

Effective malaria controls such as artemisinin 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.

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Neeraj Dhingra and colleagues<sup>1</sup> 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).<sup>2–4</sup> 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where no malaria deaths occurred in children younger than 5 years, verbal autopsy attributed 12% of deaths to malaria (unpublished data).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.<sup>5</sup> We disagree with their interpretation of the studies referenced. The U-shaped distribution of proportional mortality was not seen in Bangladesh,<sup>5</sup> and the proportional mortality in the 45–60-year age group was not higher than in children younger than 5 years in Africa.<sup>5</sup> The malaria-specific mortality rate in the older than 65 years age group was higher than in younger age groups in

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

	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 <sup>2†</sup>	582	213 (37%)	262 (45%)	69%	69%	56%	23%
Kenya (Kilifi) <sup>3</sup>	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 <sup>2</sup>	1912	345 (18%)	392 (21%)	64%	89%	56%	14%
Tanzania (Ifakara) <sup>4</sup>	315	36 (11%)	28 (9%)	36%	95%	46%	−22%
Ethiopia (Jimma) <sup>4</sup>	249	39 (16%)	22 (9%)	39%	97%	68%	−44%
Ghana (Bawku) <sup>4</sup>	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**

Ghana, but the proportional mortality was not higher than in children.

Third, Dhingra and colleagues have made no attempt to assess the validity of verbal autopsy procedures in India. The subset of deaths (14%) in this study that had occurred in a health facility could have been used in a validation exercise. Ascertaining proportional mortality attributable to malaria by use of verbal autopsy in areas of low malaria transmission has substantial limitations and the estimates of malaria mortality generated by this method should be interpreted with caution.

The letter represents the views of the authors but not the views of the US Centers for Disease Control and Prevention. We declare that we have no conflicts of interest.

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Neeraj Dhingra and colleagues<sup>1</sup> report higher estimates of annual malaria deaths in India than previously suggested. South Asia abounds in life-threatening undifferentiated febrile illnesses like malaria. Typhoid, typhus (ricketsial illness), leptospirosis, and dengue are some of the common diseases that mimic malaria. The

transmission rate of typhoid fever, for example, is 1600 per 100 000 population in some parts, and conservative annual estimates of typhoid deaths worldwide are about 200 000.<sup>2</sup> Blood cultures, when available, are only positive in about 50% of cases, and typhoid, like malaria, remains a largely undiagnosed disease in the community.

Additionally, in a large fever study<sup>3</sup> in south Asia, typhus and leptospirosis were very important causes of undifferentiated fever, yet none of the treating physicians was sufficiently informed about these diseases to put them down as differential diagnoses. Unlike for malaria, however, studies on these undifferentiated febrile illnesses, including typhoid fever, are poorly funded. Indeed, the burden of disease for these common illnesses remains unknown owing to a severe lack of proper fever diagnostics.

Against this background, more concrete proof of malaria with better methods might be required to establish

Dhingra and colleagues' claims about increased malaria mortality in India.

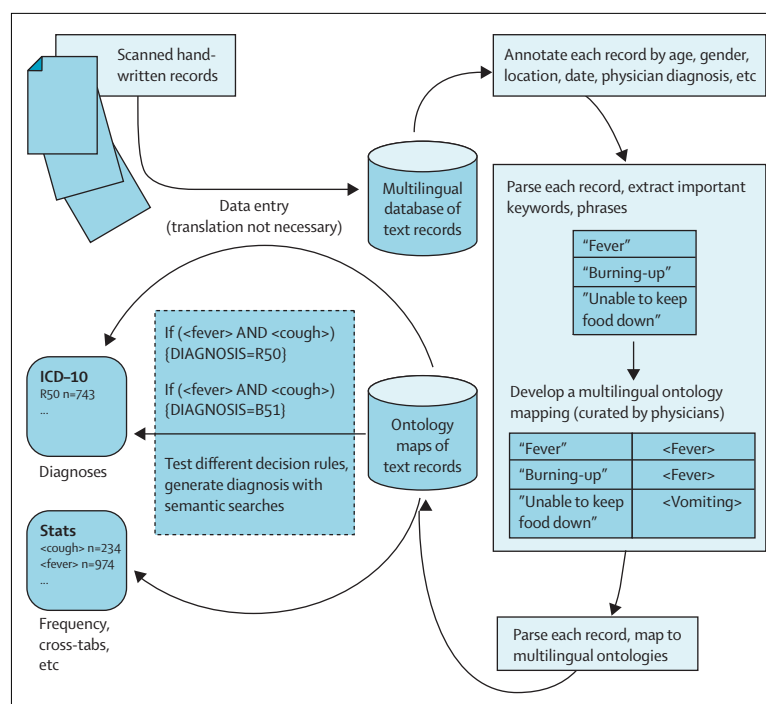
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The methods used by Neeraj Dhingra and colleagues<sup>1</sup> have some potential sources of inaccuracy and bias, which could alter the number of malaria-attributed deaths. Although Dhingra and colleagues were quite fastidious in their methods, concerns about the accuracy of diagnoses by physicians



**Figure: A computational approach to diagnosis and calculation of the number of deaths related to malaria in India**

ICD=International Classification of Diseases.