

# ASSOCIATION BETWEEN MALNUTRITION AND PNEUMOCOCCAL PNEUMONIA IN THE PERCH STUDY

Juliet Otieno Awori, PERCH Study Group

Department of International Health, International Vaccine Access Center, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland; Department of Pathology, University of Otago, Christchurch; Microbiology Unit, Canterbury Health Laboratories, Christchurch, New Zealand; Kenya Medical Research Institute-Wellcome Trust Research Programme, Kilifi, Kenya; Medical Research Council Unit, The Gambia; Departments of Pediatrics and Medicine, Center for Vaccine Development, University of Maryland School of Medicine, Baltimore, Maryland; Centre pour le Développement des Vaccins (CVD-Mali), Bamako, Mali; Boston University School of Public Health, Boston, Massachusetts; University Teaching Hospital, Lusaka, Zambia; Medical Research Council: Respiratory and Meningeal Pathogens Research Unit, University of the Witwatersrand, Johannesburg, South Africa; Department of Science and Technology/National Research Foundation: Vaccine Preventable Diseases Unit, Division of Global Health Protection, Centers for Disease Control and Prevention, Atlanta, Georgia; Global Disease Detection Center, Thailand Ministry of Public Health-US Centers for Disease Control and Prevention Collaboration, Nonthaburi, Thailand; International Centre for Diarrhoeal Disease Research, Bangladesh; Nuffield Department of Clinical Medicine, University of Oxford, United Kingdom

## INTRODUCTION

Malnutrition is an important risk factor for pneumonia and has been shown to increase the frequency and severity of pneumonia episodes<sup>1</sup>. Malnutrition is estimated to be the underlying cause of death in approximately 45% of all deaths in children under 5 years of age, increasing the risk of pneumonia mortality significantly<sup>2</sup>. The role of different aetiology on pneumonia outcomes is not well defined<sup>1</sup>. We sought to examine the association between malnutrition and pneumococcal pneumonia and pneumococcal mortality in the PERCH study.

## METHODS

PERCH is a 7-country case-control study evaluating the aetiology of hospitalized WHO-defined severe or very severe pneumonia (WHO 2005) among children 1-59 months.

Malnutrition was defined as stunting (height-for-age), wasting (weight-for-height) or underweight (weight-for-age) < -2 z-score using WHO child growth standards and Mid-Upper Arm Circumference (MUAC) < 11.5cm.

Microbiologically confirmed invasive bacterial pneumonia including pneumococcal pneumonia were defined as aetiology detected by culture in blood, lung aspirates or pleural fluid or by PCR in lung aspirates or pleural fluid.

Logistic regression analysis using healthy community controls was done to evaluate the association between malnutrition and admission to hospital with pneumonia and with pneumococcal pneumonia. The analysis was repeated separately for other pneumonia aetiologies including *S. aureus*, *H. influenzae*, *E.coli*, other invasive bacteria and RSV. Age, site and HIV status were adjusted for in the analysis.

Risk ratios were calculated for the association between malnutrition and pneumonia mortality and pneumococcal pneumonia. We further tested whether the association between malnutrition and inpatient mortality among invasive bacterial pneumonias differed for cases of pneumococcal aetiology and those due to other invasive bacterial aetiology using an interaction term in a logistic regression model.

## RESULTS

Of 4232 cases, 28% had stunting, 27% wasting, 33% underweight and 30% MUAC < 11.5cm. The distribution varied by site (Figure 1). Infants (age <1 year) comprised 59% of those who were stunted, 63% of those wasted, 57% of those who were underweight and 76% of those who had MUAC < 11.5%. Amongst the cases, 4% had an invasive bacterial aetiology: 1.4% *S.pneumoniae*, 0.6% *S. aureus*, 0.6% *H. influenzae*, 0.4% *E. coli* and 1% other invasive bacterial aetiology (Figure 2).

Malnutrition was associated with pneumonia case status and pneumococcal pneumonia (Figure 3). The association between malnutrition and pneumonia of other aetiology varied by pathogen and by malnutrition indicator (Table 1).

In the mortality analysis, 7.5% of the cases died in hospital out of which 4% had pneumococcal pneumonia and 10% any other invasive bacterial aetiology. Malnutrition was associated with a higher risk of mortality amongst the cases. RR 2.2 (95% CIs 1.7-2.63), 2.45 (1.96,3.06), 3.35 (2.7,4.17) and 4.43 (3.45-5.71) for stunting, wasting, undernutrition and MUAC < 11.5 cm, respectively.

Amongst cases with pneumococcal pneumonia, the risk of mortality was RR 0.87(95% CIs 0.3-2.27), 1.68(0.68-4.16), 2.96(1.05,8.39) and 2.42(0.83-7.06) for stunting, wasting, undernutrition and MUAC < 11.5 cm, respectively. The risk for pneumococcal pneumonia mortality was not significantly different from the risk of death from any other invasive bacterial aetiology.

TABLE 1

Association between malnutrition and pneumonia by aetiology

	Stunting		Wasting		Underweight		MUAC (< 11.5cm)
	Moderate (HAZ < -2 to -3)	Severe (HAZ < -3)	Moderate (WHZ < -2 to -3)	Severe (WHZ < -3)	Moderate (WAZ < -2 to -3)	Severe (WAZ < -3)	
<i>S.pneumoniae</i>	2.13 (0.89-5.1)	7.75 (3.67-16.4)	2.96 (1.46-5.99)	2.78 (1.13-6.85)	2.29 (1.02-5.12)	8.77 (4.31-17.86)	5.56 (2.86-10.82)
<i>S.aureus</i>	3.42 (1.15-10.14)	4.75 (1.4-16.05)	3.09 (1.01-9.41)	0.96 (0.12-7.42)	1.98 (0.56-6.79)	2.92 (0.65-13.20)	2.24 (0.69-7.30)
<i>H.influenza</i>	1.70 (0.47-6.15)	2.73 (0.7-10.72)	6.43 (2.13-19.41)	14.41 (5.42-38.33)	6.45(2.32-17.93)	18.1 (6.59-49.7)	15.33(5.85-40.15)
<i>E.coli</i>	2.82 (0.72-11.05)	7.44 (2.05-26.94)	6.74 (1.95-23.22)	11.35 (3.13 -41.18)	4.28(1.08-16.88)	17.87(95.36-59.6)	4.15(1.16-14.79)
Other invasive bacteria	2.66 (1.1-6.44)	8.87 (4.15-18.94)	4.23 (1.93-9.27)	7.14 (3.26-15.63)	5.09(2.25-11.53)	24.03(11.74-49.2)	6.43 (3.06-13.50)
Non-bacterial etiology	0.67 (0.42-1.07)	0.53 (0.35-0.80)	0.65 (0.43-0.99)	0.68 (0.44-1.05)	0.85 (0.55-1.31)	0.43 (0.2909.63))	0.65 (0.44-0.96)
RSV	0.89 (0.70-1.12)	0.88 (0.70-1.09)	0.91 (0.73-1.13)	0.59 (0.46-0.76)	0.77 (0.63-0.95)	0.58 (0.45-0.73)	0.88 (0.73-1.07)

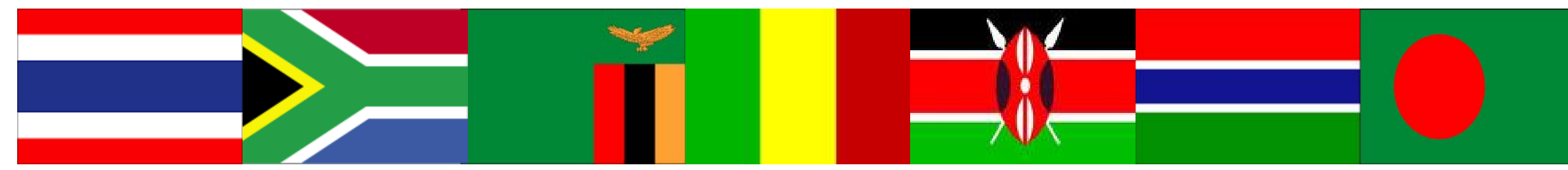


FIGURE 1

Distribution of malnutrition across PERCH sites

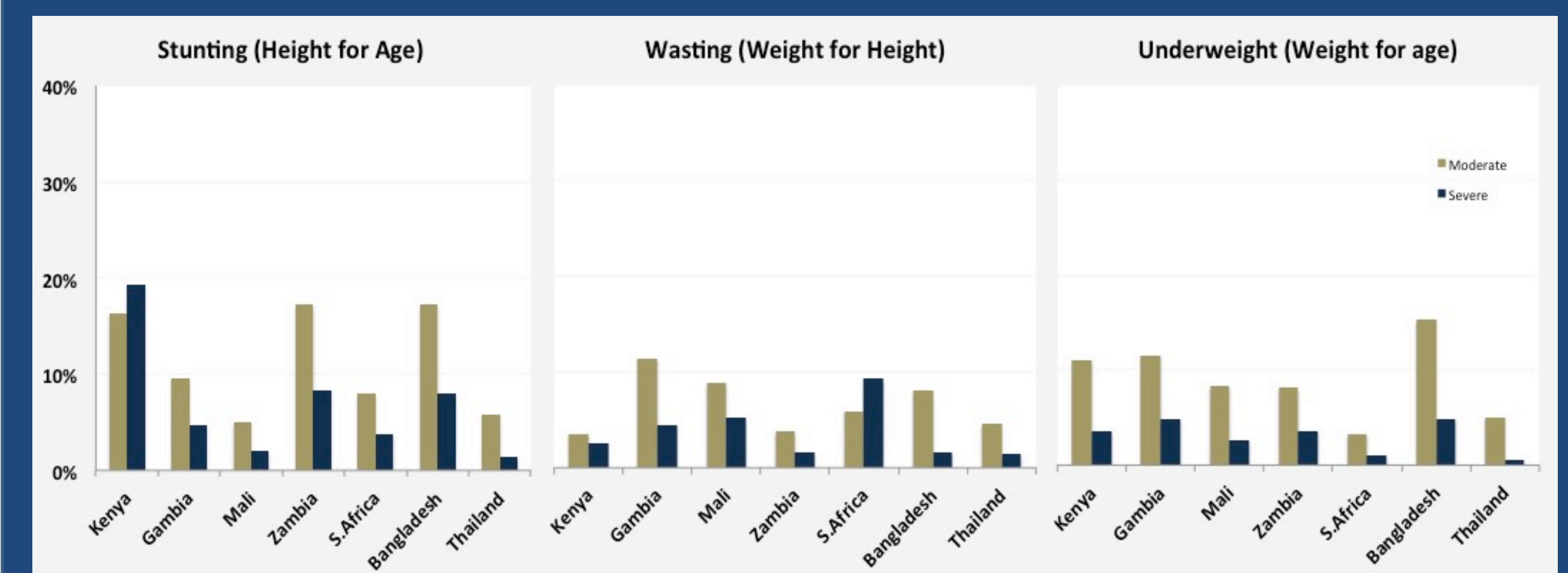


FIGURE 2

Distribution of invasive bacteria across PERCH sites

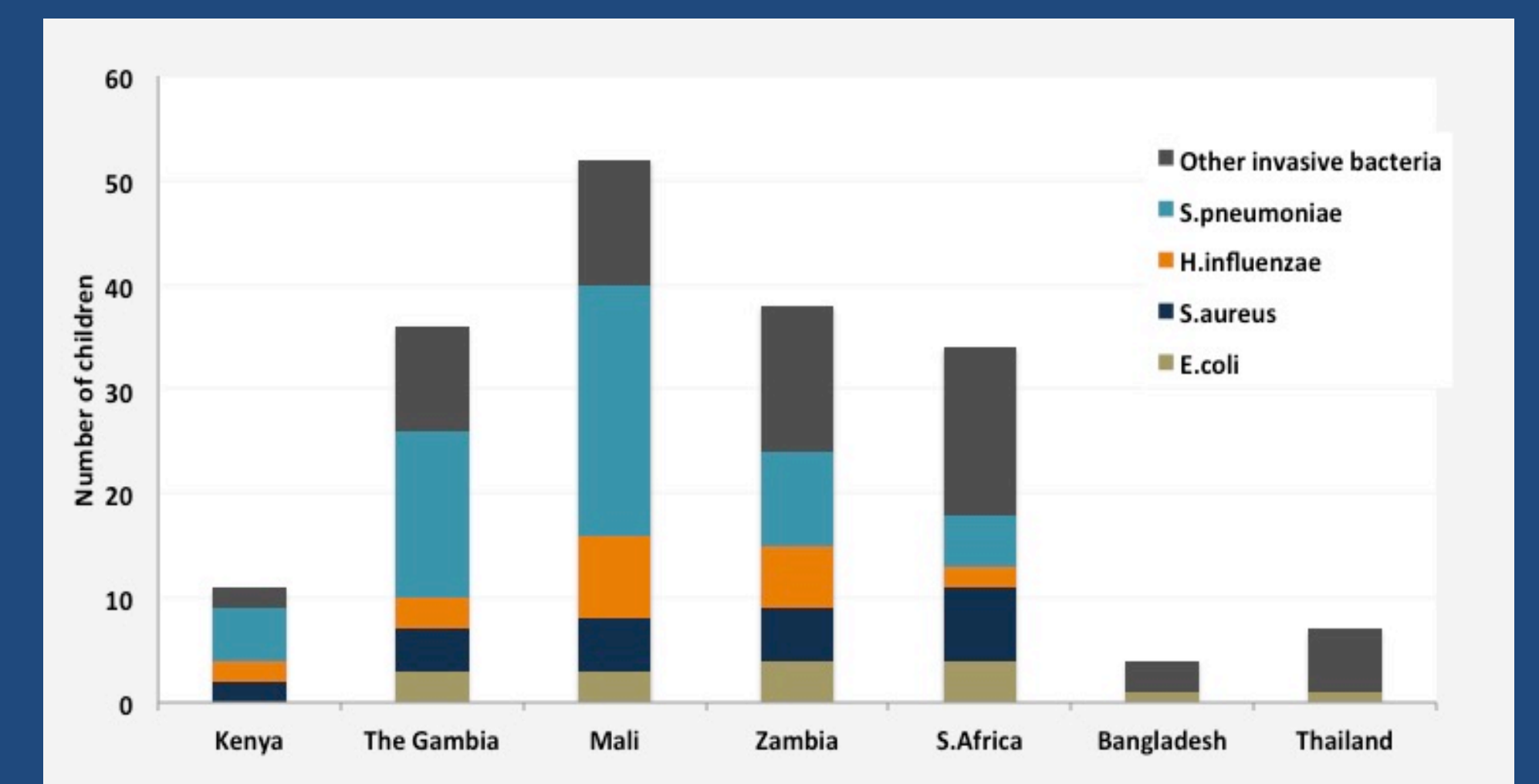
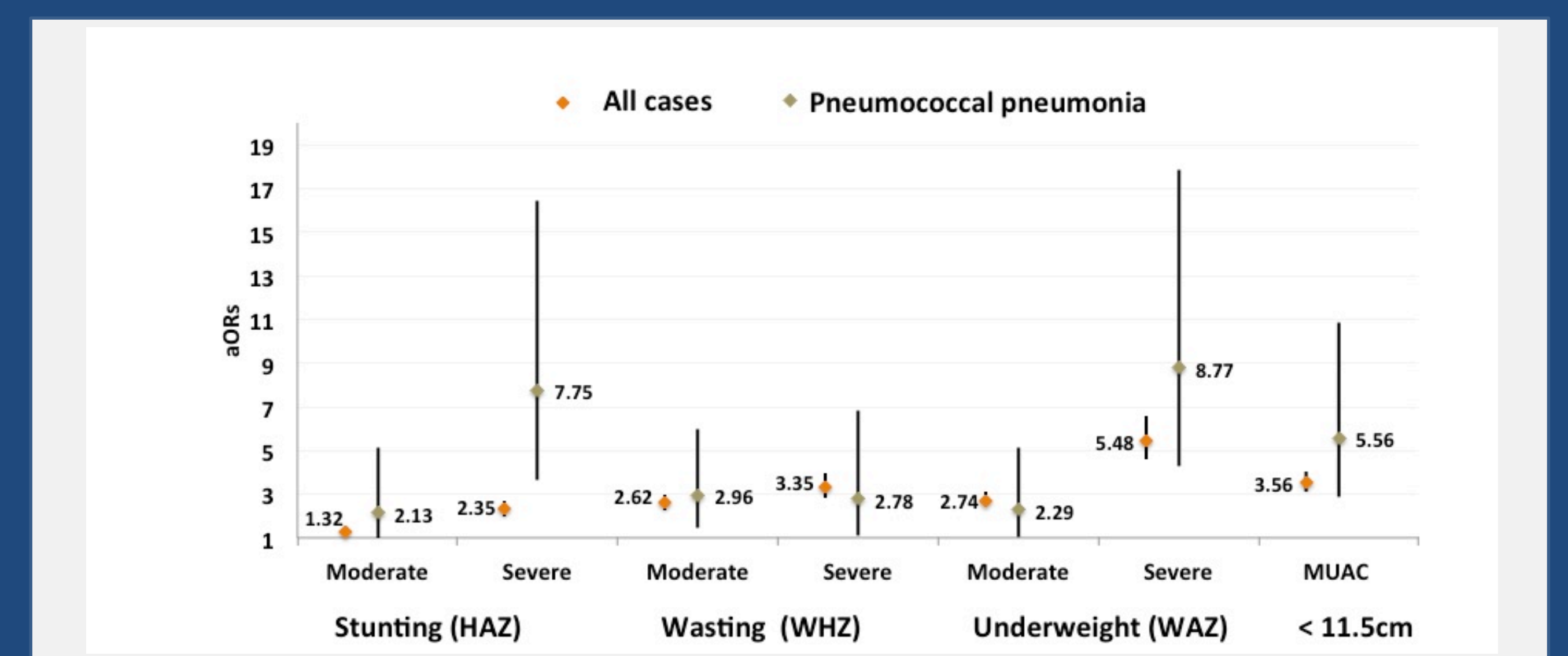


FIGURE 3

Association between malnutrition and pneumococcal pneumonia



aOR: Adjusted for age, site and HIV status

## CONCLUSIONS

- In the PERCH study, children with different markers of malnutrition were 1.7-3.6 times more likely to be admitted to hospital with pneumonia (all causes) and 4.0-5.6 times more likely to be admitted to hospital with pneumococcal pneumonia.
- Pneumonia cases with a simple marker of poor nutrition (MUAC<11.5cm) had a 4 fold increased risk of dying during admission.
- Amongst children with invasive bacterial pneumonia the excess risk of mortality associated with identification of *S. pneumoniae* was no greater than for any other aetiology.
- Altered pathophysiological responses to infections in malnourished children may explain these observations<sup>3</sup>.

### References:

- Chisti MJ, Tebruegge M, La Vincente S, et al. Pneumonia in severely malnourished children in developing countries - Mortality risk, aetiology and validity of WHO clinical signs: A systematic review, Tropical Medicine and International Health, 2009
- Black RE, Victora CG, Walker SP, et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. Lancet 2013;382:427-51.
- Ulrich E, Schaible S, Kaufmann HE. Malnutrition and Infection: Complex Mechanisms and Global Impacts, Plos Medicine May 2007

### Funding

PERCH was supported by grant 48968 from The Bill & Melinda Gates Foundation to the International Vaccine Access Center, Department of International Health, Johns Hopkins Bloomberg School of Public Health.

