

Undernutrition and pneumonia mortality



Globally, pneumonia remains the leading infectious cause of death in children younger than 5 years. Undernutrition, defined by wasting, stunting, and specific nutritional deficiencies, is associated with approximately half of all deaths in such children.¹ Beyond having a direct impact on mortality, undernutrition increases the frequency and severity of pneumonia episodes, potentially representing a secondary immune deficiency that has not been well characterised.^{2,3} Undernutrition in a child with severe pneumonia requiring hospitalisation can also be associated with a diminished metabolic capacity to overcome the amplified physical and physiological demands of the illness, such as increased temperature, cardiac output, and work of breathing. Consequently, the presence of severe acute malnutrition can increase mortality from pneumonia 15-fold, and in a score of mortality risk among infants with pneumonia, very low weight-for-age and refusal to feed contributed as much to mortality risk as hypoxia.^{4,5}

In addition to being a key determinant of the risk of acquiring infection, nutritional status is a principal determinant of the health trajectory and outcomes following discharge from hospital. Among Gambian children admitted with pneumonia, even being moderately underweight was associated with a rate ratio of 3.2 for death.⁶ In Kenya, children discharged alive from hospital had an eight-fold higher risk of death during the following year than their community peers, with undernutrition being the main determinant of mortality risk.⁷ The modifiable factors associated with these deaths following care are not well defined, but potential targets include addressing nutrient composition of therapeutic and supplementary feeds, suboptimal infant feeding practices, food insecurity, an unhealthy gut microbiome, recurrent infection due to ongoing susceptibility and exposure to pathogens, and restricted access to care.

Improved prevention, early identification, and appropriate diagnosis of undernourished children with pneumonia are critical, yet clinical presentation of pneumonia in this population is not straightforward, and the stratification of risk to identify those with greatest likelihood of mortality is currently dependent on non-specific indicators of nutritional status. Although anthropometry is relatively easy to do and is strongly associated with outcomes at the population

level, the utility of such measurements in defining risk and guiding management in individual children with pneumonia is less certain, particularly in children with moderate acute malnutrition or stunting. Furthermore, anthropometry, even when systematically done, does not differentiate between the underlying cause of undernutrition or mechanisms amenable to treatment, and might not be useful in identifying children who are most likely to respond to treatment.

Beyond the diagnostic challenges, the aetiology of pneumonia in these children can be different from that in well nourished children. Optimal treatment regimens might need to cover a broader range of pathogens, and undernourished children might also have a significantly greater need for basic supportive care than nourished children.³ Undernutrition often begins in the antenatal period, establishing a vicious cycle of low birthweight, undernutrition, and increased risk of infection in children.⁸ Although breastfeeding support among infants and appropriate nutritional rehabilitation are cornerstones of treatment, there is a dearth of robust evidence supporting guidelines on type, timing, and duration of nutritional interventions. Non-breastfed children are at higher risk of death from pneumonia, yet only two in five babies under the age of 6 months are exclusively breastfed and most children younger than 2 years do not receive a minimum acceptable diet.¹

Nearly all current recommendations for the management of undernourished children are based on small groups of children treated in the 1960s–80s without a detailed understanding of the interplaying roles of infection, inflammation, immune dysfunction, and social factors in this vulnerable group. Additionally, there has been little attempt to date to harmonise data across different populations and geographies to better understand substantial differences in reported prevalence of stunting, wasting, specific nutrient deficiencies, and comorbidities between sub-Saharan Africa and Asia, where the greatest burden lies. An improved understanding of the critical links between pneumonia and undernutrition is a first step. Increased attention and resources directed at improving prevention as well as early identification and treatment of undernourished children with pneumonia is crucial.

Pneumonia remains the leading infectious killer of children younger than 5 years and without addressing undernutrition specifically, we risk a plateau in the efforts of the global health community to reduce child mortality. In 2013, less than one in six children requiring treatment for severe acute malnutrition were treated.¹ On this World Pneumonia Day, we call on the global health community to recognise the role that undernutrition plays in the risk of death from childhood pneumonia, and the need for funding and research prioritisation to address acute illness in undernourished children in order to continue the impressive reduction in child mortality that has occurred in recent years.

*Amy Sarah Ginsburg, Rasa Izadnegahdar, James A Berkley, Judd L Walson, Nigel Rollins, Keith P Klugman
PATH, PO Box 900922, Seattle, WA 98109, USA (ASG); Bill & Melinda Gates Foundation, PO Box 23350, Seattle, WA, USA (RI, KPK); Centre for Tropical Medicine & Global Health, University of Oxford, Oxford, UK (JAB); KEMRI/Wellcome Trust Research Programme, Kilifi, Kenya (JAB); University of Washington, Seattle, WA, USA (JLW); and World Health Organization, Geneva, Switzerland (NR)
messageforamy@gmail.com

We declare no competing interests.

Copyright © Ginsburg et al. Open Access article distributed under the terms of CC BY-NC-ND.

- 1 United Nations Children's Fund. Committing to child survival: a promise renewed. Progress report 2015. http://www.unicef.org/publications/index_83078.html (accessed Oct 23, 2015).
- 2 Wiens MO, Pawluk S, Kissoon N, et al. Pediatric post-discharge mortality in resource poor countries: a systematic review. *PLoS One* 2013; **8**: e66698.
- 3 Rytter MJ, Kolte L, Briend A, Friis H, Christensen VB. The immune system in children with malnutrition—a systematic review. *PLoS One* 2014; **9**: e105017.
- 4 Chisti MJ, Tebruegge M, La Vincente S, Graham SM, Duke T. Pneumonia in severely malnourished children in developing countries—mortality risk, aetiology and validity of WHO clinical signs: a systematic review. *Trop Med Int Health* 2009; **14**: 1173–89.
- 5 Reed C, Madhi SA, Klugman KP, et al. Development of the respiratory index of severity in children (RISC) score among young children with respiratory infections in South Africa. *PLoS One* 2012; **7**: e27793.
- 6 West TE, Goetghebuer T, Milligan P, Mulholland EK, Weber MW. Long-term morbidity and mortality following hypoxaemic lower respiratory tract infection in Gambian children. *Bull World Health Organ* 1999; **77**: 144–48.
- 7 Moisi JC, Nokes DJ, Gatakaa H, et al. Sensitivity of hospital-based surveillance for severe disease: a geographic information system analysis of access to care in Kilifi district, Kenya. *Bull World Health Organ* 2011; **89**: 102–11.
- 8 Katona P, Katona-Apte J. The interaction between nutrition and infection. *Clin Infect Dis* 2008; **46**: 1582–88.