## The burden of viral respiratory infections in young children in low-resource settings



Acute lower respiratory infections (ALRI), encompassing bacterial and viral pneumonias, acute viral bronchiolitis, and bacterial and viral bronchitis, remain the leading cause of global child mortality.1 The thrust of global prevention and treatment efforts has been directed against bacterial causes of ALRI, and deaths from bacterial pneumonia have decreased substantially since 1990 because of improved access to health care and life-saving antibiotics, as well as increased use of vaccines targeted at bacterial respiratory pathogens. The leading causes of ALRI now are viral infections, with respiratory syncytial virus, influenza virus, parainfluenza virus, rhinovirus, and human metapneumovirus among the top viral causes of ALRI in children, particularly in low-resource settings.2 Prevention and treatment of viral pathogens could therefore substantially affect childhood ALRI outcomes.

In The Lancet Global Health, Xin Wang and colleagues<sup>3</sup> estimated the regional and global burden of influenzavirus-associated ALRI in children younger than 5 years in 2018. Compared with their previous estimates<sup>4</sup> in 2008 (35 per 1000 children per year [95% CI 22–55]), the authors estimated a lower incidence of influenzavirus-associated ALRI in 2018 (15.6 per 1000 children per year [uncertainty range 10·3-23·6]) for ages 0-4 years in developing countries. The estimated proportion of childhood influenza virus ALRI episodes has also decreased from 13% in 2008 to 7% in 2018. Influenza virus accounted for 5% of ALRI hospital admissions and 4% of ALRI deaths in children under 5 years. However, about 23% of the hospital admissions and 36% of the in-hospital deaths were in infants under 6 months. With 81% of the in-hospital deaths occurring in low-resource countries, the data show that much needs to be done to tackle the huge burden of influenza-associated morbidity and mortality in these settings.

Nevertheless, there are few representative data from south Asia and sub-Saharan Africa, regions with a disproportionally higher burden of global under-5 mortality, and the investigators rightly indicate the need for high-quality, in-hospital, mortality data from low-income countries to improve estimates of global

in-hospital mortality. The inclusion of only laboratory-confirmed influenza infection morbidity and mortality data is a strength of the evidence base for the estimates in this study but would invariably have precluded studies from low-to-middle-income countries where there are few adequate diagnostic tools. Such data are essential to clarify the disease burden and subsequently inform evidence-based vaccination strategies. The wide confidence intervals around the estimates in Wang and colleagues'<sup>3</sup> comprehensive systematic review highlight the diagnostic issues.

Although the overall decline in influenza virus ALRI reported by Wang and colleagues is good news,3 the absolute numbers of children affected by influenza virus ALRI with potentially serious consequences are staggering, and it is concerning that a fifth of influenza virus ALRI hospital admissions and a third of in-hospital deaths occurred in infants younger than 6 months. Gaps in the availability of supportive care options and antiviral drugs (where indicated) for viral pneumonias in low-resource settings are likely to have contributed to the subsequent poor outcomes.5 Despite the reduction in pneumonia-related childhood deaths in children under 5 years, there have been fewer reductions in pneumonia-related and sepsisrelated mortality among neonates. 6,7 The ANISA study of the aetiology of early infant deaths also identified viral infections, notably respiratory syncytial virus, as the leading cause of serious infections among neonates and young infants in south Asia.8 With no respiratory viral vaccines licensed for use in this age group, very young children will remain vulnerable. Some of the gaps in protection could be bridged by vaccinating mothers during pregnancy.9 Improvements in delivery of oxygen to newborn babies and young children affected by pneumonia are also required.10 In the meantime, we ought to ensure that the licensed influenza vaccines can reach as many target groups as possible.

BK reports grants from UKRI and other international funders for her vaccine research, and travel support from vaccine companies for attendance at advisory board meetings. OTI became an employee of Sanofi Pasteur on Jan 20, 2020, after having completed the writing of this Comment. UO declares no competing interests.

Published Online February 20, 2020 https://doi.org/10.1016/ S2214-109X(20)30037-1

See Articles page e497

Copyright © 2020 The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY 4.0 license.

## \*Uduak Okomo, Olubukola T Idoko, Beate Kampmann uokomo@mrc.qm

Vaccines & Immunity Theme, Medical Research Council Unit, The Gambia at London School of Hygiene and Tropical Medicine, Fajara, PO Box 273, The Gambia (UO, OTI, BK); Vaccine Centre, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK (BK)

- 1 UN Inter-agency Group for Child Mortality Estimation. Levels & trends in child mortality: report 2019, estimates developed by the UN Inter-agency Group for Child Mortality Estimation, 2019. https://www.unicef.org/ media/60561/file/UN-IGME-child-mortality-report-2019.pdf (accessed Jan 10, 2020).
- Pneumonia Etiology Research for Child Health Study Group. Causes of severe pneumonia requiring hospital admission in children without HIV infection from Africa and Asia: the PERCH multi-country case-control study. Lancet 2019; 394: 757–79.
- Wang X, Li Y, O'Brien KL, et al. Global burden of respiratory infections associated with seasonal influenza in children under 5 years in 2018: a systematic review and modelling study. Lancet Glob Health 2020; published online Feb 20. https://doi.org/10.1016/S2214-109X(19)30545-5.

- 4 Nair H, Brooks WA, Katz M, et al. Global burden of respiratory infections due to seasonal influenza in young children: a systematic review and meta-analysis. *Lancet* 2011; **378**: 1917–30.
- 5 Turner TL, Kopp BT, Paul G, Landgrave LC, Hayes D Jr, Thompson R. Respiratory syncytial virus: current and emerging treatment options. Clinicoecon Outcomes Res 6: 217–25.
- 6 Klugman KP, Rodgers GL. PERCH in perspective: what can it teach us about pneumonia etiology in children? Clin Infect Dis 2017; 64 (suppl 3): S185–87.
- 7 Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of under-5 mortality in 2000-15: an updated systematic analysis with implications for the Sustainable Development Goals. *Lancet* 2016; 388: 3027-35.
- 8 Saha SK, Schrag SJ, El Arifeen S, et al. Causes and incidence of communityacquired serious infections among young children in south Asia (ANISA): an observational cohort study. Lancet 2018; 392: 145-59.
- 9 Saso A, Kampmann B. Vaccination against respiratory syncytial virus in pregnancy: a suitable tool to combat global infant morbidity and mortality? Lancet Infect Dis 2016; 16: e153-63.
- 10 Duke T, Graham SM, Cherian MN, et al. Oxygen is an essential medicine: a call for international action. Int J Tuberc Lung Dis 2010; 14: 1362–68.