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others might not. Additionally, individual genetic variation in the three major histocompatibility complex (MHC) class 1 genes have been reported to affect the severity of SARS-CoV-2 infection,¹⁴ which could also explain the manifestation of Kawasaki disease in some infected children observed in Europe and the USA who might share a different MHC class 1 gene from that of Asian children. Genetic studies in SARS-CoV-2-infected children worldwide can provide more information regarding the association of certain MHC class 1 genes with Kawasaki disease, MIS-C, or PIMS-TS.

More questions than answers emerge from our collective experience in managing children with COVID-19. Why is there a lack of description of this inflammatory clinical phenotype in the Asia-Pacific region? What is the natural history of the cardiac lesions associated with this clinical phenotype? More work remains to be done, especially in long-term follow-up of paediatric COVID-19 survivors.

We declare no competing interests. The authors would like to pay tribute to Tomisaku Kawasaki, who passed away at age 95 on June 10, 2020.

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The burden of childhood pneumonia in India and prospects for control



Pneumonia continues to be the leading cause of mortality in children worldwide, with India accounting for 20% of those deaths and a higher burden of childhood pneumonia than any other country.¹ In *The Lancet Child & Adolescent Health*, Brian Wahl and colleagues² report the first comprehensive evaluation of state-specific pneumonia incidence in children in India using a risk factor-based modelling approach. By calculating the effect of temporal changes in prevalence of well-known pneumonia risk factors

such as malnutrition, incomplete immunisation, and exposure to indoor air pollution on incidence, the authors estimated the change in pneumonia morbidity over time. Wahl and colleagues obtained individual-level data from the National Family Health Survey in India to model the number of children with each combination of risk factors, thereby accounting for interactions between risk factors, which is a novel aspect of the study when compared with previous models that have considered that the prevalence of

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risk factors were independent.² Vital insights obtained from this study regarding national and subnational estimates of pneumonia burden could inform data-driven interventions to address pneumonia morbidity.² At the national level, the estimated number of pneumonia cases in Indian HIV-uninfected children markedly reduced from 83·8 million cases (95% uncertainty interval [UI] 14·0–300·8) in 2000 to 49·8 million cases (9·1–174·2) in 2015. State-level estimates highlight the considerable heterogeneity in incidence and progress towards mitigation that exists between states. In Uttar Pradesh and Madhya Pradesh, more than half of all children aged younger than 5 years were estimated to have pneumonia in 2015 (565 cases per 1000 children [95% UI 94–2047] in Uttar Pradesh; 563 cases per 1000 children [88–2084] in Madhya Pradesh). By contrast the states of Kerala and Tamil Nadu had the lowest incidence of pneumonia (137 cases per 1000 children in Kerala and 169 per 1000 children in Tamil Nadu).² Although a considerable need for progress remains throughout India, the reductions in pneumonia incidence observed in Kerala and Tamil Nadu between 2000 and 2015, can inform strategies to achieve comparable reductions in other states and other countries.

Since the health-care system in India is primarily administered by the 36 states and union territories, subnational policies and investments are fundamental to health outcomes. Kerala and Tamil Nadu have among the highest per-capita health expenditure in India, although these states are not the most affluent. The number of health-care workers per 100 000 population in 2001, was substantially higher in Kerala (394) and Tamil Nadu (223) than Bihar (110) and Uttar Pradesh (135).³ Additionally, disparities in public health services between rural and

urban areas are the lowest in Kerala and Tamil Nadu. By contrast, childhood mortality varies markedly between rural and urban areas in Uttar Pradesh and Bihar. The availability of health care also affects the likelihood that people will seek care for pneumonia. Specifically, 90% of people in rural Kerala seek care for pneumonia compared with 60% of people in rural Bihar.⁴ A pentavalent vaccine for *Haemophilus influenzae* type b, a leading bacterial cause of pneumonia and meningitis, was introduced in Kerala and Tamil Nadu before expansion to the rest of the country by the end of 2015.

In 2010, pneumococcal pneumonia was estimated to account for 30% of all pneumonia deaths in India.⁵ In 2017, the Ministry of Health and Family Welfare of India allocated national funding to offer the pneumococcal conjugate vaccine, with prioritised roll-out to the states with the highest pneumonia burden. Application of the methodology developed by Wahl and colleagues to district-level data on risk factors for pneumonia will also facilitate prioritisation within states.

At present, India has the largest population of children (<14 years) worldwide. To enable these children to have a healthy and productive life, it is imperative to mitigate the challenge of pneumonia through the implementation of multifaceted preventive measures. Several policies, including improving nutrition and reducing pollution, which could reduce pneumonia incidence, are also aligned with the UN Sustainable Development Goals and have effects on other diseases. For example, malnutrition in children is recognised as a risk factor for many diseases such as HIV, tuberculosis, and malaria.⁶ Therefore, Indian Government initiatives such as the Integrated Child Development Service programme, the National Health Mission, and the Village Health Sanitation and Nutrition Committee will also be instrumental in reducing the burden of pneumonia.⁷ Another national programme, Pradhan Mantri Ujjwala Yojana,⁸ which aims to replace unclean cooking fuel in rural Indian households with liquid petroleum gas for cooking, will also minimise indoor pollution, a key risk factor for pneumonia.

The nationwide lockdown implemented in India from March 24 to July 3, 2020, to combat COVID-19 has interrupted provision of these services. Moreover, economic repercussions of the COVID-19 pandemic might delay the expansion of the pneumococcal conjugate vaccine, which could potentially stall



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progress towards decreasing the burden of pneumonia. Future studies investigating the cost-effectiveness of preventive measures for pneumonia across other diseases could supplement the findings of Wahl and colleagues, and lead to the galvanisation of resources required to strengthen and expand these vital interventions.

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NICE guidelines on neonatal parenteral nutrition: a step towards standardised care but evidence is scarce



Globally, neonatal conditions are the leading cause of reductions in disability-adjusted life-years and affect outcomes that extend throughout life.¹ Providing neonatal care to optimise such long-term outcomes is challenging because short-term research outcomes might conflict, even within individual trials.² Evidence-based guidelines are a welcome tool to translate research into practice and reduce variation in care. Such standardisation of care can improve outcomes for patients. For example, adherence to a standardised guideline for enteral feeding is protective against necrotising enterocolitis, despite the heterogeneity in the content of the individual guidelines.³ The latest guideline by the UK's National Institute for Health and Care Excellence (NICE) on neonatal parenteral nutrition is a welcome addition to neonatal practice, and is particularly important given the deficiencies frequently found in the provision of neonatal nutritional care in the UK.⁴

The guideline makes recommendations for both preterm and term neonates. For preterm neonates, the guideline recommends commencing parenteral nutrition for all babies born before 31 gestational weeks, for those unlikely to establish sufficient enteral feeding because of comorbidities, or where insufficient progress is made establishing enteral feeding in the first 72 h after

birth. For term babies, the guideline recommends that parenteral nutrition be administered to babies who are unlikely to establish enteral feeding and to all babies for whom feeding has been stopped for more than 72 h. The guideline recommends administering parenteral nutrition via a central venous catheter whenever possible, and that a standardised bag should be used initially. The guideline details how blood variables should be monitored, and when parenteral nutrition should be discontinued. The recommendations are clear, should be straightforward to implement, and represent an effort to standardise what is considered to be good practice.

The guideline will affect the care received by thousands of babies in the UK each year, which makes it imperative that recommendations are based on robust evidence. Unfortunately, however, the evidence upon which this guideline is based is scarce. Although there are areas with considerable research to draw on, such as the composition of certain macronutrients, there is a paucity of evidence to inform other fundamental aspects, such as indications and timings for commencing parenteral nutrition in neonates. Guidelines should clearly reflect and acknowledge the quality of evidence on which they are based. The NICE's guideline on early onset sepsis has been criticised for an over-reliance on measurements of C-reactive protein of



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For more on the NICE guideline see <https://www.nice.org.uk/guidance/ng154>