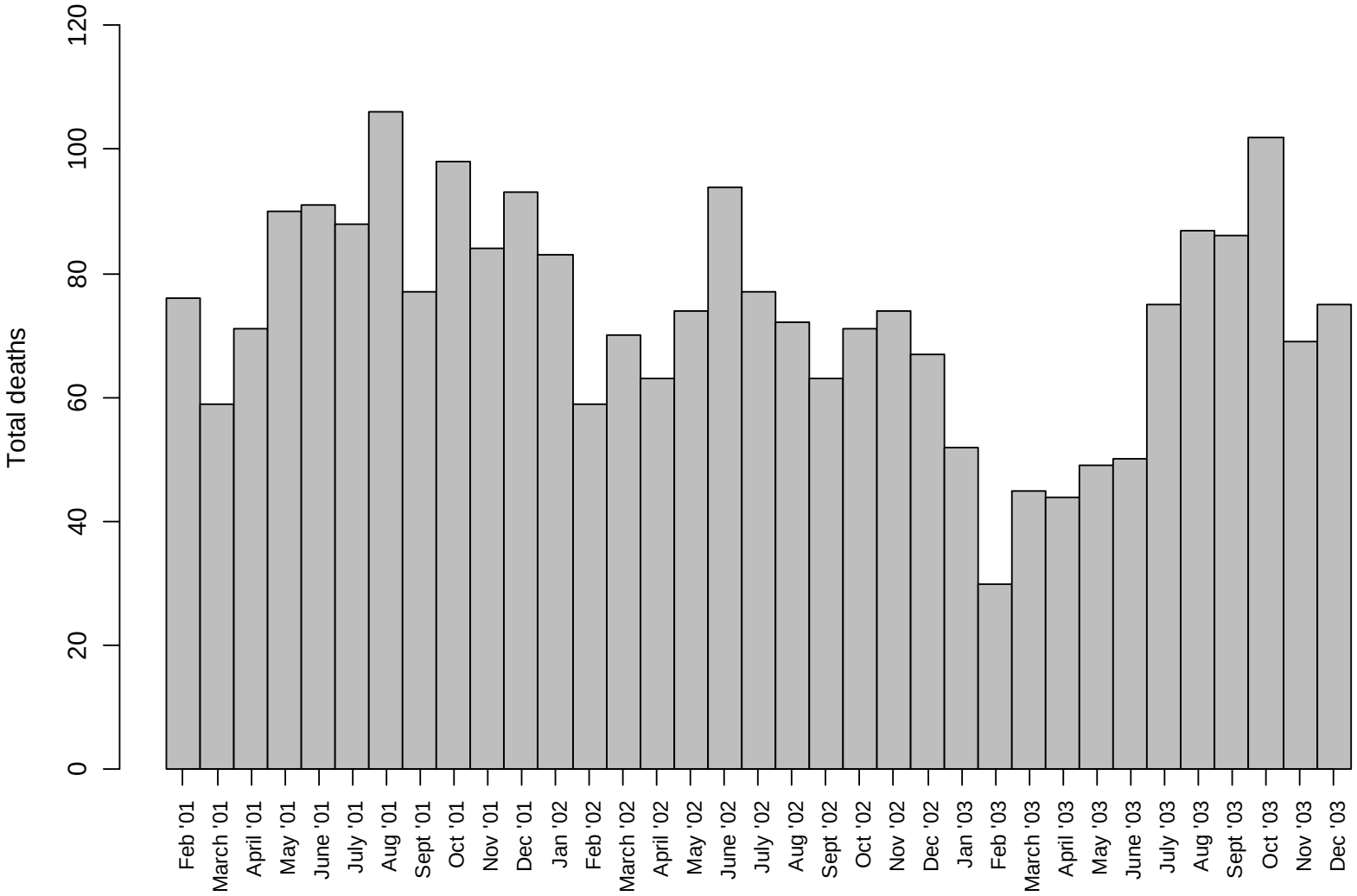

Figure S3: Seasonality of observed deaths attributed to malaria ages 0-69 years

MILLION DEATH STUDY COLLOBORATORS

Indian Academic Partners (in alphabetical order):

1. Clinical Epidemiology Resource and Training Centre Trivandarum: KB Leena, KT Shenoy (until 2005)
2. Department of Community Medicine Gujarat Medical College Ahmedabad: DV Bala, P Seth KN Trivedi
3. Department of Community Medicine Kolkatta Medical College Kolkatta: SK Roy
4. Department of Community Medicine Regional Institute of Medical Sciences Imphal: L Usharani
5. Department of Community Medicine S.C.B. Medical College Cuttack Orissa: Dr. B Mohapatra
6. Department of Community Medicine SMS Medical College Jaipur: AK Bharadwaj, R Gupta
7. Epidemiological Research Center Chennai: V Gajalakshmi, CV Kanimozhi
8. Gandhi Medical College Bhopal: RP Dikshit, S Sorangi
9. Healis-Seskarhia Institute of Public Health Mumbai: PC Gupta, MS Pednekar, S Sreevidya
10. Indian Institute of Health & Family Welfare, Hyderabad: P Bhatia
11. Institute of Health Systems Research Hyderabad: P Mahapatra (until 2004)
12. St. John's Research Institute St. John's Academy of Health Sciences Bangalore: A Kurpad, P Mony, M Vaz, R Jotkar, S Rao-Seshadri, S Shrihari, S Srinivasan
13. King George Medical College Lucknow: S Awasthi
14. Najafgarh Rural Health Training Centre Ministry of Health Government of India New Delhi: N Dhingra, J Sudhir, I Rawat (until 2007)
15. National Institute of Mental Health and Neurosciences Bangalore: G Gururaj (until 2004)
16. North Eastern Indira Gandhi Institute of Regional Medical Sciences Shillong Meghalaya: FU Ahmed (until 2005), DK Parida
17. Regional Medical Research Center ICMR Institute Bhubaneshwar: AS Karketta, SK Dar
18. School of Preventative Oncology Patna: DN Sinha
19. School of Public Health Post Graduate Institute of Medical Education and Research Chandigarh: N Kaur, R Kumar, JS Thakur
20. Tata Memorial Hospital Mumbai: RA Badwe, RP Dikshit, K Mohandas

Lead Partners:

1. Office of the Registrar-General India RK Puram New Delhi India: C Chandramouli (Registrar General of India [RGI]), RC Sethi, B Mishra, S Jain (until 2008), DK Dey (until 2009), AK Saxena, MS Thapa, N Kumar, JK Banthia and DK Sikri (former RGIs)

2. Million Death Study Coordinating Centre for Global Health Research (CGHR) Li Ka Shing Knowledge Institute Keenan Research Centre St. Michael's Hospital Dalla Lana School of Public Health University of Toronto Canada: DG Bassani, P Jha (Principal Investigator), R Jotkar, R Kamadod, B Pezzack, S Rao-Seshadri, P Rodriguez, J Sudhir, C Ramasundarahettige, W Suraweera

Affiliated Partners:

1. Indian Council of Medical Research New Delhi India: VM Katoch (Director General or DG from 2008), NK Ganguly (DG tol 2008), L Kant, B Bhattacharya
2. School of Population Health The University of Queensland Australia: AD Lopez, C Rao
3. World Health Organisation Geneva and SEARO Office New Delhi: T Boerma, T Evans, A Fric, S Habayeb (WHO Representative-India), S Khanum, C Mathers, DN Sinha, N Singh, P Singh (Deputy Regional Director)
4. Clinical Trial Service Unit and Epidemiological Studies Unit (CTSU) University of Oxford England: N Bhala, J Boreham, Z Chen, J Godwin, R Collins, R Peto, G Whitlock

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