Do regional differences in under-5 mortality in India reflect the burden of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b disease?

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In 2015, India had the largest number of global deaths in children younger than 5 years. In their systematic analysis in *The Lancet Global Health*, Li Liu and colleagues[1] estimate all-cause and cause-specific deaths in 2000–15 for children younger than 5 years in India. To calculate mortality in children younger than 5 years, infant mortality rates, and neonatal mortality rates, the authors extrapolated 1991, 2001, and 2011 census data to estimate the crude birth rate for 2015. All-cause mortality was calculated from the sample registration system (SRS) for 20 large states in India. From these data the authors imputed under-5 mortality and infant mortality rates for the remaining 15 states and union territories. Assignment of cause of death beyond the neonatal period was based on verbal autopsies done in the SRS. For neonatal deaths, causes were assigned according to verbal autopsies done in high-mortality countries.

In India, there were 1·2 million deaths in children younger than 5 years in 2015, with 0·7 million (57·9%) of these deaths occurring in the neonatal period. The leading causes of neonatal deaths were preterm birth complications (25·5%), intrapartum-related events (11·1%), and sepsis or meningitis (7·9%). In the post-neonatal period, pneumonia and diarrhoea were the leading causes of death. The authors report large disparities in all-cause and cause-specific mortality in children across the different states of India. However, the causes of geographical disparities in under-5 mortality, infant mortality rate, and neonatal mortality rate have not been assessed. The association of these estimates with socioeconomic indicators, education status, and health-systems performance has not been reported. Also, the authors did not estimate the effect of vaccine coverage on mortality since vaccine coverage data were included in their model for adjustment of estimates. These results therefore cannot be used to inform immunisation programmes and policies.

The study by Liu and colleagues nonetheless identifies certain gaps in the knowledge base. All-cause and cause-specific mortality estimates in children younger than 5 years have been calculated meticulously and all assumptions used in the modelling have been specified. Such nationwide surveillance data must be collected at regular intervals, and verbal autopsies of neonatal deaths must also be done at a national level. The key message of this study is that geographical disparities exist in the causes of death in children younger than 5 years in India. Since neonatal mortality accounts for more than half of under-5 deaths in the country, national efforts are needed to address these causes and improve neonatal outcomes.

Also published in *The Lancet Global Health* is a modelling study by Brian Wahl and colleagues,[2] estimating the national, regional, and state-level disease burden due to *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) for 2000–15 in children aged 1–59 months in India. Census data were used to estimate the annual population at risk.

The authors used data from multiple sources to estimate the pathogen-specific disease burden. Data from clinical trials of the pneumococcal conjugate vaccine (PCV) and Hib vaccine done outside of India were used to estimate pneumonia deaths due to these two pathogens. For pathogen-specific deaths due to meningitis, the authors used various surveillance data. From the above estimates, they modelled the burden of pathogen-specific non-pneumonia, non-meningitis (NPNM) invasive disease. Next, they applied pathogen-specific proportions to cause-specific mortality in children aged 1–59 months, which was obtained from verbal autopsies done as a part of the SRS.

The authors report that between 2000 and 2015 there was a 58% decline in pneumococcal deaths and an 81% decline in Hib deaths. They report geographical variation in the burden of disease due to these two pathogens. *S pneumoniae* caused the highest number of deaths in the states of Uttar Pradesh and Odisha, as did Hib in the states of Uttar Pradesh and Bihar. Pneumonia accounted for the largest proportion of pathogen-specific mortality in India.

Reasons for the reduction in pathogen-specific mortality during the 15-year period remain unclear.

Notably, immunisation against Hib began in a phased manner in India in 2012 and there was no immunisation programme against *S pneumoniae* during the time period studied.

A Hib probe vaccine study done in India[3] has shown that there are regional differences in the incidence of severe pneumonia requiring admission to hospital. However, Wahl and colleagues have broadly applied a fixed proportion of the pathogen-specific burden for pneumonia, meningitis, and NPNM invasive disease across all states. Therefore, regional differences in disease burden could be largely attributed to regional variations in mortality, as reported by Liu and colleagues.[1] The first degree of uncertainty is in estimation of the proportion of pathogen-specific deaths while applying a fixed proportion across all regions in the 15-year period. The second degree of uncertainly is in estimation of the causes of death by verbal autopsies done through the SRS, specifically for those with the most severe disease or who died at home or before being admitted to hospital. The authors have also highlighted this as a limitation of their study.

In the absence of prospective epidemiological data, results from the study by Wahl and colleagues[2] could be used as a baseline comparator for assessing the effectiveness of Hib vaccine and PCV programmes in India. The key message of this study—that regional variation exists in the pathogen-specific disease burden in children younger than 5 years—requires validation. Scaling up PCV and Hib vaccine coverage across the country could diminish these regional differences.

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We declare no competing interests.

1 Liu L, Chu Y, Oza S et al. National, regional, and state-level all-cause and cause-specific under-5 mortality in India in 2000–15: a systematic analysis with implications for the Sustainable Development Goals. *Lancet Glob Health* 2019; **7:** e721–34.

2 Wahl B, Sharan A, Deloria Knoll M, et al. National, regional, and state-level burden of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b disease in children in India: modelled estimation for 2000–15. *Lancet Glob Health* 2019; **7:** e735–47.

3 Gupta M, Kumar R, Deb AK, et al. Multi-center surveillance for pneumonia & meningitis among children (<2 yr) for Hib vaccine probe trial preparation in India. *Ind J Med Res* 2010; **131:** 649–58.