## Malaria-attributed death rates in India

As a component of the Million Death Study, Neeraj Dhingra and colleagues (Nov 20, p 1768)[1] estimate by verbal autopsy that about 200 000 people die of malaria in India each year. This estimate is much higher than the WHO estimate of between 10 000 and 21 000 deaths in 2006.[2] New efforts to obtain estimates of the number of malaria deaths are welcome, but there are several reasons why Dhingra and colleagues' results should be viewed with caution.

First, deaths that occurred in 2001–03 were assessed an average of 2 years later (in 2003–05), risking recall bias. Second, any adult member of the family or even a neighbour was interviewed during verbal autopsy, and how well interviewees knew patients during the period of illness before death is not clear. Third, confirmation bias might have led to overdiagnosis of malaria among fever deaths in endemic areas; coding physicians were aware of the state in which each death occurred.

These diagnostic problems, in addition to the use of non-specific symptoms for classification, were highlighted in a small WHO-funded study that examined the accuracy of verbal autopsy in populations served by six hospitals in three Indian states (University of Toronto, unpublished data). Of 48 deaths coded as malaria by verbal autopsy, only four were medically certified as malaria. Others were caused by septicaemia, viral encephalitis, and pneumonia. Additionally, of 69 hospital deaths for which a parasitological test result was available (microscopy or a rapid diagnostic test), 30 deaths were medically certified as malaria, but only 15 were confirmed. The implication is that as few as 4% of deaths attributed to malaria by verbal autopsy were actually due to malaria in that setting.

The limitations of Dhingra and colleagues' study are further exposed when estimates are examined for particular states. Dhingra and colleagues' estimate of 1·24 malaria deaths per 1000 population in Orissa is close to one estimate for Africa (1·47 per 1000 per year).[3] If the case–fatality rate in Orissa were in the range 0·1–0·3%, there would be 17–50 million falciparum cases in a population of 40 million. This is a very high attack rate for the whole state, exceeding that measured in tribal populations living in high-risk forested areas of Orissa.[4] In 2009, only 381 000 malaria cases were found in Orissa of more than 5 million blood slides taken from fever cases.

Dhingra and colleagues argue that various spatial and temporal correlations lend credibility to their estimates. None is compelling. Their malaria deaths coded by verbal autopsy were correlated geographically with malaria deaths recorded by the National Vector-Borne Disease Control Programme, with the distribution of *Plasmodium falciparum* determined by microscopy, and with self-reported fever rates. These associations simply show that there are more malaria deaths where there are more fevers, which is plausible but does not exclude the possibility that verbal autopsy overestimates malaria mortality. They also report that malaria deaths were seasonal, but the seasonality was inconsistent across 3 years and not obviously or formally linked with malaria transmission.

In summary, although routine reports of malaria cases and deaths in India are incomplete, this new estimate of malaria deaths in India cannot be accepted without further validation.

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1 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; **376:** 1768–74.
2 World Health Organization. World malaria report. Geneva: World Health Organization, 2009.
3 Breman JG, Mills A, Snow RW, et al. Conquering malaria: disease control priorities in developing countries, 2nd edn. New York: Oxford University Press, 2006: 413–31.
4 Sharma SK, Tyagi PK, Padhan K, et al. Epidemiology of malaria transmission in forest and plain ecotype villages in Sundargarh District, Orissa, India. *Trans R Soc Trop Med Hyg* 2006; **100:** 917–25.

Neeraj Dhingra and colleagues[1] estimate that, between 2001 and 2003, there were 205 000 malaria deaths annually in India—13 times the WHO estimate.[2] For 1997 and 1998, we reviewed the Medical Certification of Cause of Death under the Civil Registration Scheme that covered 8000 hospitals across India.[3,4] Of the 6·1 million deaths registered, 0·9 million (15%) were medically certified, a sample large enough to be representative of nationally registered deaths. Of these, 8048 were due to malaria. Using these estimates, and after adjustment for the variation in certification in different states, we calculated the probable number of malaria deaths to be 146 032 in 1997 and 141 050 deaths in 1998 (table).[5]

| | Total deaths registered | Number of medically certified deaths | Number of certified malaria deaths | Direct estimation of malaria deaths* | Probable number of malaria deaths† |
|---|---|---|---|---|---|
| 1997 | 2 789 834 | 419 353 (15%) | 3572 (0·85%) | 80 919 | 146 032 |
| 1998 | 3 353 703 | 498 586 (15%) | 4476 (0·89%) | 84 550 | 141 050 |

In 1997, Bihar, Jharkhand (then part of Bihar), Assam, Gujarat, Mizoram, West Bengal, Jammu and Kashmir, and Sikkim did not report. In 1998, Bihar, Assam, Mizoram, Uttar Pradesh, West Bengal, and Jammu and Kashmir did not report. *Assuming 9·5 million annual deaths in India—ie, crude death at 8·5–9·0% from 1997 to 2000. †Adjusted by percentage of medically certified malaria deaths to total registered in different states and union territories.

***Table:*** **Estimated and probable number of malaria deaths in India on the basis of Medical Certification of Cause of Death in rural and urban hospitals across India under civil registration system in 1997 and 1998**

Effective malaria controls such as artemesinin combination therapy, rapid diagnostic tests, and longlasting insecticide-treated bednets have been in widespread use in India over the past 5 years. Additionally, thousands of village health workers have been treating malaria in remote villages with rapid diagnostic tests and antimalarials. Dhingra and colleagues' findings, if valid, are of academic interest since these effective interventions were not in use between 2001 and 2003.

We recognise the importance of prospectively collected, high-quality data. Presently, the US National Institute of Allergy and Infectious Diseases has undertaken a major global initiative to establish International Centres of Excellence for Malaria Research (ICEMRs) in ten different regions around the globe. Two of these ICEMRs have been designated for India. We hope that this collaboration between US and Indian scientists, with research and surveillance across multiple field sites including areas with little or no information on malaria, will provide accurate and reliable estimates to support the national programme.

For more on **ICEMRs** see http://www.niaid.nih.gov/LabsAndResources/resources/icemr/Pages/programOverview.aspx

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2 World Health Organization Country Office for India. Burden of disease. http://www.whoindia.org/en/section2/section427_1348.htm (accessed March 2, 2011).
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5 Jha P, Gajalakshmi V, Gupta PC, et al, for the RGI-CGHR Prospective Study Collaborators. Prospective study of one million deaths in India: rationale, design, and validation results. *PLoS Med* 2006; **3:** e18.

Neeraj Dhingra and colleagues[1] use verbal autopsy procedures to estimate that 205 000 deaths attributable to malaria occur annually in India before 70 years of age (with plausible lower and upper bounds of 125 000–277 000 deaths annually). We believe that Dhingra and colleagues might have substantially overestimated the number of malaria deaths in India for the following reasons.

First, previous validation studies show that verbal autopsy procedures tend to overestimate malaria deaths in areas where malaria transmission is low or absent. Verbal autopsy overestimated malaria deaths in children by 47% in a low-transmission setting in Uganda (Kampala), and overestimated malaria deaths in adults by 200% in a high-transmission setting in Ghana where the proportional mortality of malaria among adults was very low (table).[2–4] In Kisoro, Uganda, where no malaria deaths occurred in children younger than 5 years, verbal autopsy attributed 12% of deaths to malaria (unpublished data).

Second, Dhingra and colleagues report that the increasing proportional mortality in older adults compared with children has been noted previously.[5] We disagree with their interpretation of the studies referenced. The U-shaped distribution of proportional mortality was not seen in Bangladesh,[5] and the proportional mortality in the 45–60-year age group was not higher than in children younger than 5 years in Africa.[5] The malaria-specific mortality rate in the older than 65 years age group was higher than in younger age groups in

| | Total number of deaths | Deaths attributable to malaria | | Sensitivity | Specificity | Positive predictive value | Proportion of malaria mortality underestimated or overestimated by verbal autopsy* |
|---|---|---|---|---|---|---|---|
| | | Medical records | Verbal autopsy | | | | |
| **Verbal autopsy of child deaths** | | | | | | | |
| Tanzania[2]† | 582 | 213 (37%) | 262 (45%) | 69% | 69% | 56% | 23% |
| Kenya (Kilifi)[3] | 217 | 52 (24%) | 42 (19%) | 46% | 89% | 57% | –19% |
| Uganda (Tororo)‡ | 67 | 33 (49%) | 24 (36%) | 61% | 88% | 83% | –27% |
| Uganda (Kampala)‡ | 600 | 60 (10%) | 88 (15%) | 50% | 89% | 34% | 47% |
| Uganda (Kisoro)‡ | 52 | 0 | 6 (12%) | 0 | 88% | 0 | NA |
| **Verbal autopsy of adult deaths** | | | | | | | |
| Tanzania[2] | 1912 | 345 (18%) | 392 (21%) | 64% | 89% | 56% | 14% |
| Tanzania (Ifakara)[4] | 315 | 36 (11%) | 28 (9%) | 36% | 95% | 46% | –22% |
| Ethiopia (Jimma)[4] | 249 | 39 (16%) | 22 (9%) | 39% | 97% | 68% | –44% |
| Ghana (Bawku)[4] | 232 | 10 (4%) | 30 (13%) | 0 | 87% | 0 | 200% |

*(Percentage of malaria deaths estimated by verbal autopsy – percentage of malaria deaths in medical records) / percentage of malaria deaths in medical records. †Validation study was done in tertiary hospitals in adult morbidity and mortality study areas in Dar es Salaam, Morogoro, and Hai districts. ‡Unpublished data.

***Table:*** **Validity of verbal autopsy for ascertaining malaria deaths in children and adults**