Change in national, regional, and state-level pneumonia and severe pneumonia morbidity in India:

Change in national, regional, and state-level pneumonia and severe pneumonia morbidity in India: modelled estimates for 2000 and 2015

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SUMMARY

Background: Pneumonia remains the leading cause of mortality in children in India despite the fact that the absolute number of pneumonia deaths in the country has declined substantially since 2000. As deaths due to pneumonia continue to decline, it will be imperative to also consider interventions that target pneumonia morbidity. We used an improved risk factor-based method to calculate pneumonia and severe pneumonia morbidity in Indian states for 2000 and 2015.

Methods: We estimated the burden of pneumonia and severe pneumonia in children less than five years using a risk factor-based model. A systematic literature review was conducted to identify published data on the incidence of pneumonia from community-based longitudinal studies and a summary estimate was calculated. We estimated state-specific incidence rates for WHO-defined clinical pneumonia for 2000 and 2015 using Poisson regression and the prevalence of risk factors in each state obtained from National Family Health Surveys (NFHS). From clinical pneumonia studies, we identified studies reporting the proportion of clinical pneumonia cases with lower chest wall indrawing to estimate WHO-defined severe pneumonia cases. We used the estimate of the proportion of cases with lower chest wall indrawing to estimate WHO-defined severe pneumonia cases for each state.

Findings: We estimated there were 49.8 (95% uncertainty interval [UI]: 9.1-174.2) million pneumonia cases in HIV-uninfected children less than five years in India in 2015—a 41% reduction since 2000 when there were an estimated 83.8 (95% UI: 14.0- 300.8) million pneumonia cases in this age group. The national incidence of pneumonia in children in India was 657 (95% UI: 110-2 357) cases per 1000 children less than five in 2000 and 403 (74-1408) cases per 1000 children in 2015. We also estimated there were 8.4 (95% UI: 1.2-31.8) million severe pneumonia cases with a corresponding incidence rate of 68 (9-257) cases per 1000 children less than five years and a case fatality ratio of 0.38% (0.11-2.10%) in 2015. The greatest number of pneumonia cases in HIV-uninfected children in 2015 was estimated to have occurred in Uttar Pradesh (12.4 [95% UI: 2.1-45.0] million), Bihar (7.3 [1.3-26.1] million), and Madhya Pradesh (4.6 [0.7-17.0] million) in 2015. Kerala had the greatest reduction with an 82% reduction between 2000 and 2015. Two states were estimated to have pneumonia incidence rates greater than 500 cases per 1000 children less than five years in 2015: Uttar Pradesh (565 [95% UI: 94-2 047]) and Madhya Pradesh (563 [88-2084]).

Interpretation: Pneumonia and severe pneumonia cases were estimated to have decreased between 2000 and 2015. Improvements in socioeconomic indicators and specific government initiatives are likely to have contributed to declines in the prevalence of pneumonia risk factors in many states. However, pneumonia incidence rates in many states remain worryingly high. The introduction of new vaccines that target pneumonia pathogens and reduce risk factors will help further reduce the burden of pneumonia in the country.

RESEARCH IN CONTEXT

Evidence before this study

We searched PubMed for modelled national and subnational estimates of pneumonia and severe pneumonia morbidity in children since 1 January 2000 to 31 December 2018. WE included lower respiratory infections and severe lower respiratory infections in our search. Several national estimates of pneumonia and severe pneumonia morbidity have been published in the literature by the Child Health Epidemiology Reference Group (CHERG) collaboration (now the WHO Maternal and Child Epidemiology Estimation collaboration). In the most contemporary of these estimates, there were an estimated 45 million pneumonia cases and 7 million severe pneumonia cases in 2015. National and subnational estimates of severe pneumonia morbidity for 2010 were published in 2015. Based on these estimates, there were 3.6 million severe pneumonia cases in India in 2010. The same researchers published deaths due to pneumonia. The case fatality ratio based on these estimates was approximately 1% for children less than five years.

Added value of this study

These estimates represent, to our knowledge, the most contemporary estimates of national pneumonia and severe pneumonia morbidity in India. While there have been estimates of severe pneumonia cases in India, we believe these are also the first subnational estimates for pneumonia and severe pneumonia together. In addition, we have updated the risk factor prevalence-based model used to derive pneumonia case estimates. Our updated model uses seven risk factors for pneumonia instead of the five or six risk factors used in previous models. Earlier models assumed that pneumonia risk factors were independent. The completeness of the India survey data allowed us to directly observe the number of children with each combination of risk factors using individual-level survey data. This meant that we were able to build the risk factor model using the observed correlation between risk factors.

Implications of all the available evidence

These updated estimates highlight the recent reductions in pneumonia and severe pneumonia morbidity in India, as a result of changes in the prevalence of seven pneumonia risk factors. These data, together with all the available evidence, should be used to inform policies and programs for addressing pneumonia morbidity in India through new policies and programs. In addition, the new methods developed for this study can be used with data from other settings.

INTRODUCTION

While pneumonia remains the leading cause of mortality in children after the neonatal period in India, efforts to improve access to primary health services in the country have contributed to substantial reductions in pneumonia mortality in recent years.[1] In 2015, there were an estimated 192,000 pneumonia deaths in children less than five years, representing a reduction in the pneumonia mortality rate of 57% since 2000.[1] As deaths due to pneumonia continue to decline, reducing the burden of pneumonia morbidity through primary interventions in particular will become increasingly imperative. Updated subnational estimates of pneumonia morbidity can help monitor progress in this regard.

The World Health Organization (WHO) has identified several interventions for the prevention of pneumonia in children.[2] Many of these interventions are related to improving nutrition and reducing exposure to environmental and social risk factors, and include: exclusive breastfeeding for the first six months of life, adequate complementary feeding, vitamin A supplementation, handwashing with soap, reducing exposure to indoor air pollution, and immunization.[2] The urgent need to focus on pneumonia prevention is compounded by the increasing prevalence of antibiotic resistance that threatens to make treatment for bacterial causes of pneumonia more challenging and expensive in countries such as India.[3]

Etiologic contributors to pneumonia morbidity globally include *Streptococcus pneumoniae* (pneumococcus), *Haemophilus influenzae* type b (Hib), respiratory syncytial virus (RSV), influenza, and human metapneumovirus.[4,5] India introduced the Hib-containing pentavalent vaccine in two states in 2011.[6] It is now used routinely throughout all states and union territories in India.[7] The 13-valent pneumococcal conjugate vaccine (PCV) was introduced in three states in 2017, which was expanded to three additional states in 2018 with plans to expand its routine use in coming years.[5,7] The government is also currently implementing other programs that could reduce the burden of pneumonia in India, including the Integrated Child Development Services (ICDS) scheme that aims improve the nutritional status of children[8] and the Mothers' Absolute Affection (MAA) program that promotes exclusive breastfeeding for the first six months of life.[9]

Previous national and subnational estimates of pneumonia morbidity have been published for India.[10,11] Using subnational inputs, researchers estimated there were 3.6 million severe pneumonia cases in 2010 in children less than five years in India.[11] This model used a risk factor-based approach originally developed by the WHO and the Maternal and Child Epidemiology Estimation (MCEE) collaboration—then called the WHO Child Health Epidemiology Reference Group (CHERG).[12] Using a similar approach, the WHO and MCEE collaboration estimated that nationally there were 45.0 million pneumonia cases and 7.2 million severe pneumonia cases among children in India in 2015.[13] However, for simplicity, these models assumed that the prevalence of pneumonia risk factors were independent, such that children with, for example, low birth weight are no more likely to have malnutrition than children who did not have low birth weight. To support policy making related to child health interventions in India, we used a method which instead uses the observed risk factor combinations to calculate pneumonia and severe pneumonia morbidity in Indian states for 2000 and 2015.

METHODS

Literature review

We estimated the burden of pneumonia and severe pneumonia using a risk factor-based model previously described elsewhere.[13] Briefly, we used data from an earlier systematic literature review that identified published data on the incidence of pneumonia from community-based longitudinal studies around the world and to identify summary estimates of risk factors associated with pneumonia in children. Only studies that reported incidence of WHO-defined clinical pneumonia case definition in children aged younger than five years and those that were carried out for a minimum period of one year and in multiples of 12 months to account for seasonal variations in incidence were included in the analysis. From clinical pneumonia studies, the earlier review identified studies that report the proportion of clinical pneumonia cases with lower chest wall indrawing to estimate WHO-defined severe pneumonia cases. For pneumonia risk factors, we used data from another previous review to identify factors that had strong and consistent statistically significant associations with pneumonia in a published meta-analysis—see Table 1.[14] Additional details for the literature review are described in the appendix (pp 3-5) .

Analysis

Model parameters and their sources for each state are described in Table 1. We obtained data on the prevalence of identified risk factors (except HIV infection) in each state from the National Family Health Survey (NFHS), which uses standardized Demographic and Health Survey (DHS) data collection methods.[15] This survey is supposed to be conducted every five years in India and provides data on a range of demography and health indicators. For small states that were not included in NFHS rounds, we used prevalence estimates from neighbouring states with similar demographics. The prevalence of HIV infection in children was estimated using the proportion of children in each state with mothers infected with HIV and the UNAIDS estimate of the odds ratio for HIV infection in children born to mothers infected with HIV infection in India. We used India census data from 2001 and 2011 to estimate annual population growth rates for each state, which were extrapolated to 2015.[16] We normalized population data to sum to the total national UN population estimates for India.

We estimated state-specific pneumonia incidence by combining: (i) overall incidence estimates from published papers for the WHO South East Asia region, (ii) published effect estimates for associations between risk factors and pneumonia, and (iii) risk factor prevalence data from state-level survey data. We combined each of these estimates in a risk-factor based model, sampling from our previous model, log-normal distributions, and Dirichlet distributions for the regional incidence, risk factor associations, and survey data respectively. We also calculated the incidence of clinical pneumonia in children with HIV and incidence of pneumonia attributable to HIV. To calculate state-level WHO-defined clinical pneumonia cases, we applied the estimate of the proportion of cases with lower chest wall indrawing to estimate WHO-defined severe pneumonia cases for each state. Additional details for the modelling are in the appendix and the model code is available on request.

After calculating pneumonia and severe pneumonia cases for each state, we used estimates of Hib vaccine efficacy against invasive Hib disease,[17] the proportion of clinical pneumonia cases attributable to Hib,[18] and state-level vaccine coverage estimates to account for the proportion of

children who would have been protected by Hib vaccine. We used coverage of the third dose of diphtheria-tetanus-pertussis vaccine (DTP3) from subnational surveys for coverage with three doses of Hib vaccine. This is justified, as Hib vaccine is provided as part of a pentavalent combination that includes DTP in the national immunization program. We adjusted coverage estimates to account for the time of year when Hib vaccine was introduced. Linear interpolation was used when data were missing for relevant years. PCV was only available in India through the private sector in 2015 with low estimated population-level coverage.[19] Therefore, we assumed PCV had no impact on pneumonia morbidity in children prior to 2015. We then used published state-level estimates of pneumonia deaths in children from 2015[1] to independently infer case fatality ratios.

We used a simulation approach to calculate state-specific rates along with uncertainty estimates, as uncertainty ranges (UR; appendix p 5). All statistical analyses were done using R (version 3.2; Vienna, Austria) and JAGS (version 3.4). This study was conducted in accordance with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) recommendations (appendix p 2).[20]

Reporting
We report pneumonia and severe pneumonia morbidity estimates for six geographically contiguous and socio-economically similar regions: north, east, northeast, central, west and south. For state-level model results, union territories (UT) except Delhi and states in the Northeast except Assam have been grouped together. Telangana separated from Andhra Pradesh in June 2014. We projected population and mortality data for Andhra Pradesh and modelled the pneumonia and severe pneumonia burden for Andhra Pradesh and Telangana together for 2015. We also report on the pneumonia and severe pneumonia morbidity together for the nine high-focus states—see Table 2. Since state and region estimates are related to the total estimate only through the estimated rate in the unexposed group, the model does not impose the constraint that the state counts will sum to the national counts.

Ethical approval
This study did not require ethical approvals.

Role of the funding source
The sponsor of this study had no role in the study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit this report for publication. All authors had full access to all the data used in the study and the corresponding author had final responsibility for the decision to submit for publication.

RESULTS
We estimated there were 49.8 (95% UI: 9.1-174.2) million pneumonia cases in HIV-uninfected children less than five years in India in 2015. This represents a 41% reduction since 2000 when there were an estimated 83.8 (95% UI: 14.0- 300.8) million pneumonia cases in this age group. National incidence of pneumonia in children in India decreased by 39% from 657 (95% UI: 110-2 357) cases per 1000 children less than five years in 2000 to 403 (74-1 408) cases per 1000 children in 2015. We also estimated there were 8.4 (95% UI: 1.2-31.7) million severe pneumonia

cases with a corresponding incidence rate of 68 (9-257) cases per 1000 children less than five years in 2015.

There remained disparities in the calculated burden of pneumonia by region in India. The pneumonia incidence in the central region (540 [95% UI: 89-1 967] cases per 1000 children less than five years) was more than twice the pneumonia incidence in the south region (251 [55-810] cases per 1000 children) in 2015. Pneumonia incidence in the north region declined by an estimated 53% between 2000 and 2015, more than any other region. Pneumonia incidence in the west region only reduced by 22% during the same timeframe. The central region also had the greatest estimated severe pneumonia incidence with 91 (95% UI: 11-355) cases per 1000 children less than five years in 2015.

The estimated pneumonia incidence rate was higher in the high-focus states in 2015 with 513 (95% UI: 87-1847) cases per 1000 children less than five years compared with non-high-focus states in the same year when the pneumonia incidence was estimated to be 331 (64-1134) cases per 1000 children. Pneumonia incidence in high-focus states declined by approximately the same amount compared to non-high-focus states between 2000 and 2015. In 2015, the severe pneumonia incidence rate in high-focus states was 87 (95% UI: 11-336) cases per 1000 children compared with 56 (8-208) cases per 1000 children in non-high-focus states in the same year.

The incidence rates and number of cases of pneumonia and severe pneumonia for each state in 2000 and 2015 are included in Table 3. The greatest number of pneumonia cases in children uninfected with HIV were estimated to have occurred in Uttar Pradesh (12.4 [95% UI: 2.1-45.0] million), Bihar (7.3 [1.3-26.1] million), and Madhya Pradesh (4.6 [0.7-17.0] million) in 2015. All states were estimated to have reduced the number of pneumonia cases between 2000 and 2015. Kerala had the greatest reduction with an 73% reduction and Gujarat had the smallest with a 18% reduction during this timeframe. Two states were estimated to have pneumonia incidence rates greater than 500 cases per 1000 children less than five years in 2015: Uttar Pradesh (565 [95% UI: 94-2 047]) and Madhya Pradesh (563 [88-2 084).

In 2015, there were an estimated 143,000 (UR: 22,500-531,000) and 24,200 (UR: 2,900-95,200) cases of pneumonia and severe pneumonia among children infected with HIV, respectively. Uttar Pradesh had the highest incidence of pneumonia and severe pneumonia among children infected with HIV in 2015, with 1.9 (UR: 0.3-7.2) and 0.3 (UR: 0.0-1.3) cases per 1000 children less than five years, respectively. Incidence rates for pneumonia and severe pneumonia in HIV infected children increased in Rajasthan, Jharkhand, Bihar, Odisha, Jammu and Kashmir, and Haryana between 2000 and 2015.

Using state-level estimates of pneumonia mortality for 2015 published by the WHO/MCEE collaboration,[1] we estimated pneumonia and severe pneumonia case fatality ratios in all states in 2000 and 2015. The national pneumonia case fatality in 2015 was estimated to be 0.38% (95% UI: 0.11-2.10%). Severe pneumonia case fatality in 2015 was estimated 2.26% (95% UI: 0.60-16.30%). Pneumonia and severe pneumonia case fatality in 2015 ranged from 0.87% (95% UI: 0.26-4.37%) and 5.20% (1.40-36.42%) in Assam, respectively, to 0.12% (0.03-0.69%) and 0.72% (0.19-5.31%) in Maharashtra, respectively. Pneumonia mortality decreased in all states between 2000 and 2015.

The national prevalence all seven pneumonia risk factors, except non-exclusive breastfeeding, decreased between 2000 and 2015 (Figure 1). The prevalence of non-exclusive breastfeeding increased from 20% to 22% between 2000 and 2015. HIV infection was estimated to have the lowest prevalence of all pneumonia risk factors, at 0.3% in both 2000 and 2015. National prevalence of malnutrition decreased marginally; however, the prevalence of malnutrition in many of the high-focus states largely remained constant or increased, with the exception of Rajasthan and Odisha in which the malnutrition prevalence decreased by 8% and 7%, respectively. The prevalence of incomplete immunization decreased more than the other six pneumonia risk factors from 25% to 19% between 2000 and 2015. The range of prevalence estimates for indoor air pollution at the state level increased substantially between 2000 and 2015.

DISCUSSION

We calculated national- and state-level estimates of pneumonia and severe pneumonia morbidity in India for 2000 and 2015 using an improved risk factor-based approach. To our knowledge, these estimates represent the first subnational pneumonia morbidity estimates and the most contemporary severe pneumonia morbidity estimates for India. Together with pneumonia mortality estimates prepared by the WHO/MCEE collaboration,[1] these estimates can be used by policy makers for tracking progress toward reducing the burden of pneumonia and prioritizing the introduction of new child health interventions. An important use of these estimates is that they can be used to estimate the cost effectiveness of pneumonia interventions.

We estimate that pneumonia and severe pneumonia cases in India decreased by approximately 41% since 2000. This is greater than the 22% reduction globally in pneumonia cases during the same period. The reduction in India corresponds with an overall reduction in the proportion of children who are unimmunized and state-specific reductions in low birthweight, malnutrition, and exposure to indoor air pollution. Many risk factors for pneumonia are associated with low socioeconomic status. While there remain worrying socioeconomic inequities in India, overall improvements in socioeconomic status would have contributed to a reduction in the prevalence of critical pneumonia risk factors.

In addition, the launch of the National Rural Health Mission in 2005, now the National Health Mission, has helped to expand and improve access to many primary health services for women and children in the country, including immunization.[21,22] Researchers have also found that nutrition outcomes have been improving in several states in India at least in part due to improved infant and young child feeding practices encouraged by the ICDS program.[23] Additional government efforts aimed at addressing the prevalence of risk factors for pneumonia morbidity, including Mission Indradhanush to improve full immunization coverage and Pradhan Mantri Ujjwala Yojana to extend access to liquid petroleum gas and therefore reduce exposure to indoor air pollution, could help further reduce the burden of pneumonia morbidity in the country.

Despite these reductions, there remained considerable disparities in pneumonia morbidity between states in India. These disparities arise largely as a result of substantial differences in the prevalence of risk factors for pneumonia. All states in India had introduced the Hib-containing pentavalent vaccine by December 2015. However, the states with the lowest pneumonia burden

(i.e., Kerala and Tamil Nadu) were the first to introduce the vaccine in 2012. Many high burden states only introduced the vaccine in 2015. Uttar Pradesh, the state with the highest estimated incidence of pneumonia and severe pneumonia, only introduced the pentavalent vaccine in December 2015. In addition, differences in care seeking behaviors between states have also likely contributed to disparities in the case fatality ratios we estimated using state-level estimates of pneumonia mortality for 2015 from the WHO/MCEE collaboration.[1]

While the prevalence of pneumonia risk factors in many states declined since 2000, in many states the increase or flattening of prevalence for many risk factors in some states remains worrying and should be the target of strategies to address the burden of pneumonia in India. The introduction of PCV in 2017 in Uttar Pradesh, Bihar, and Himachal Pradesh—some of the states with the highest pneumonia incidence—diverges from the introduction approach for Hib vaccine which was introduced first in Tamil Nadu and Kerala. The introduction of PCV in Uttar Pradesh and Bihar was initiated in several districts in these states. In the future, district-level estimates of pneumonia burden will be helpful for policy making related to the introduction of new vaccines that target respiratory pathogens including respiratory syncytial virus (RSV) and influenza.

The current national estimates of pneumonia and severe pneumonia in 2015, approximately 49.8 million and 8.4 million cases, respectively, are marginally greater than previously published pneumonia and severe pneumonia estimates— 45.0 million and 7.2 million cases respectively.[13] The current estimates allow for pneumonia risk factors to be correlated (i.e., the previous model assumed independence of risk factors). As such, we would expect higher estimates, holding all other factors constant, in settings with high correlation of risk factors. In addition, the current severe pneumonia estimates are also greater than the national estimate published for 2010.[11] At the state-level, the number and incidence of severe pneumonia also differs substantially—the current estimates are higher than those for 2010 for every state. While the rank order of states based on severe pneumonia cases is similar between the two models, the rank order according to incidence differs substantially. This suggests differences in the denominator used to calculate incidence rates. The previously published estimates used a summary estimate comprising radiography-confirmed pneumonia rather than WHO-defined severe pneumonia to calculate severe pneumonia cases. The incidence of radiography-confirmed pneumonia from the three studies comprising the summary estimate[24-26] are lower than severe pneumonia incidence.

A prospective and cross-sectional study was recently conducted in India and provides estimates of community acquired pneumonia incidence for 2016 for Bihar and Uttar Pradesh.[27] In two districts in Uttar Pradesh, the incidence of community-acquired pneumonia was estimated to be 87 and 177 per 1000 children. The incidence in Bihar was estimated to be 208 and 221 per 1000 children in two districts in that state. In the current study, we calculated the incidence of pneumonia in Uttar Pradesh and Bihar to be 524 and 495 cases per 1000 children less than five years. The authors of these estimates suggest their estimates are likely lower than the true incidence of community acquired pneumonia in the four districts of these two states. They note that gender biases related to access to care and pneumonia patients dying prior to reaching a health facility might have contributed to the underestimation of community-acquired pneumonia incidence in these two states.

We updated our methods for estimating pneumonia and severe pneumonia cases. First, our updated model uses seven risk factors for pneumonia instead of the five or six risk factors used in previous models.[10,11] Our earlier models also assumed that the risk factors were mutually exclusive (e.g., a child with malnutrition did not also have low birth weight), with later models making the less stringent assumption that the risk factors were independent. The completeness of the India survey data, however, allowed us to directly observe the number of children with each combination of risk factors using individual-level survey data. This meant that, other than for HIV, we were able to build the risk factor model using the observed correlation between risk factors. For HIV, we assumed that within each state and combination of risk factors, the number of children with HIV was proportionally related to the proportion of children whose mothers had HIV. Code for the updated model is available at [github repository when paper published].

We accounted for several sources of uncertainty in our estimates of pneumonia morbidity, including pneumonia incidence rates, the proportion of pneumonia that is severe, odds ratios for pneumonia risk factors, the proportion of children with pneumonia risk factors, and coverage of PCV and Hib vaccine in children. The wide uncertainty intervals reported reflect the multiple sources of uncertainty in our model. However, these uncertainty estimates might be too conservative. For example, the upper uncertainty range for pneumonia cases in 2015 in India was estimated to be 174 million. This exceeds the total populations in this age group, approximately 119 million children.[28] Improved methods for estimating uncertainty from all potential sources of uncertainty, or preferably increased empirical data collection, could help to address this challenge.

The *post hoc* adjustment for immunization with Hib vaccine assumes homogenous vaccine coverage within each state. However, there are known differences in vaccine coverage within states and based on demographic and socioeconomic indicators.[29] Failing to account for these disparities in immunization coverage likely overestimates the impact of vaccination and therefore underestimates the burden of pneumonia morbidity in each of the Indian states. Subnational PCV coverage estimates from the private sector have been published for 2012.[19] However, we did not use these estimates in our model as the overall national coverage was reported to be <1% in this year. In addition, those who received PCV through the private sector are likely at lower risk of pneumococcal disease compared with those who did not receive PCV in the private sector.

Our model accounts for the prevalence of indoor air pollution as an independent risk factor for pneumonia. However, we were unable to account for the prevalence of exposure to ambient air pollution, (AAP) which has been observed to be associated with short- and long-term increased risk of pneumonia in children.[30] Given the high prevalence of AAP exposure throughout India, this could lead to an underestimate in our pneumonia morbidity estimates. In addition, we were unable to account for the increased risk associated with having a family member with an upper or lower respiratory infection, which are known risk factors for pneumonia in India.[31,32]

India has made substantial progress toward reducing childhood pneumonia mortality in the last decade and a half. The country is now home to more children less than five years than any other country. This cohort of children will soon become the largest working population in the world. Ensuring that these children are able to live healthy, productive lives will require the scale-up of

a comprehensive package of important interventions that protect against and prevent pneumonia, including breastfeeding for the first six months, adequate nutrition, immunization with pertussis, measles, Hib, and PCV, and reduced exposure to air pollution. Increasing utilization of these interventions will protect many of the most vulnerable children from pneumonia and could help prevent long-term sequelae, including restrictive lung disease, obstructive lung disease, and asthma.[33] Doing so will be critical for India to reap the benefits of its growing workforce.

Contributions

BW supported data collection, contributed to the data analysis, and wrote the first draft of this manuscript. DAM collected the data and led the data analysis. LL and YC prepared the state-specific pneumonia death estimates in children used to calculate case fatality ratios. HC and HN conceptualized the study, led the data collection, and oversaw the manuscript writing. REB had oversight responsibility for the project. All coauthors contributed to the interpretation of the results and manuscript revisions.

Declaration of interests

BW reports grants from the Bill & Melinda Gates Foundation during the conduct of the study; and grants from Gavi, the Vaccine Alliance, the Bill & Melinda Gates Foundation, and Pfizer, outside the submitted work. MDK reports grants from the Bill & Melinda Gates Foundation during the conduct of the study; and personal fees from Merck; and grants from Pfizer, outside the submitted work. AS reports grants from the Bill & Melinda Gates Foundation and Pfizer, outside the submitted work. LL reports grants from the Johns Hopkins Bloomberg School of Public Health during the conduct of the study. YC and MS report grants from the Bill & Melinda Gates Foundation outside the submitted work. KLO reports grants from the Bill & Melinda Gates Foundation during the conduct of the study; grants from the Bill & Melinda Gates Foundation, Gavi, the Vaccine Alliance, GlaxoSmithKline, and Pfizer outside the submitted work. HC reports grants and personal fees from the Bill & Melinda Gates Foundation during the conduct of the study; grants and personal fees from the World Health Organization, UN IMI, UK NIHR; and grants and personal fees from Sanofi, outside the submitted work. HN reports grants and personal fees from Innovative Medicines Initiative and Sanofi; grants from the World Health Organization and the National Institute of Health Research; and personal fees from the Bill & Melinda Gates Foundation, Janssen, and Abbvie outside the submitted work. All other co-authors have nothing to disclose.

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TABLES AND FIGURES

Table 1: Model parameters and data sources

Model component	Model parameter	Sources of data	Value (95% confidence interval or interquartile range)
Pneumonia and severe pneumonia morbidity	Baseline pneumonia incidence (per child year), community	Published summary estimate[13]	0.22 (IQR: 0.11–0.51)
	Proportion of pneumonia that are severe	Published summary estimate[13]	11.5% (IQR: 8.0–33.0%)
Pneumonia risk factors	Odds ratio for low birth weight (i.e., <2.5 kg)	Published summary estimate[14]	3.6 (95% CI: 0.8-16.3)
	Odds ratio for the lack of exclusive birth feeding	Published summary estimate[14]	2.7 (95% CI: 1.7-4.4)
	Odds ratio for crowding (i.e., seven or more persons per household)	Published summary estimate[14]	1.9 (95% CI: 1.5-2.5)
	Odds ratio for indoor air pollution exposure	Published summary estimate[14]	1.6 (95% CI: 1.1-2.3)
	Odds ratio for malnutrition (i.e., weight for age <-2 standard deviations)	Published summary estimate[14]	4.5 (95% CI: 2.1-9.5)
	Odds ratio for incomplete immunization at 12 months	Published summary estimate[14]	1.8 (95% CI: 1.3-2.5)
	Odds ratio for HIV infection	Published summary estimate[34]	6.5 (95% CI: 5.9-7.2)
Population at risk and demographic model parameters	Child population	2001 and 2011 census data from Government of India	State-specific values
	Hib vaccine coverage	Inferred from DTP3 coverage estimates from AHS, DLHS, and NFHS	State-specific values
	Pneumonia mortality	Estimates of pneumonia mortality from WHO/MCEE collaboration[1]	State-specific values

AHS = Annual Health Survey; DLHS = District Level Household and Facility Survey; NFHS = National Family Health Survey; WHO/MCEE = World Health Organization and Maternal Child Epidemiology Estimation.

Table 2: Indian states by region and categories

Region	States
Central	Chhattisgarh, Madhya Pradesh, Rajasthan, Uttar Pradesh
East	Bihar, Jharkhand, Odisha, West Bengal
North	Chandigarh, Delhi, Haryana, Himachal Pradesh, Jammu & Kashmir, Punjab, Uttarakhand
Northeast*	Arunachal Pradesh, Assam, Manipur, Meghalaya, Mizoram, Nagaland, Sikkim, Tripura
South	Andaman & Nicobar Islands, Andhra Pradesh, Karnataka, Kerala, Lakshadweep, Puducherry, Tamil Nadu
West	Dadra & Nagar Haveli, Daman & Diu, Goa, Gujarat, Maharashtra
Union territories	Andaman & Nicobar Islands, Chandigarh, Dadra & Nagar Haveli, Daman & Diu, Delhi, Lakshadweep, Puducherry
High-focus states	Assam, Bihar, Chhattisgarh, Jharkhand, Madhya Pradesh, Odisha, Rajasthan, Uttar Pradesh, Uttarakhand

* Northeast states exclude Assam for estimates reported at the state-level

Table 3: National and state-level estimates of pneumonia and severe pneumonia morbidity among children less than five years

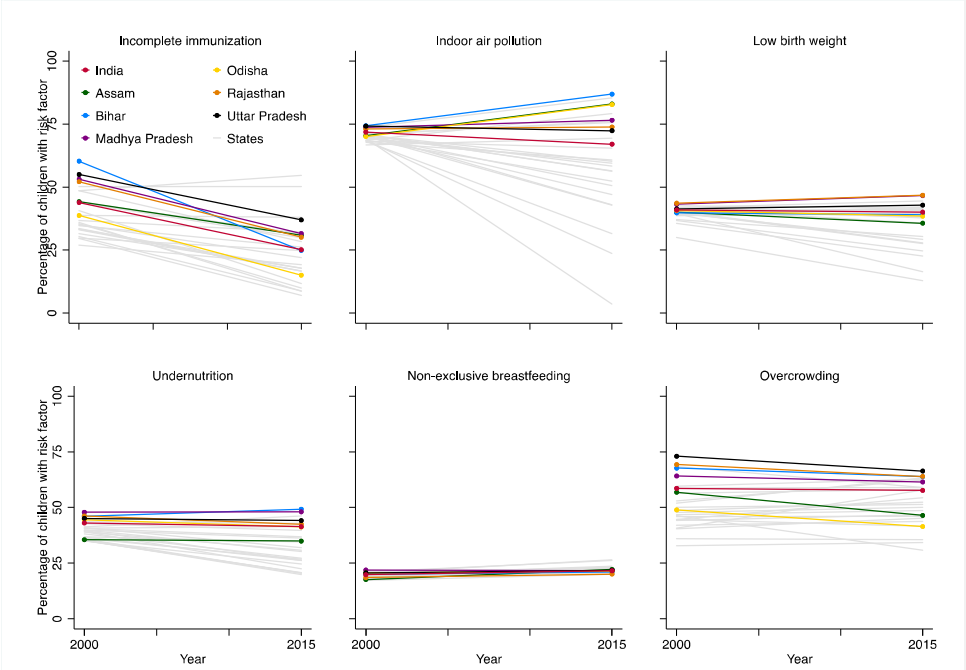
Geography	2000				2015			
	Pneumonia cases in thousands (95% UI)	Pneumonia incidence (95% UI)	Severe pneumonia cases in thousands (95% UI)	Severe pneumonia incidence (95% UI)	Pneumonia cases in thousands (95% UI)	Pneumonia incidence (95% UI)	Severe pneumonia cases in thousands (95% UI)	Severe pneumonia incidence (95% UI)
States								
Andhra Pradesh and Telangana	3 920 (700-13 680)	504 (90-1 758)	660 (90-2 510)	85 (11-323)	1 830 (380-6 110)	275 (57-918)	310 (50-1 120)	46 (7-169)
Assam	2 000 (340-7 220)	574 (98-2 068)	340 (40-1 300)	97 (13-371)	1 250 (250-4 230)	350 (69-1 184)	210 (30-780)	59 (9-218)
Bihar	10 860 (1 730-39 510)	865 (138-3 148)	1 840 (220-7 250)	147 (18-578)	7 330 (1 290-26 060)	498 (87-1 773)	1 240 (160-4 720)	84 (11-321)
Chhattisgarh	2 520 (380-9 320)	892 (136-3 294)	430 (50-1 710)	151 (17-603)	1 120 (200-3 960)	401 (71-1 416)	190 (30-730)	68 (9-260)
Delhi	900 (150-3 180)	566 (97-1 997)	150 (20-580)	96 (13-364)	430 (80-1 480)	285 (54-983)	70 (10-280)	48 (7-184)
Goa	70 (10-230)	542 (91-1 943)	10 (0-40)	92 (12-356)	20 (0-70)	203 (44-667)	0 (0-10)	34 (6-124)
Gujarat	3 620 (610-12 900)	596 (101-2 123)	610 (80-2 380)	101 (13-391)	2 960 (500-10 770)	493 (83-1 792)	500 (60-1 960)	83 (11-326)
Haryana	1 420 (240-5 050)	540 (92-1 926)	240 (30-930)	91 (12-353)	850 (170-2 870)	326 (65-1 100)	140 (20-530)	55 (8-205)
Himachal Pradesh	330 (60-1 170)	502 (87-1 801)	60 (10-210)	85 (11-327)	190 (40-650)	320 (60-1 112)	30 (0-120)	54 (8-206)
Jammu & Kashmir	690 (110-2 450)	642 (107-2 282)	120 (10-450)	109 (14-422)	390 (90-1 240)	218 (49-695)	70 (10-230)	37 (6-131)
Jharkhand	3 240 (520-11 780)	865 (138-3 148)	550 (70-2 160)	147 (18-578)	1 920 (340-6 720)	464 (83-1 625)	320 (40-1 220)	78 (11-296)
Karnataka	3 130 (560-10 690)	548 (99-1 873)	530 (70-1 990)	93 (12-349)	2 000 (380-6 820)	362 (69-1 235)	340 (50-1 260)	61 (9-228)
Kerala	1 300 (250-4 360)	402 (79-1 346)	220 (30-800)	68 (10-248)	350 (100-930)	137 (40-365)	60 (10-180)	23 (5-69)
Madhya Pradesh	7 600 (1 150-28 050)	892 (136-3 294)	1 290 (150-5 140)	151 (17-603)	4 590 (720-16 990)	563 (88-2 084)	780 (90-3 060)	95 (12-375)
Maharashtra	6 320 (1 100-22 240)	572 (99-2 012)	1 070 (140-4 060)	97 (13-368)	4 350 (770-15 520)	431 (76-1 538)	740 (100-2 810)	73 (10-279)
Northeast	800 (140-2 830)	540 (94-1 900)	140 (20-520)	91 (12-351)	420 (100-1 280)	248 (60-750)	70 (10-240)	42 (7-139)
Odisha	2 570 (430-9 140)	622 (104-2 215)	430 (60-1 680)	105 (13-408)	1 580 (280-5 540)	394 (71-1 386)	270 (40-1 020)	67 (9-254)
Punjab	1 420 (230-5 140)	576 (93-2 086)	240 (30-950)	98 (12-385)	600 (120-2 040)	258 (50-879)	100 (10-380)	44 (6-164)
Rajasthan	6 930 (1 090-25 310)	828 (130-3 026)	1 170 (140-4 590)	140 (17-549)	3 970 (650-14 520)	499 (81-1 826)	670 (80-2 630)	84 (10-331)
Tamil Nadu	2 420 (460-8 200)	411 (78-1 395)	410 (60-1 520)	70 (10-259)	980 (260-2 850)	169 (44-491)	170 (30-540)	29 (6-92)
Union Territories	150 (30-530)	526 (91-1 859)	30 (0-100)	89 (12-342)	80 (20-260)	257 (54-857)	10 (0-50)	43 (7-158)
Uttar Pradesh	20 120	838	3 410	142	12 410	565	2 100	96

	(3 200-73 050)	(133-3 041)	(410-13 410)	(17-558)	(2 070-44 960)	(94-2 047)	(270-8130)	(12-370)
Uttarakhand	890 (140-3 240)	838 (133-3 041)	150 (20-600)	142 (17-558)	320 (60-1 120)	321 (60-1 118)	50 (10-210)	54 (8-206)
West Bengal	5 650 (930-20 270)	638 (105-2 291)	960 (120-3 730)	108 (13-421)	2590 (500-8 880)	331 (64-1 133)	440 (60-1630)	56 (8-208)
Regions								
Central	37 170 (5,850-135 840)	850 (134-3 105)	6 290 (750-24 700)	144 (17-565)	22 090 (3630-80 430)	540 (89-1 967)	3 740 (470-14 530)	91 (11-355)
East	22 310 (3 620-80 490)	762 (124-2 749)	3 780 (460-14 800)	129 (16-506)	13 420 (2410-47 090)	437 (79-1 534)	2270 (310-8 620)	74 (10-281)
North	5 700 (950-20 340)	596 (99-2 127)	960 (120-3 720)	101 (13-389)	2 790 (560-9 420)	282 (56-952)	470 (70-1 760)	48 (7-177)
Northeast	2 810 (480-10 020)	564 (97-2 010)	480 (60-1 810)	95 (12-363)	1 670 (350-5 490)	317 (67-1 040)	280 (40-1 020)	54 (8-193)
South	10 830 (2 000-37 230)	476 (88-1 636)	1 830 (250-6 840)	81 (11-301)	5 180 (1140-16 750)	251 (55-810)	880 (140-3 100)	42 (7-150)
West	10 040 (1 730-35 380)	580 (100-2 044)	1 700 (220-6 520)	98 (13-377)	7 370 (1 270-26 360)	453 (78-1 619)	1 250 (160-4 780)	77 (10-294)
National								
India*	83 830 (14 000-300 800)	657 (110-2 357)	14 190 (1 790-54 730)	111 (14-429)	49 800 (9 100-174 180)	403 (74-1 408)	8 430 (1170-31730)	68 (9-257)

UI = uncertainty interval

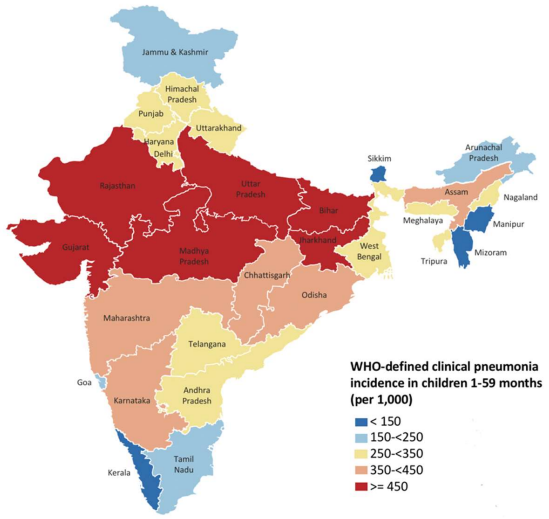
* Since state and region estimates are related to the total estimate only through the estimated rate in the unexposed group, the model does not impose the constraint that the state counts will sum to the national counts.

Figure 1: Prevalence of six pneumonia risk factors in India and select high-focus states[†] in 2000 and 2015



[†] Risk factor prevalence data for Chhattisgarh, Jharkhand, and Uttarakhand in 2000 are unavailable as they were part of Madhya Pradesh, Bihar, and Uttar Pradesh, respectively, until late 2000.

Figure 2: Map of pneumonia incidence in India in 2015[‡]



[‡] Andhra Pradesh and Telangana are calculated together for 2015