

The role of pneumococcal conjugate vaccination in reducing pneumonia mortality



In *The Lancet Global Health*, Cynthia Schuck-Paim and colleagues¹ examine pneumonia mortality in Brazilian children younger than 5 years from 1980 to 2014, to assess the effect of ten-valent pneumococcal conjugate vaccine (PCV10) that was introduced nationwide in 2010. These data are unique because there are few post-marketing PCV effectiveness studies with a mortality endpoint, and clinical trials generally do not have the power to detect significant mortality reductions. Furthermore, the 3 million infants born in Brazil every year grow up in a wide variety of socioeconomic circumstances. Therefore, the dataset has both the power to detect mortality endpoints and the diversity to draw parallels with many other global settings.

At first glance, the results of Schuck-Paim and colleagues' study might seem disappointing. The authors found a modest, non-significant reduction of about 10% in national childhood pneumonia mortality after PCV introduction. By examining the 95% credible intervals, we can deduce that their analysis had sufficient power to rule out a reduction in mortality greater than about 20%. If 10% reductions are reproduced elsewhere, this could still represent a substantial improvement in child survival, but it falls short of the expectations raised by some studies, particularly those done in low-income settings.

However, as Schuck-Paim and colleagues note, the results warrant a more nuanced interpretation. First, PCV introduction in Brazil coincided with a change in antibiotic use policy towards a prescription-only system and, therefore, with a probable reduction in antibiotic use. Hence, estimates presented in Schuck-Paim and colleagues' study might be conservative, particularly for the lower-income regions of the country, as highlighted by the large mortality reductions from broad-spectrum antibiotic use in the MORDOR trial.²

Additionally, the authors found a generally larger effect on child survival in the less wealthy municipalities than in the more wealthy ones, where PCV introduction might have reduced pneumonia-associated mortality by about 20% (though with wide credible intervals); the largest decrease was observed in children aged 3–23 months in municipalities with low maternal education (24%, 95% credible interval 7–35). This

decrease is similar to published estimates from low-income settings. It is an important result, because childhood pneumonia mortality is strongly and increasingly concentrated among the poorest people in the poorest countries. Over 75% of global pneumonia mortality in children younger than 5 years in 2010 occurred in the African and Southeast Asian WHO regions.³ Even within countries, most pneumonia deaths occurred among the poorest wealth quintiles.⁴ Hence, Schuck-Paim and colleagues' study suggests that PCV seems to be performing in line with expectations in those settings where the vaccine is most needed. To put things in perspective, a 20% reduction in pneumonia mortality in children younger than 5 years would translate to 200 000 deaths prevented annually if this result could be reproduced across the African and Southeast Asian WHO regions.

In upper-middle-income and high-income settings, the health and economic rationale for PCV is clear, despite a smaller burden of childhood mortality associated with pneumococcal pneumonia than that of low-income settings. The large burden of non-fatal pneumococcal disease results in hospitalisations, health-care expenses, bed shortages in the winter in temperate settings, and productivity losses for patients and their caregivers,⁵ giving a good economic reason for PCV use.

One reason why reductions in vaccine-attributable mortality were difficult to detect outside of the more deprived municipalities is because childhood pneumonia mortality had already been steadily decreasing in Brazil long before PCV10 introduction. This observation highlights another crucial finding of the study: the contribution of non-vaccine factors to reductions in pneumonia mortality. What could have caused the 90% reduction in pneumonia mortality between 1980 and 2010, the year when PCV10 was introduced? Over those 30 years, Brazil transitioned from lower-middle-income to upper-middle-income status and, in the process, the prevalence of poverty declined by 75%, female illiteracy by 70%, and childhood underweight by more than 50% (on the basis of World Bank's World Development Indicators for Brazil). Access

See [Articles](#) page e249

For the World Development Indicators see <https://data.worldbank.org>

to care and to antibiotics for pneumonia have also improved greatly over the same period.

Which of these factors contributed the most to reductions in childhood pneumonia mortality? Such a question is beyond the scope of Schuck-Paim and colleagues's study to answer, but will be essential to address in the future. Evidence about the broader socioeconomic determinants of pneumonia deaths could literally be life-saving and could not come at a more important juncture in Brazil, where economic and political developments in the past years might have implications on public investment and welfare. And globally, this question will be crucial as we seek to bring mortality in children younger than 5 years below 25 per 1000 livebirths by 2030 as part of the Sustainable Development Goals. Ultimately, our aim should be a world in which PCV has little effect on mortality because there are few pneumonia deaths left to prevent; however, in the meantime, PCVs play a key part in the concerted effort to reduce childhood mortality in low-income settings.

*Mark Jit, Stefan Flasche

Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London WC1E 7HT, UK (MJ, SF); and Modelling and Economics Unit, Public Health England, London, UK (MJ)

mark.jit@lshtm.ac.uk

We declare no competing interests.

Copyright © 2019 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.

- 1 Schuck-Paim C, Taylor RJ, Alonso WJ, Weinberger DM, Simonsen L. Effect of pneumococcal conjugate vaccine introduction on childhood pneumonia mortality in Brazil: a retrospective observational study. *Lancet Glob Health* 2019; **7**: e249–56.
- 2 Keenan JD, Bailey RL, West SK, et al. Azithromycin to reduce childhood mortality in sub-Saharan Africa. *N Engl J Med* 2018; **378**: 1583–92.
- 3 Walker CLF, Rudan I, Liu L, et al. Global burden of childhood pneumonia and diarrhoea. *Lancet* 2013; **381**: 1405–16.
- 4 Chang AY, Riumallo-Herl C, Salomon JA, Resch SC, Brenzel L, Verguet S. Estimating the distribution of morbidity and mortality of childhood diarrhea, measles, and pneumonia by wealth group in low- and middle-income countries. *BMC Med* 2018; **16**: 102.
- 5 Zhou F, Kyaw MH, Shefer A, Winston CA, Nuorti JP. Health care utilization for pneumonia in young children after routine pneumococcal conjugate vaccine use in the United States. *Arch Pediatr Adolesc Med* 2007; **161**: 1162.