Biologic Basis and Epidemiologic Relationship of Anthropometry with Child Development

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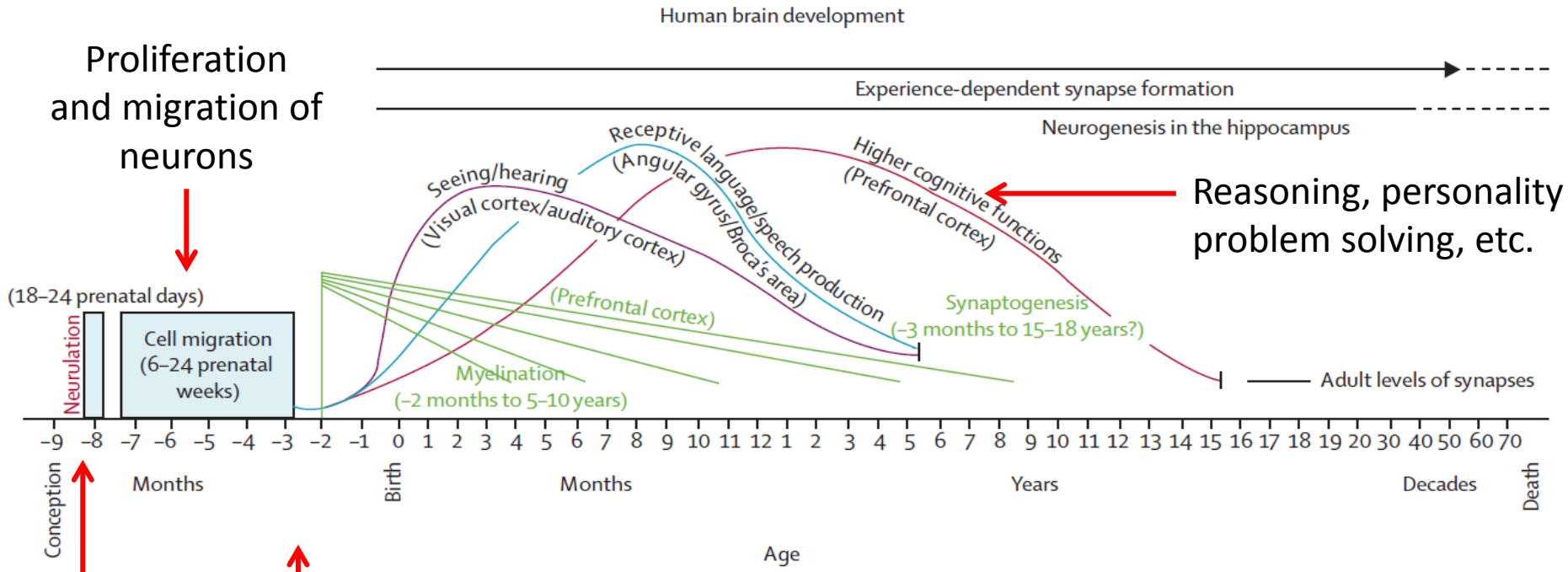
Brain Development



Proliferation and migration of neurons

Reasoning, personality problem solving, etc.

Formation neural tube

Myelination and Synaptogenesis begin during 3rd trimester

Grantham-McGregor 2007

Height-for-Age Z-scores

- Stunting is an ***Indicator*** of chronic malnutrition resulting from nutritional deficiency and/or infection

- Causes of stunting are multifactorial and differ in timing and magnitude of risk (maternal iron deficiency in pregnancy, SGA, child zinc deficiency, child diarrhea, etc)

- **HAZ is not a uniform indicator but stunting gives indication of exposure to multiple risk factors over time**

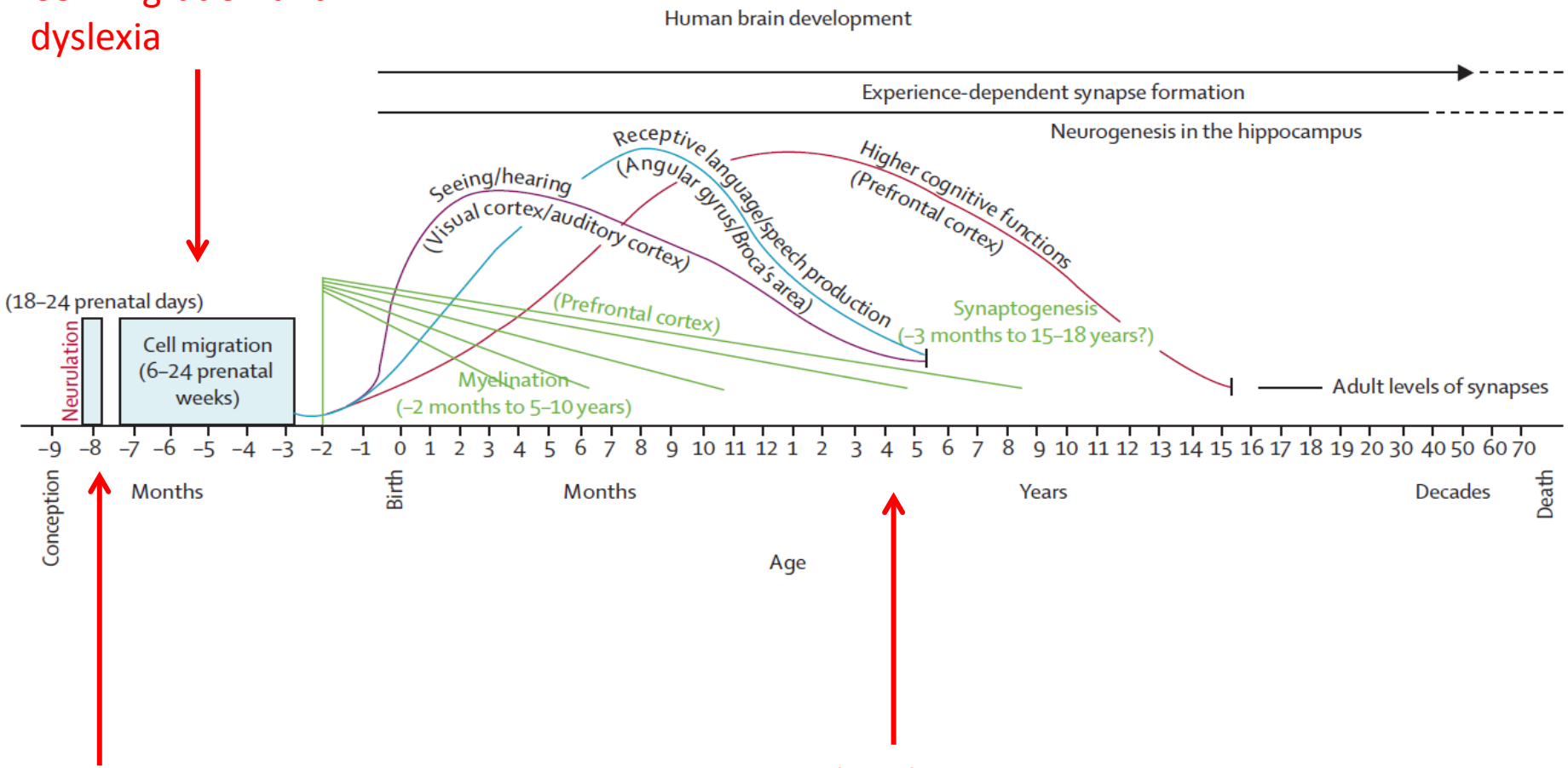
HAZ and Brain Development

- Stunting is an ***indicator*** of exposure to factors that can simultaneously induce effects on brain growth and development and physical growth

- Biological effects on brain development for HAZ risk factors differ by mechanism and timing

- Non-structural effects—malnourished children are lethargic and do not explore

Cell migration and dyslexia

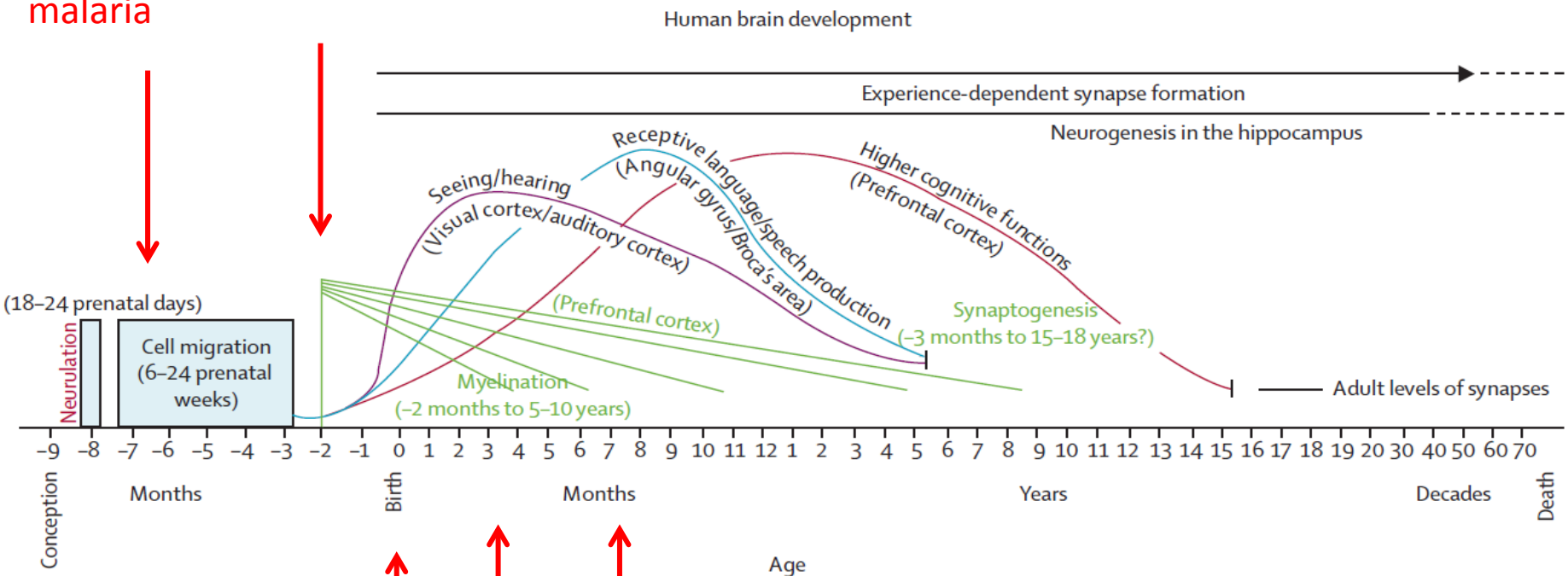


Folate deficiency and neural tube defects

Lead and cognitive function

Maternal malaria

Maternal iron deficiency in pregnancy



Low birth weight and SGA

Suboptimal Breastfeeding

Diarrhea and zinc deficiency

Summary of HAZ and Brain Development

- HAZ or stunting is as an indicator of early life exposure to risk factors which may have direct or indirect impact on brain development

- *Limitation of using stunting: Causes and timing of risk factors for stunting vary and the magnitude of their relationship and its specific cognitive, motor, socioemotional effects are likely to differ*

Epidemiologic Relationship of HAZ with Child Development

Porter WT. The Physical Basis of Precocity and Dullness. Academy of Science of St. Louis; 1893.

THE PHYSICAL BASIS OF PRECOCITY AND DULLNESS.*

W. TOWNSEND PORTER.

(From the Laboratory of Physiology in the St. Louis Medical College.)

In December, 1891, I received the permission of the St. Louis Board of Public Schools to collect physical measurements of the school children.

The investigation began on January 4, 1892, and was finished the fourth week in March, having extended over eleven of the fourteen weeks of winter. The weight, height, length and breadth of head, vital capacity of chest, acuteness of vision, nationality of parents, and many other facts were secured from thirty-three thousand five hundred boys and girls. The larger part of the measurements were made by the teachers, whose hearty co-operation and efficient service in this work should earn them the gratitude of every friend of science.

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Linear Growth and Child Development in Low- and Middle-Income Countries: A Meta-Analysis

Christopher R. Sudfeld, ScD[a], Dana Charles McCoy, PhD[b], Goodarz Danaei, MD, ScD[a,c], Günther Fink, PhD[a], Majid Ezzati, PhD[d], Kathryn G. Andrews, MPH[a], Wafaie W. Fawzi, MBBS, DrPH[a,c,e]

Linear Growth and Child Development Review

Produce estimates of the cross-sectional and prospective *observational* relationship of HAZ/stunting with cognitive, motor, and socioemotional development for children <12 years of age in LMICs

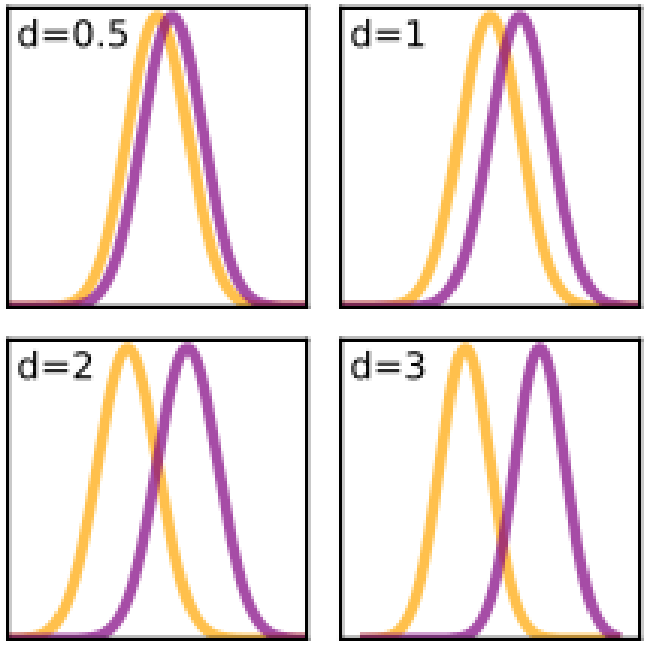
Identified 68 studies from 29 LMICs

- 52 cognitive scores
- 22 motor scores
- 13 socioemotional scores
- *Over 50 tests with Bayley most frequent at 15 studies*

Standardized Mean Difference

Due to differences in *points* or *scores* between the development tests we need to use a uniform effect measure

$$\text{SMD} = \frac{Mean\ Group\ 1 - Mean\ Group\ 2}{Standard\ Deviation\ of\ Population}$$



Statistical Adjustment

- Want to adjust for upstream factors (confounders) which will produce independent estimate

  -Wealth, maternal/paternal education, district, etc

- Do not adjust for factors we are trying to capture within indicator

Stunting

Cross-sectional Association of HAZ with Cognitive Development

Association varied significantly with child age

[effect modification by age]

≤2 years of age: Each unit increase in HAZ associated with **+0.24** SD (95% CI: 0.14-0.33) increase in cognition

>2 years of age: Each unit increase in HAZ associated with **+0.09** SD (95% CI: 0.05-0.13) increase in cognition

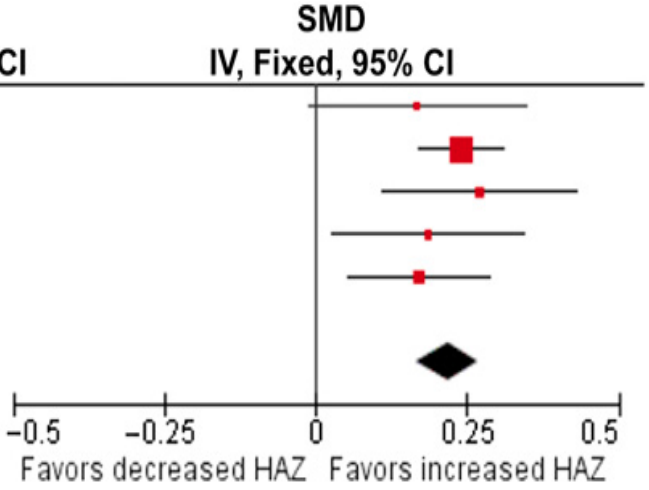
Prospective association of HAZ with Development2 years of age and cognition at 5-11 years of age

Each unit increase in HAZ at 2 years of age was associated with **+0.22 SD** (95% CI: 0.17-0.27) increase in cognition at 5-11 years

Study or Subgroup	SMD	SE	Weight	SMD IV, Fixed, 95% CI
Berkman* (Peru) 2002	0.168	0.092	8.0%	0.17(-0.01, 0.35)
Cheung (Philippines) 2009a	0.24	0.036	52.5%	0.24 (0.17, 0.31)
Hamadani (Bangladesh) 2013	0.27	0.082	10.1%	0.27 (0.11, 0.43)
Niehaus* (Brazil) 2002	0.186	0.081	10.4%	0.19 (0.03, 0.34)
Pollitt* (Guatemala) 1993	0.17	0.06	18.9%	0.17 (0.05, 0.29)
Total (95% CI)			**100.0%**	**0.22 (0.17, 0.27)**

Heterogeneity: $\chi^2 = 1.87$, $df = 4$ ($P = 0.76$); $I^2 = 0\%$

Test for overall effect: $z = 8.37$ ($P < 0.00001$)



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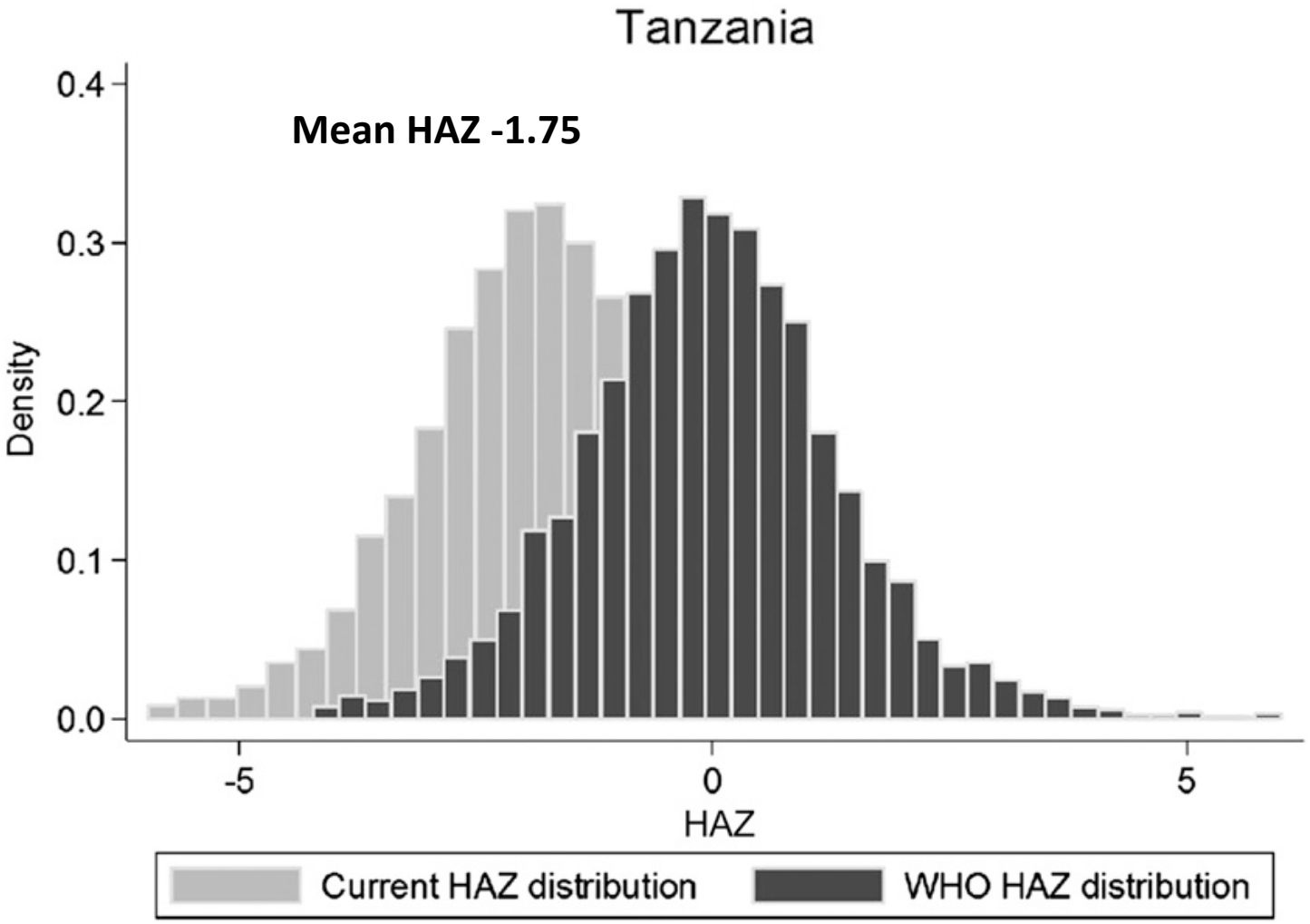
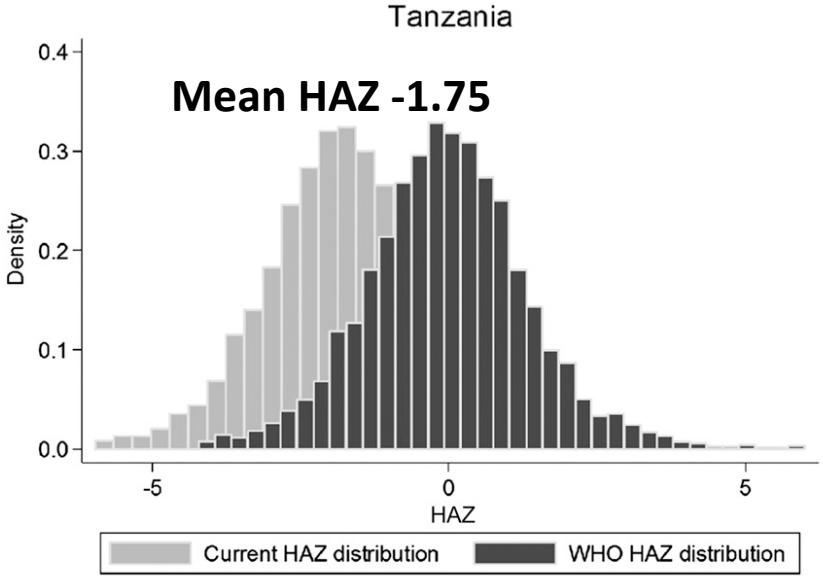
Motor and Socioemotional Development

- Cross-sectional each unit increase in HAZ associated with +0.38 increase in motor score
- Prospective each unit increase in HAZ associated with +0.29 increase in motor score
- Socioemotional not able to be estimated due to differences in measures of behavior problems, attachment, social competence and temperament

What does this mean at population level?



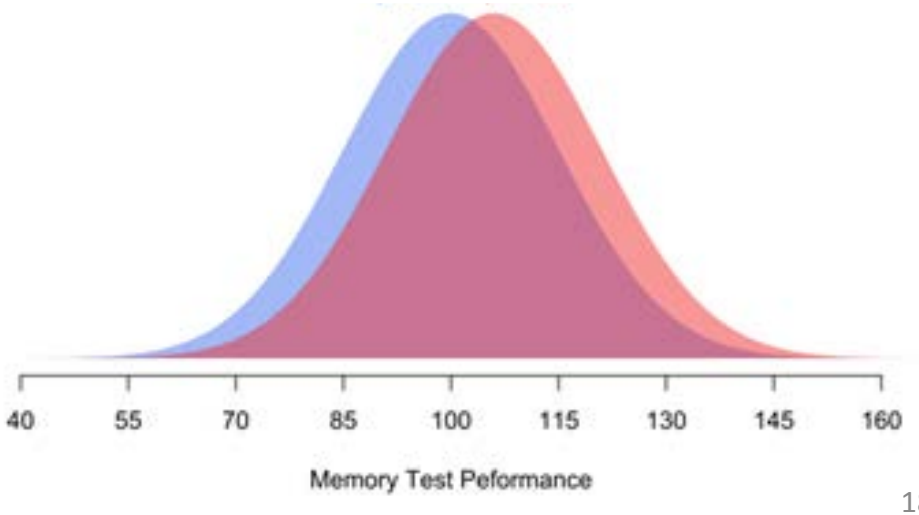
What does this mean at population level?



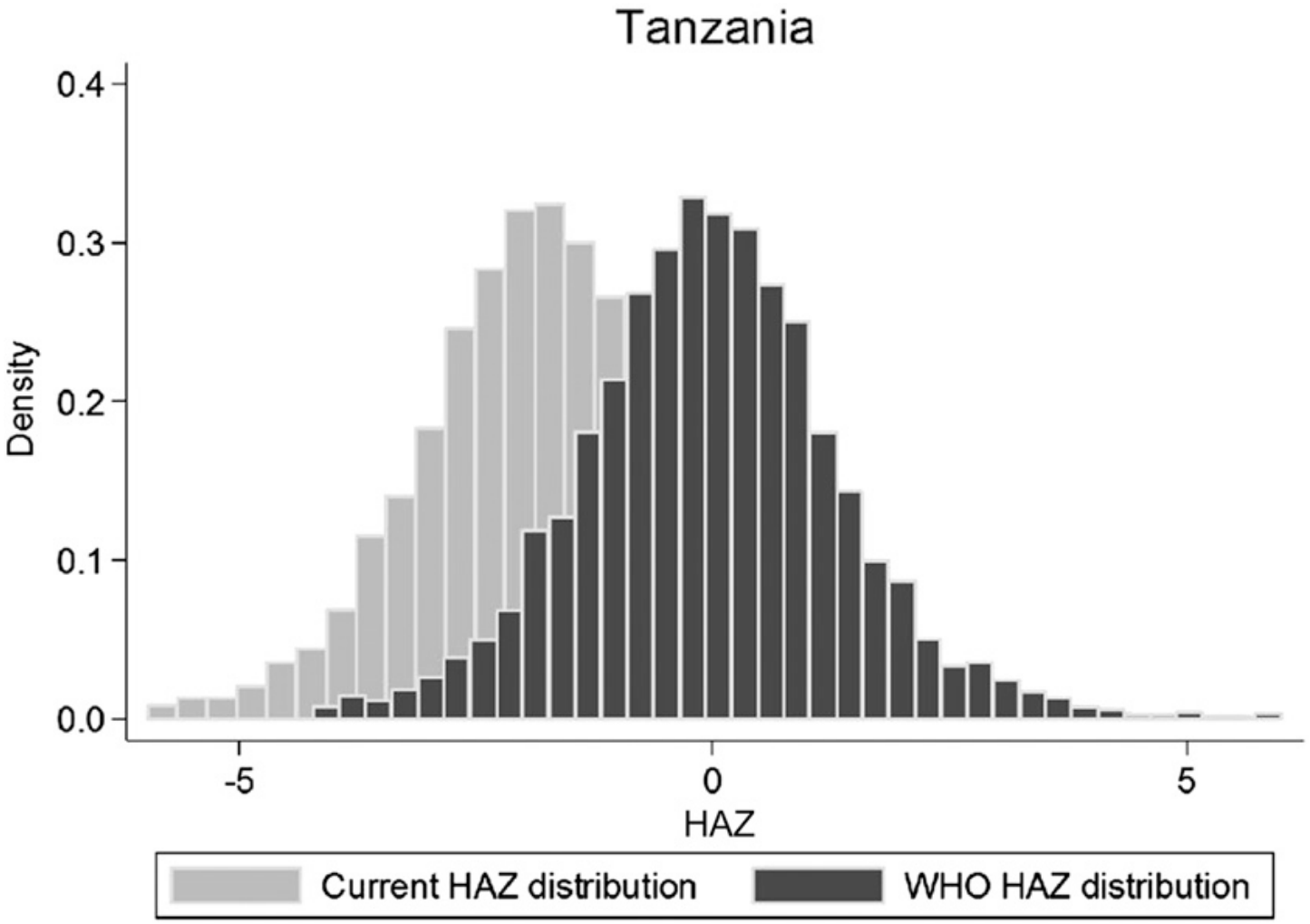
Each unit increase HAZ associated +0.22 SD cognitive z-scores so we would expect 0.385 SD shift in 'cognition' ------Equal 5.8 IQ point shift

The effect size of individual interventions (maternal iron) will likely be less than that of stunting

Effect size of SMD of +0.10 would need 3,142 trial participants to have 80% power



Is the effect of increasing HAZ equal across its distribution?



The Journal of Nutrition
Nutritional Epidemiology

Malnutrition and Its Determinants Are Associated with Suboptimal Cognitive, Communication, and Motor Development in Tanzanian Children[1–3]

Christopher R Sudfeld,[4]* Dana Charles McCoy,[8] Günther Fink,[4] Alfa Muhihi,[9] David C Bellinger,[7,10] Honorati Masanja,[9] Emily R Smith,[4] Goodarz Danaei,[4,5] Majid Ezzati,[11] and Wafaie W Fawzi[4–6]

Departments of [4]Global Health and Population, [5]Epidemiology, [6]Nutrition, and [7]Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA; [8]Center on the Developing Child, Schools of Education and Public Health, Harvard University, Cambridge, MA; [9]Ifakara Health Institute, Dar es Salaam, Tanzania; [10]Department of Neurology, Boston Children's Hospital, Boston, MA; and [11]Medical Research Council-Public Health England (MRC-PHE) Centre for Environment and Health, Departments of Epidemiology and Biostatistics, Imperial College London, London, United Kingdom

Tanzania Child Development Follow-up Study

- Enrolled 1,036 children 18-36 months of age who were previously enrolled in neonatal vitamin A study in rural Ifakara, Tanzania

Tanzania Child Development Follow-up Study

- Child cognitive, communication, and motor development assessed with an adapted Bayley Scales of Infant Development –III

- Height and Weight measured at home or clinic visits

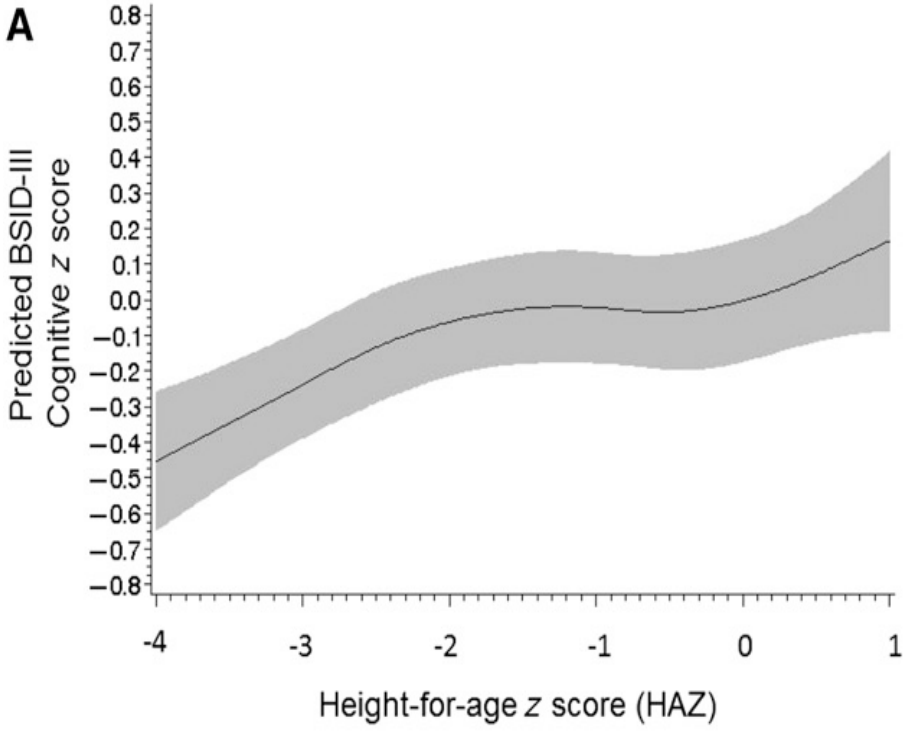
Adapting BSID-III to Tanzania

Anthropometry Distribution at 18-36 months of Age

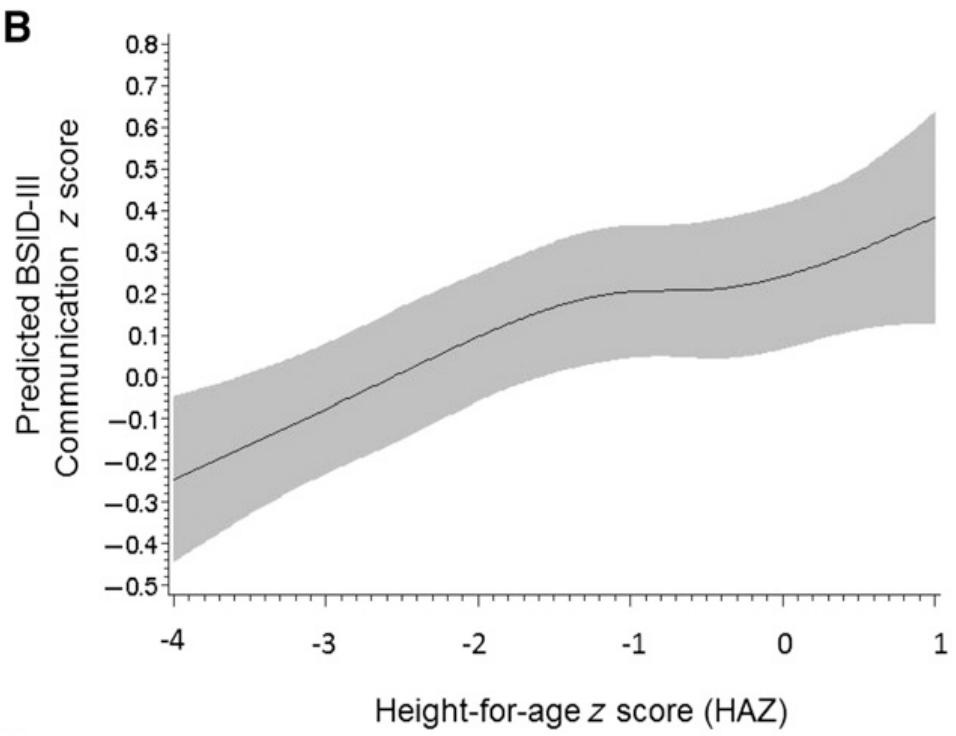
Child anthropometry 18–36 mo of age	
HAZ	−1.64 ± 1.10
Stunted (HAZ <−2)	375 (36.2)
WHZ	0.27 ± 1.08
Wasted (WHZ <−2)	15 (1.5)
WAZ	−0.67 ± 0.98
Underweight (WAZ <−2)	92 (9.0)

Shape of the HAZ and Child Development Relationship

Cognitive



Communication

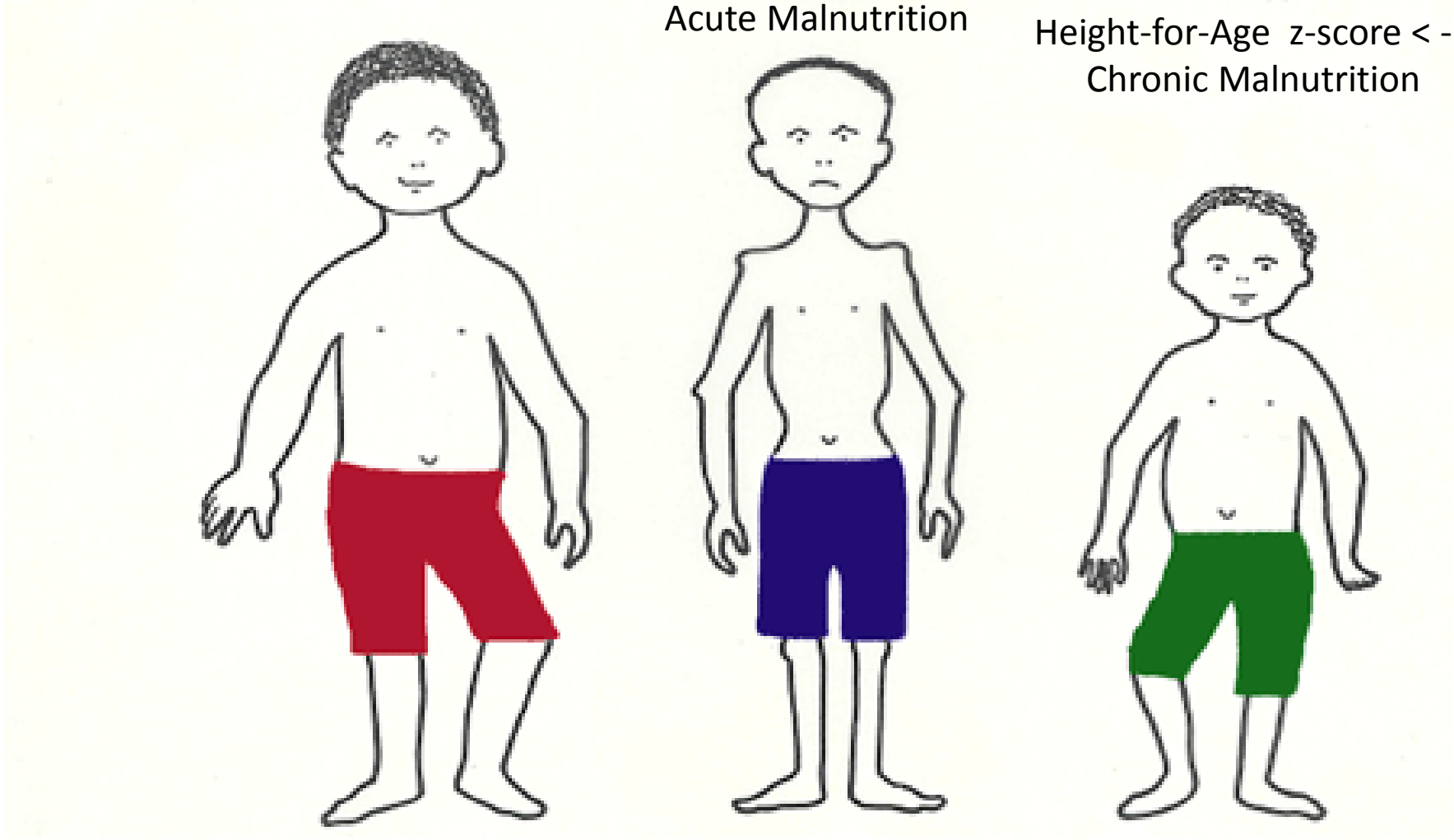


Adjusted for: infant sex, infant age, maternal education, wealth quintile, stimulation tertile

Sudfeld et al. J Nutr 2015

Weight-for-height z-score < -2
Acute Malnutrition

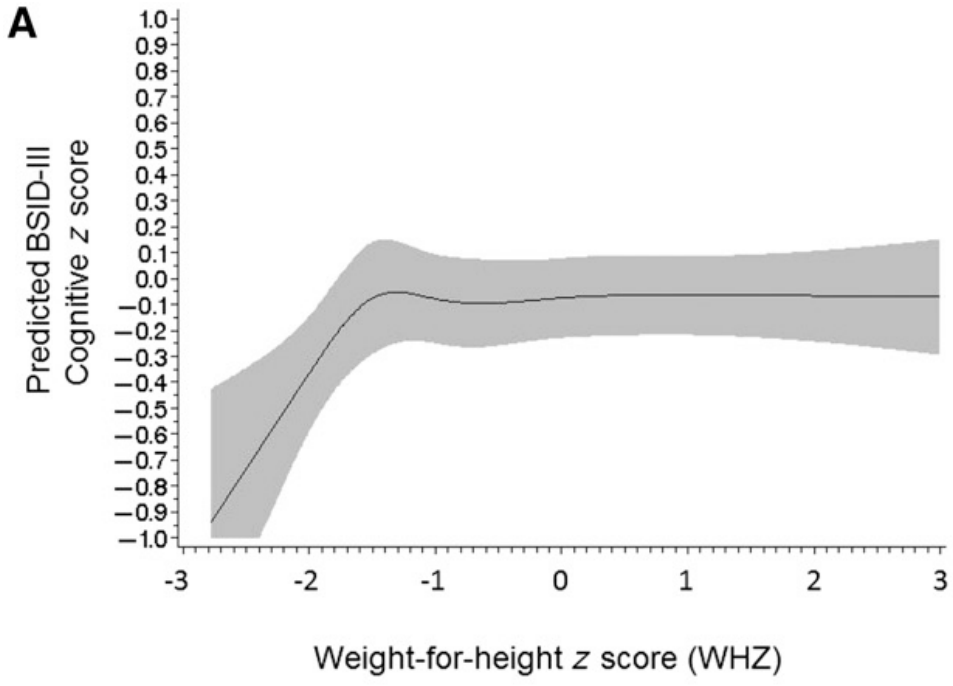
Height-for-Age z-score < -2
Chronic Malnutrition



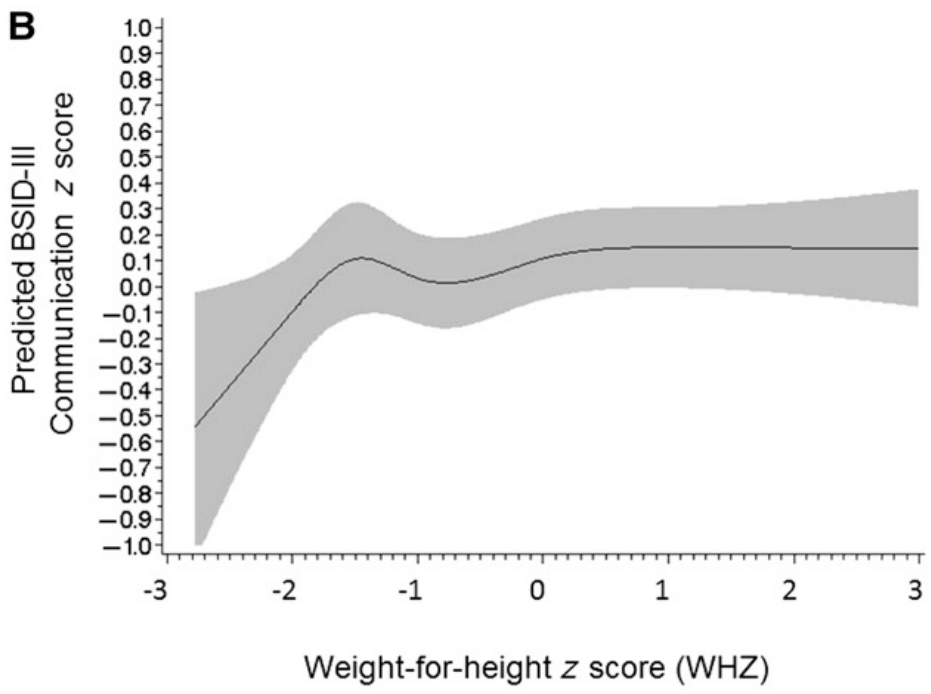
Wasted	No	Yes	No
Stunted	No	No	Yes

Shape of the WHZ and Child Development Relationship

Cognitive



Communication



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Sudfeld et al. J Nutr 2015

Conclusions and Way Forward

- Observational evidence suggests robust relationship of HAZ/stunting with child cognitive, communication, and motor development. More studies needed?

- We need to start to dissect stunting to determine effect of individual risk factors on cognition (i.e. what is effect of zinc supplementation on child cognition?)

- Packages of stunting interventions and integration with stimulation interventions need to be evaluated

Acknowledgements

- Saving Brains and Neovita Team

- Ifakara Health Institute

  -Dr. Honorati Masanja

  -Dr. Alfa Muhihi

  -Geofrey Ashrey

  -Nurses, Trackers, Motorbike drivers, Accountants, Procurement, Village Informants…

  -Caregivers and their children