Risk-differentiated care: a paradigm shift to improve child mortality

The worst form of inequality is to try to make unequal things equal
Aristotle

USAID

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WHO

World Health Organization

Acknowledgments

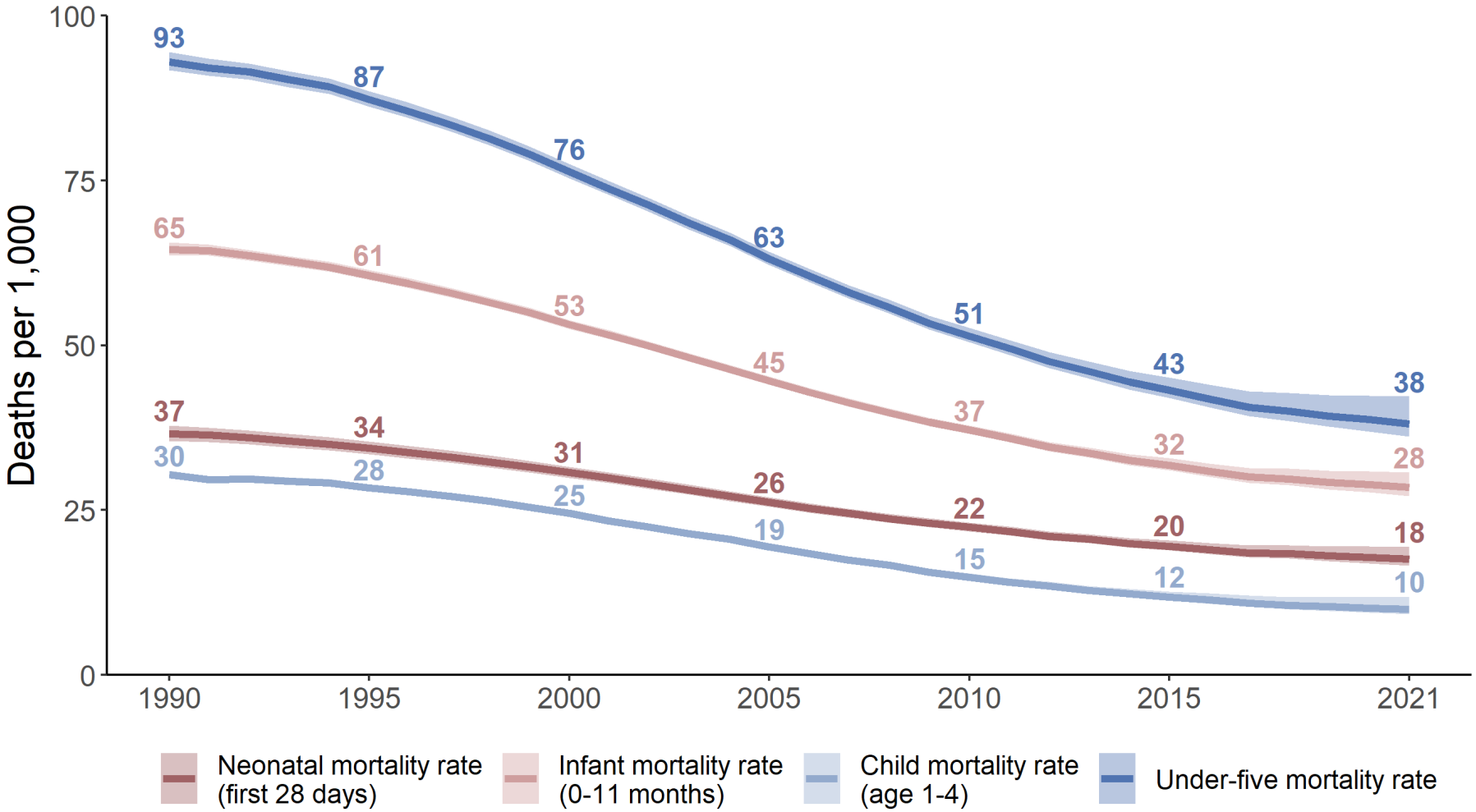
- WHO Risk Stratification Working Group
- Analysis team at University of Bergen and Innlandet Trust, Lillehammer, Norway
  - Catherine Schwinger, Siri Kaldenbach and Tor Strand

  and
  - Jay Berkley, University of Oxford and Judd Walson, Johns Hopkins

The next 25 minutes …

- Share findings from the Risk stratification individual data pooled analysis
- Consider the implications and opportunities for health programmes
- Mention other analyses in the pipeline
- Next steps

Neonatal, infant and child mortality: declining changes
What more is needed?



In 2021, WHO convened a Risk Stratification Working Group to conduct analyses to understand better the influence of physical and social factors on infant and child mortality

In particular, to examine the interactions between certain exposures and outcomes and if/how they possibly accumulate or are synergistic

Background

Well-recognised, in principle, that infants and children have different risks for mortality and morbidity

- Anthropometric deficits
- Severity of presenting morbidity
- Co-morbidities and disabilities
- Social and environmental factors

Reflected, to some extent, in WHO guidance and clinical decision pathways i.e. IMCI and Hospital Pocketbook

- Red, Yellow, Green classifications
- Complicated and uncomplicated severe acute malnutrition

The effect of multiple anthropometric deficits on child mortality: meta-analysis of individual data in 10 prospective studies from developing countries[1–3]

Christine M McDonald, Ibironke Olofin, Seth Flaxman, Wafaie W Fawzi, Donna Spiegelman, Laura E Caulfield, Robert E Black, Majid Ezzati, and Goodarz Danaei for the Nutrition Impact Model Study

ABSTRACT
Background: Child stunting, wasting, and underweight have been individually associated with increased mortality. However, there has not been an analysis of the mortality risk associated with multiple anthropometric deficits.
Objective: The objective was to quantify the association between combinations of stunting, wasting, and underweight and mortality among children <5 y of age.
Design: We analyzed data from 10 cohort studies or randomized trials in low- and middle-income countries in Africa, Asia, and Latin America with 53,767 participants and 1306 deaths. Height-for-age, weight-for-height, and weight-for-age were calculated by using the 2006 WHO growth standards, and children were classified into 7 mutually exclusive combinations: no deficits; stunted only; wasted only; un-

fact that multiple deficits may occur simultaneously, especially because all deficits are associated with poverty, disease history, and poor dietary intake (6, 7). The association between simultaneous multiple anthropometric deficits and the risk of mortality has not yet been analyzed in prospective studies, partly because it requires a large sample size that has not yet been available. Therefore, it is unclear how multiple anthropometric deficits amplify the risk of mortality and which combination is associated with the greatest risk. We quantified the association between multiple anthropometric deficits and all-cause mortality among children <5 y of age using data from 10 large cohort studies and randomized trials in 10 low- and middle-income countries.

Public Health Nutrition: 26(6), 1210–1221 doi:10.1017/S1368980023000149

Prognostic value of different anthropometric indices over different measurement intervals to predict mortality in 6–59-month-old children

André Briend[1,2,*], Mark Myatt[3,4], James A Berkley[5,6], Robert E Black[7], Erin Boyd[8,9], Michel Garenne[10,11,12], Natasha Lelijveld[4], Sheila Isanaka[13,14], Christine M McDonald[15], Martha Mwangwome[5,16], Kieran S O'Brien[17], Catherine Schwinger[18], Heather Stobaugh[19,9], Sunita Taneja[20], Keith P West[7] and Tanya Khara[4]

Public Health Nutrition: 26(4), 803–819 doi:10.1017/S136898002300023X

Systematic Review and Meta-Analysis

Anthropometric criteria for best-identifying children at high risk of mortality: a pooled analysis of twelve cohorts

Tanya Khara[1,*], Mark Myatt[2], Kate Sadler[1], Paluku Bahwere[3], James A Berkley[4,5], Robert E Black[6], Erin Boyd[7], Michel Garenne[8,9,10,11], Sheila Isanaka[12,13], Natasha Lelijveld[1], Christine McDonald[14,15], Andrew Mertens[16], Martha Mwangome[5], Kieran O'Brien[17], Heather Stobaugh[18,19], Sunita Taneja[20], Keith P West[21] and André Briend[22,23]

Prior analyses

- Often restricted to one geographic area
- Old datasets
- Focused on one risk area
  - Anthropometric outcomes only e.g. wasting and stunting
  - Syndrome or diagnoses based
- Presented findings as relative or odds ratios
- *In utero* growth not considered

Gaps and emerging insights

Risk differentials less well captured re.

- Age
- Gestational age
- Low birth weight
- Interactions between known risks
- Socio-economic factors e.g. maternal literacy, parental vital status
- Others …

Growing awareness re.

- Post discharge risks / mortality
- Use of in-patient risk assessments

Explanatory models vs. characterising predictors

Risk stratified analyses

Aim

To estimate the individual and cumulative effects of the main clinical and social/environmental risks on survival, (growth) and development of children

Objectives

1. What are the age-specific mortality risks associated with:
    a. Anthropometric deficit
    b. Common infectious diseases
    c. Being born small (Preterm / small for gestational age / LBW)
    d. History of breastfeeding
2. What are the age-specific mortality risks when individual exposures are combined?

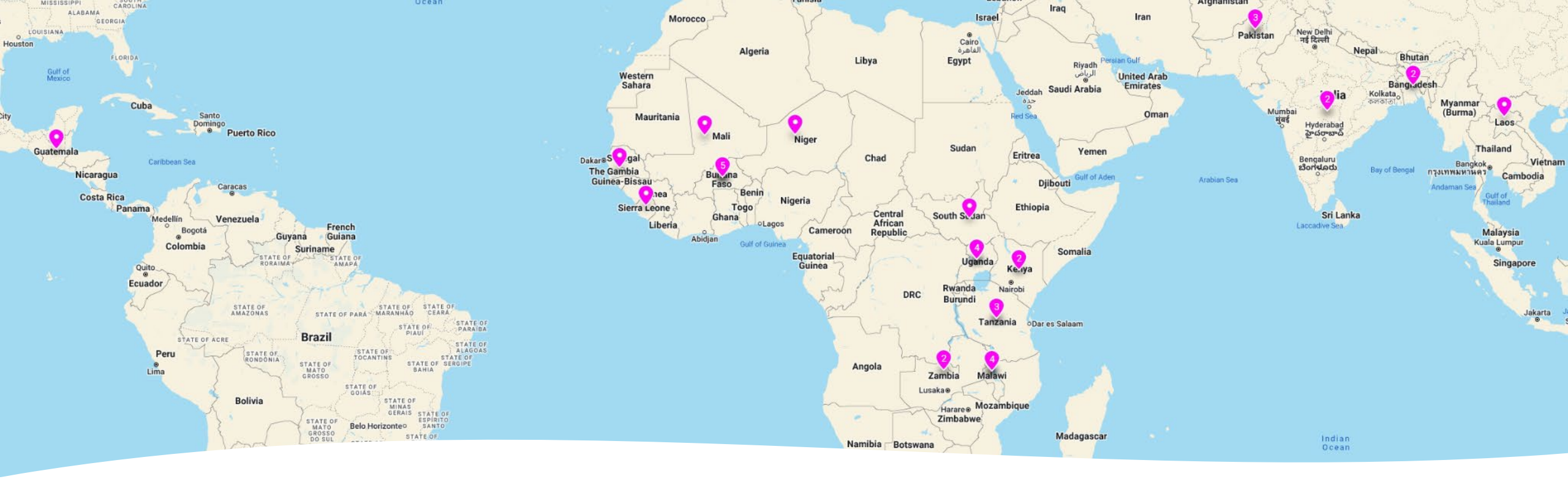
Individual data pooled analyses

Support from USAID

Search for existing datasets: inclusion criteria

The study has:

1. Data on **mortality, age, sex and weight**. Data on other anthropometric indicators, and indicators within the other categories of exposures including morbidity, pregnancy outcomes, and clinical signs and symptoms requested, but not required
2. Data on children **<60 months**
3. Conducted in a **low-or middle-income country** (World Bank definitions)
4. Followed individual children **longitudinally**, i.e. cross-sectional studies excluded
5. An **adequate description of the study population** including the sampling strategy, random vs. convenience sampling, inclusion and exclusion criteria, location, etc. and of the assessment procedures is available



Data included

33 studies
75 287 children
546 459 observations

~149 090	<6 months
~151 555	6-11 months
~178 165	12-23 months
~ 51 824	24-59 months

2 805 death events (2 660 with age at death)

Analysis approach

- Mortality risk
  - Relative (OR from GEE models) taking into account “time at risk”
  - **Absolute (margins after GEE models)**

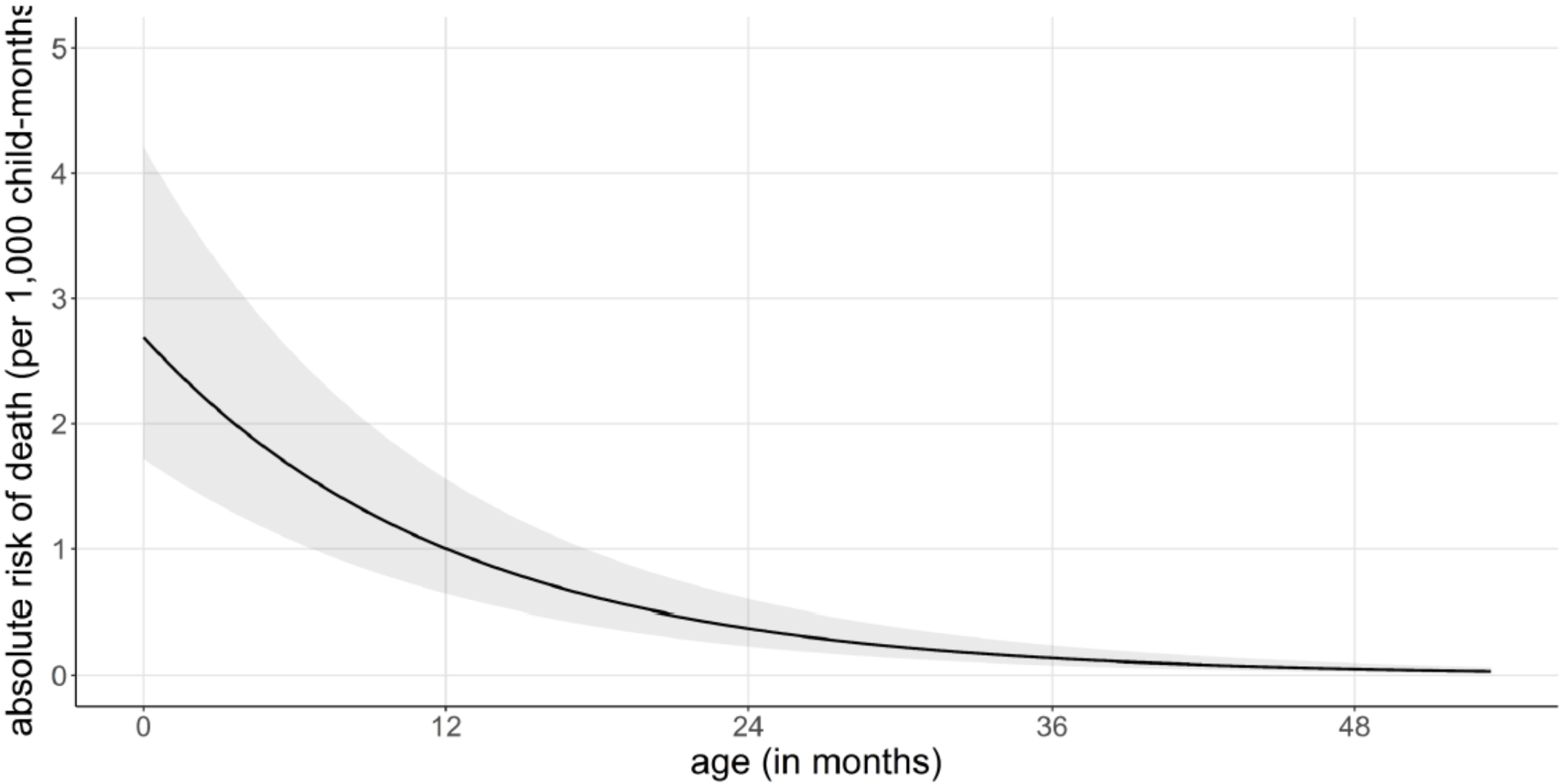
- Population types based on study inclusion criteria
  - General Population (GP)
  - Selected on basis of anthropometric deficit (Anthropometry selected: A-S)
  - Selected on basis of presence of an illness (Illness selected: I-S)

Single predictors

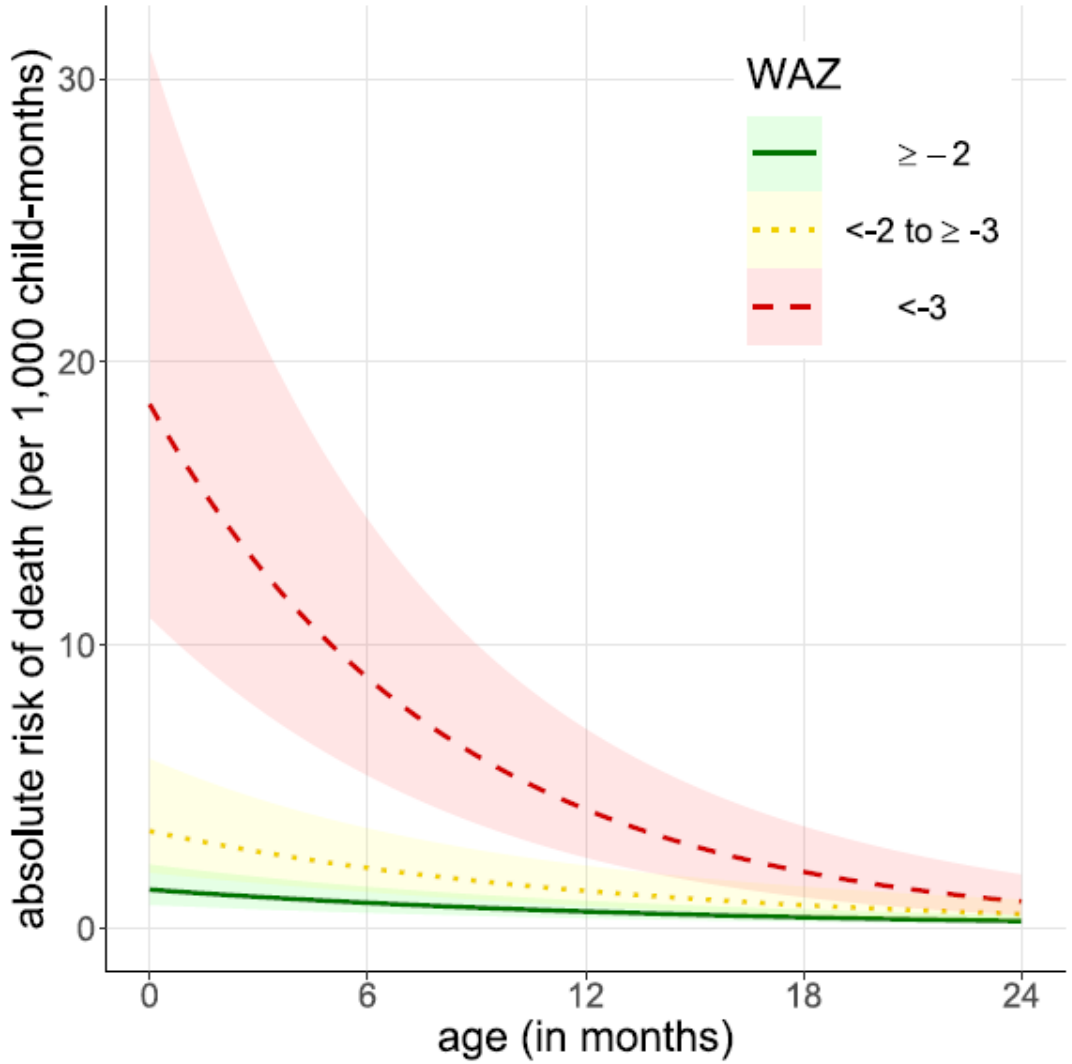
What is the relative and **absolute** risk among children with a certain ‘exposure’?

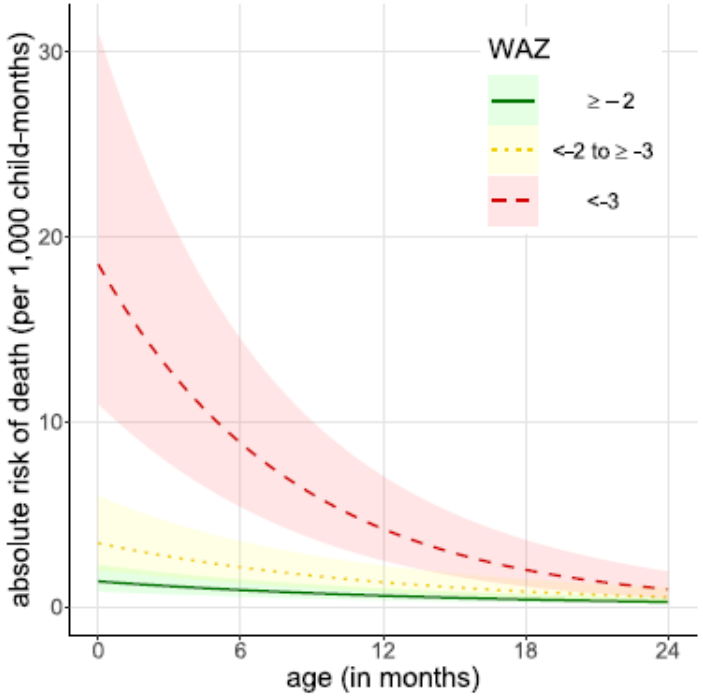
- WAZ / WHZ / HAZ / MUAC *(3 categories)*
- Diarrhoea / Illness / Number of Illnesses / Malaria *(y/n)*
- Low birthweight / preterm birth *(y/n)*
- Any breastfeeding *(y/n)*

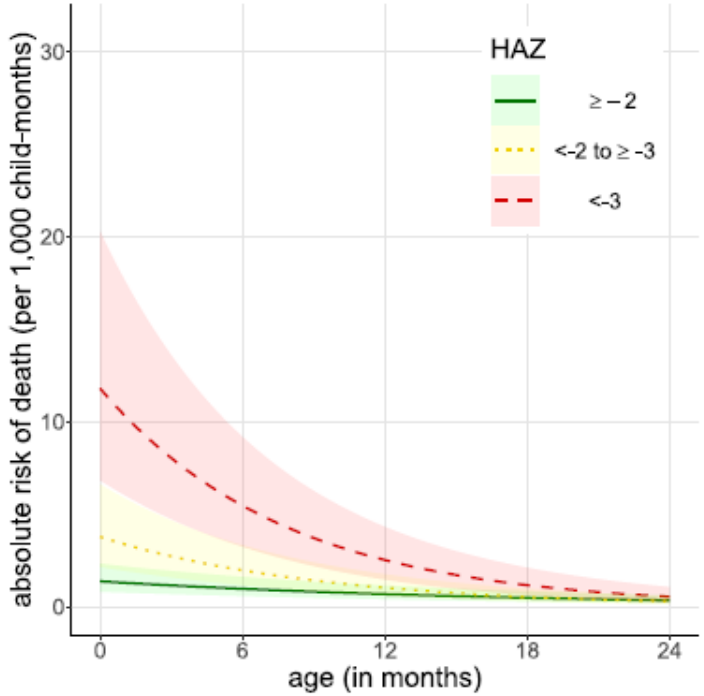
Modelled risk of death for all children

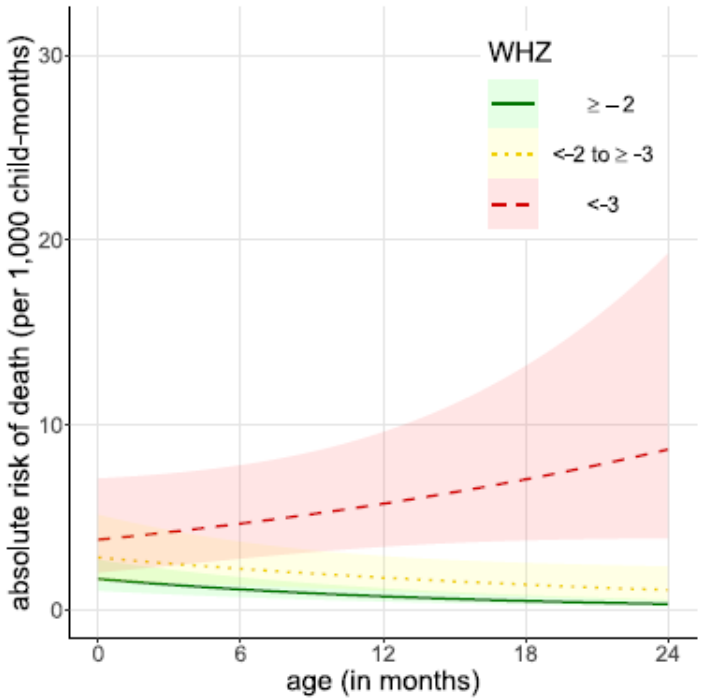


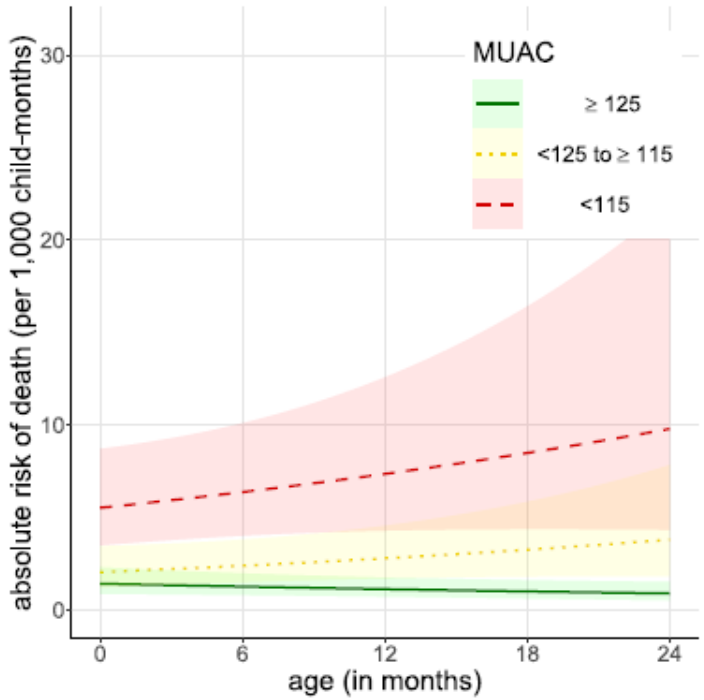
Risk of death for WAZ categories







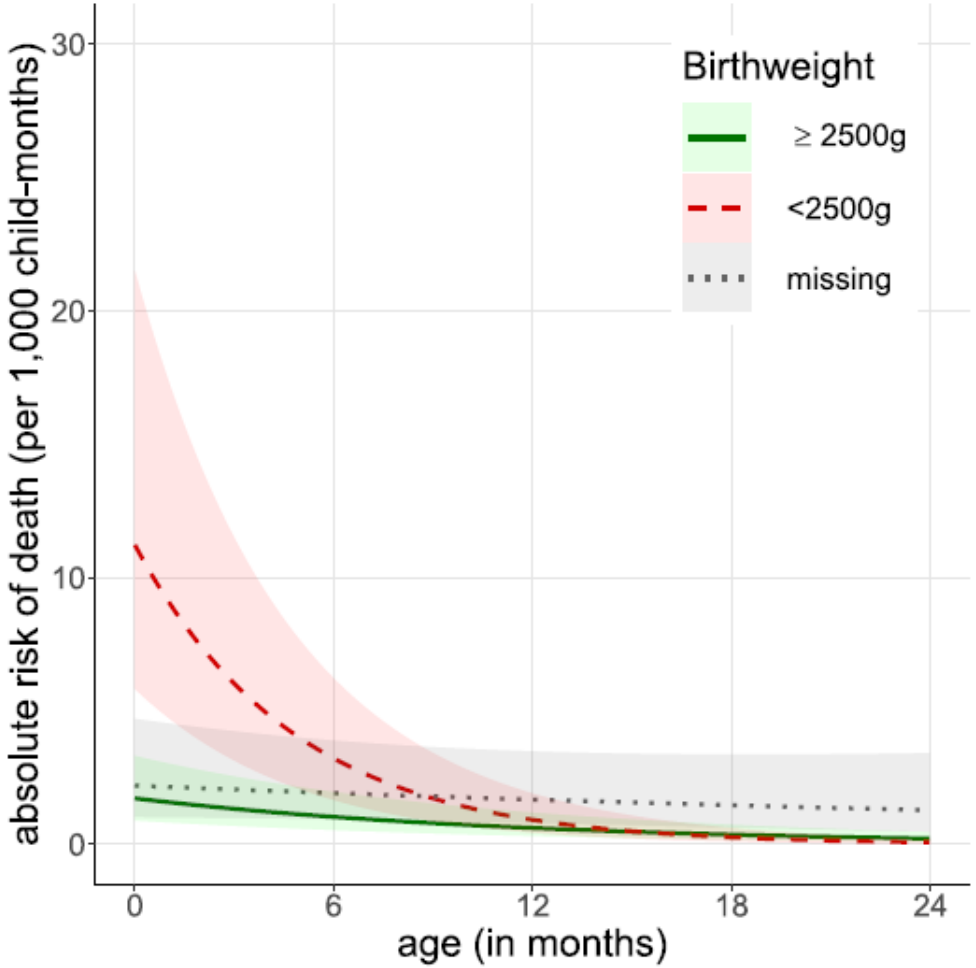


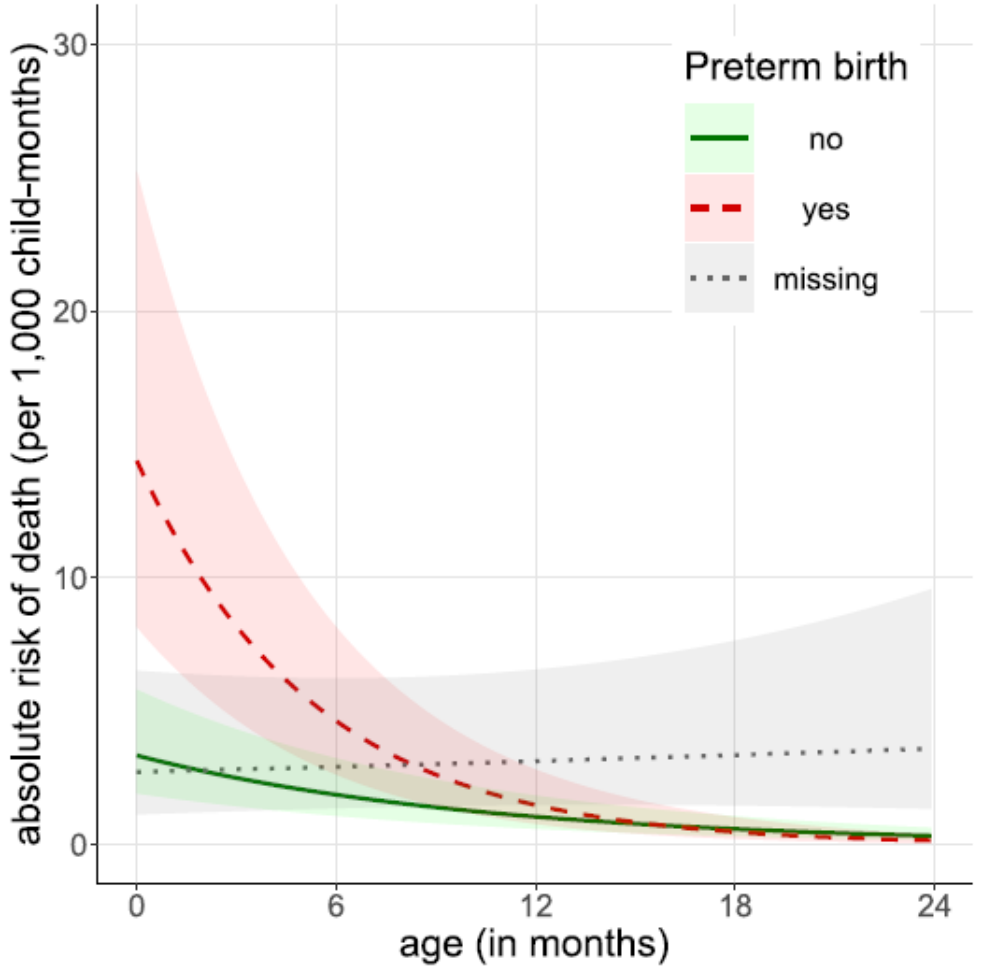


High absolute risk of dying with severe deficit in all 4 anthropometric indices

Highest risk: WAZ <-3 & <12 mo

Different age pattern WHZ & MUAC
(NB: small n!)





LBW or reported PTB: high mortality risk <6 mo but still raised until 12 mo

NB:

- % of missing information increases with age
- Children with missing information higher risk >~9 mo

No differences between sexes

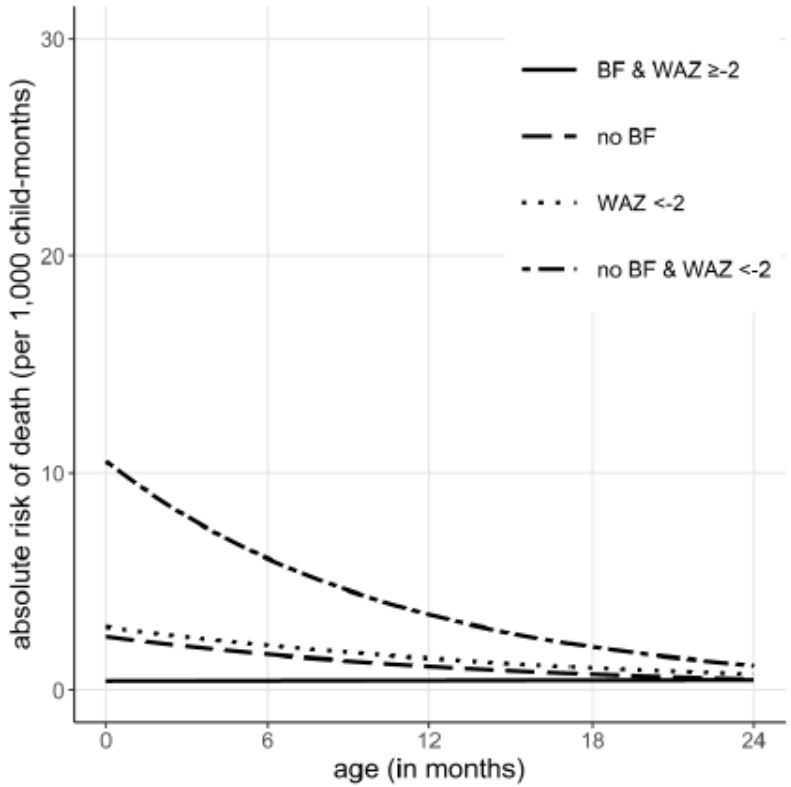
Example WAZ:

		<6 mo		6-11 mo		12-23 mo		24-59 mo	
	Indicator	**Risk[1]**	**95% CI**	**Risk[1]**	**95% CI**	**Risk[1]**	**95% CI**	**Risk[1]**	**95% CI**
Male	WAZ								
	≥-2	**1.1**	0.7, 1.9	**0.8**	0.5, 1.2	**0.5**	0.3, 0.8	**0.3**	0.2, 0.6
	<-2, ≥-3	**2.8**	1.6, 4.9	**1.8**	1.1, 3.0	**1.2**	0.6, 2.1	**0.7**	0.4, 1.6
	<-3	**12.3**	7.2, 20.7	**6.4**	3.9, 10.6	**3.4**	1.9, 6.1	**1.8**	0.8, 3.7
Female	WAZ								
	≥-2	**1.3**	0.8, 2.1	**0.7**	0.5, 1.2	**0.4**	0.2, 0.7	**0.2**	0.1, 0.5
	<-2, ≥-3	**2.6**	1.4, 4.6	**1.7**	1.0, 2.9	**1.2**	0.6, 2.2	**0.8**	0.4, 1.8
	<-3	**8.2**	8.2, 24.4	**6.8**	4.0, 11.4	**3.3**	1.7, 6.2	**1.6**	0.7, 3.7

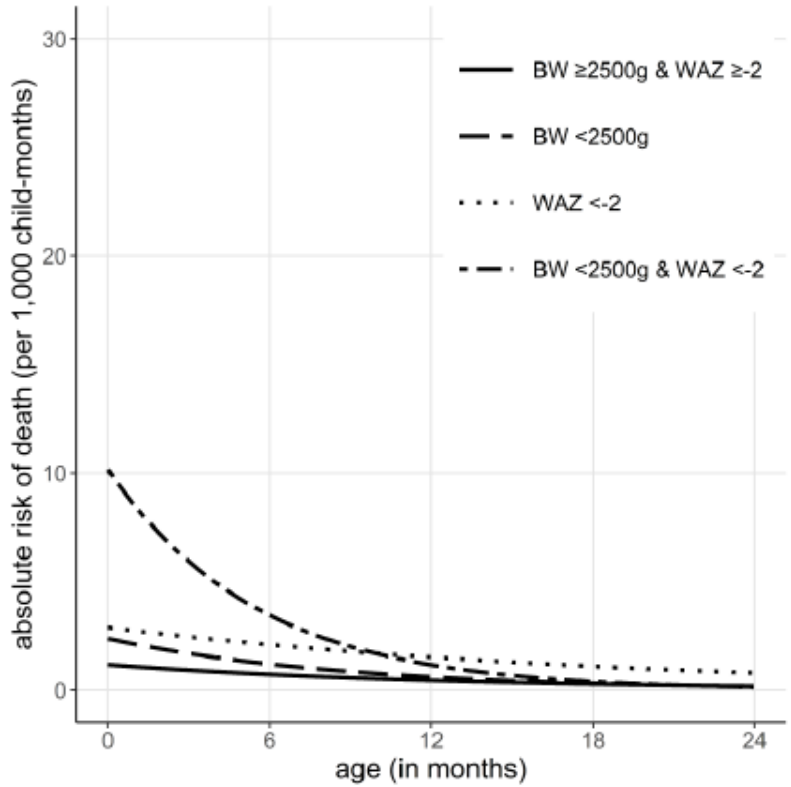
[1] Risk = absolute mortality risk per 1,000 child months

WAZ <-2 in combination with…

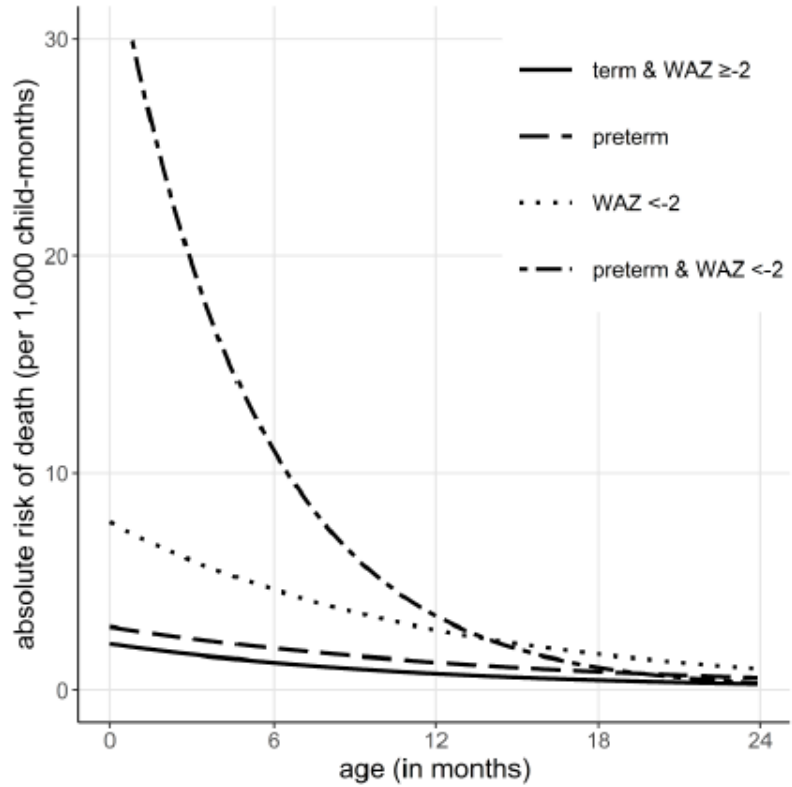
…no breastfeeding



…low birthweight



…preterm birth



Risk Stratification analyses: main findings

- Four readily assessable child-level characteristics -- age <2yrs; WAZ**<-3**; LBW/PTB; non-breastfeeding -- identify infants and young children at high risk of mortality
- Infants born small (LBW/reported preterm) are at high risk of mortality until at least 12 months of age
- WAZ **<-2** in combination with any other exposure -- LBW or reported PTB or non-BF -- substantially increase mortality risks
- Presenting to a hospital with an illness significantly increases overall risks
- Mortality risks of admitted infants/children extend substantially beyond the duration of the acute illness
- Reported symptoms of diarrhoea or pneumonia do not identify the infant/child at higher risk of mortality

Findings prompt ➔ Risk differentiated care

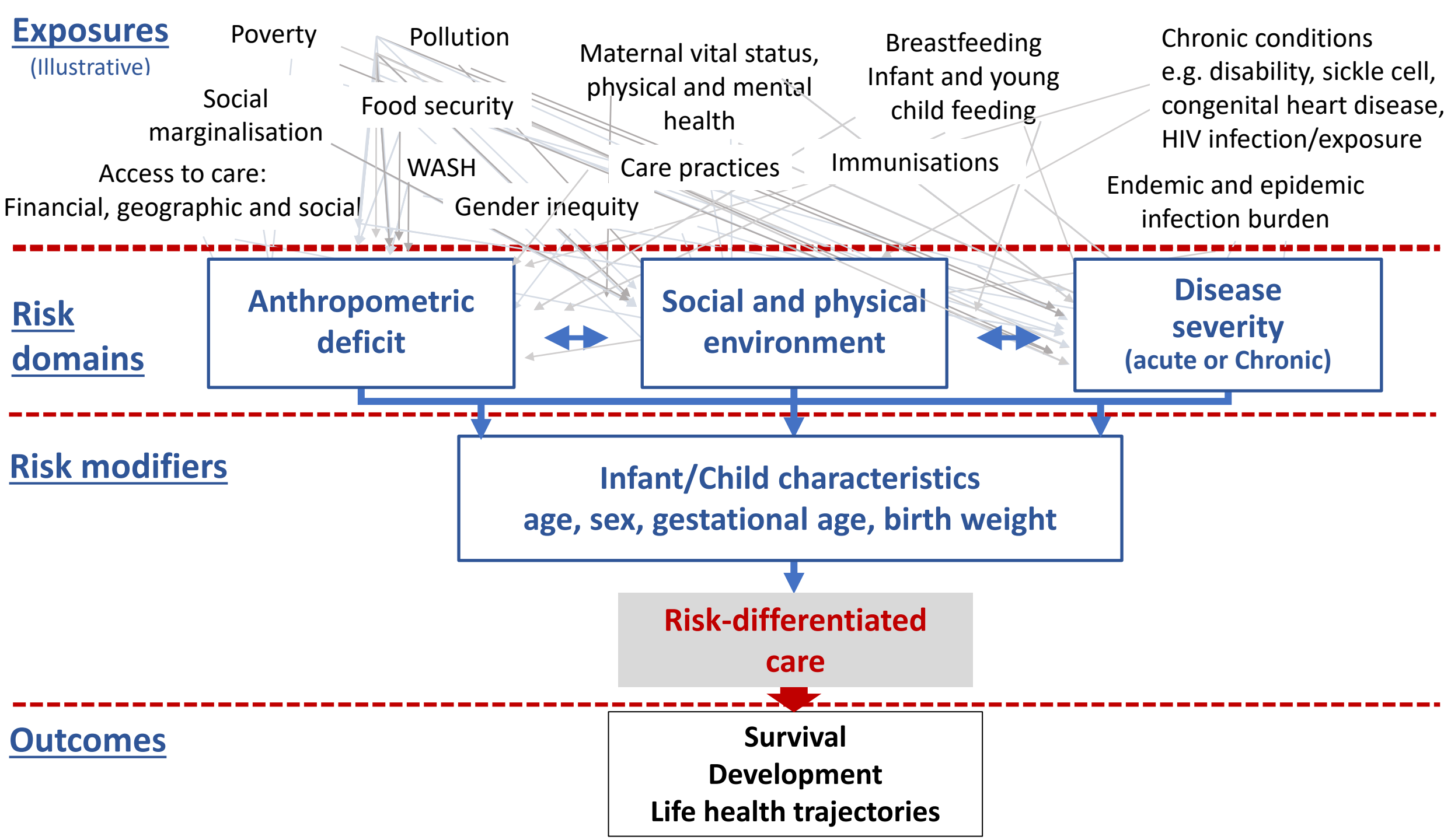
- Care reflects the underlying risk of the child – both high and low – in addition to consideration of the severity of the presenting illness

<u>At present</u>

- An 9m infant with a history of LBW, non-BF, who is low WFA and presenting with diarrhoea/dehydration

  is managed the same as

- A 3 yr child with normal BW, h/o BF, normal WFA and also presenting with diarrhoea/dehydration


Exposures
(Illustrative)
Poverty
Pollution
Maternal vital status, physical and mental health
Breastfeeding
Infant and young child feeding
Chronic conditions
e.g. disability, sickle cell, congenital heart disease, HIV infection/exposure
Social marginalisation
Food security
Access to care:
Financial, geographic and social
WASH
Care practices
Immunisations
Gender inequity
Endemic and epidemic infection burden
Risk domains
Anthropometric deficit
Social and physical environment
Disease severity
(acute or Chronic)
Risk modifiers
Infant/Child characteristics
age, sex, gestational age, birth weight
Risk-differentiated care
Outcomes
Survival
Development
Life health trajectories

Paradigm shift

- Paradigm shift to reframe ‘Risk’ ➔ child-centred risk assessment in addition to illness classification
- WHO is reviewing implementation tools e.g. IMCI, Hospital care, iCCM to consider how to include initial risk assessment of individual young children (<2 years / combination of risks e.g. h/o LBW and non-BF)
- Based on evidence, will refine and establish packages of risk-differentiated care for high risk infants and young children
  - Illness-specific interventions
  - Follow-up strategies for LBW/PTB and post-discharge

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There are immediate opportunities to make a difference
but more research is always needed

Implications and opportunities

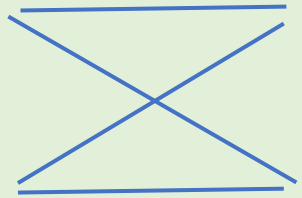
Entry points

Prevention

- Birth (if LBW or PTB identified)
- Well child visits
- Community health worker programmes

Treatment

- PHC
- Referral facilities



- Immediate Rx
  - High risk
  - Lower risk
- Follow-up care

What might this mean for care packages?

The nature of the ‘identifier’ does not necessarily point to the intervention(s) needed to mitigate the risk of that child

- Cannot change some risk ‘exposures’
  - Birth weight or preterm
  - History of breastfeeding
- Direct treatment of some risk exposures may not change the child’s risk status
  - Post-discharge mortality
- Risk identifiers e.g. weight-for-age are indicators of ‘all’ health status and not only one specific area of health

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Care packages may need to reflect not only the risk exposure – but also other intervention(s) e.g. targeted counselling for care-seeking and increased follow-up

What do these data mean for growth monitoring and wasting programmes?

Increase the importance of anthropometric assessments/monitoring and broadens the required response

- Anthropometry is a sign of general health not only dietary intake
- Wasting is one risk for mortality but not the only risk. WFA together with other identifiers identifies a larger group of infants and children at risk of mortality
- Adequate high quality diet is certainly needed to recover weight and lean tissue but may not be sufficient
- Greater understanding of anthropometric assessments and how to respond to routine assessments will serve to improve care and management of at-risk infants and children

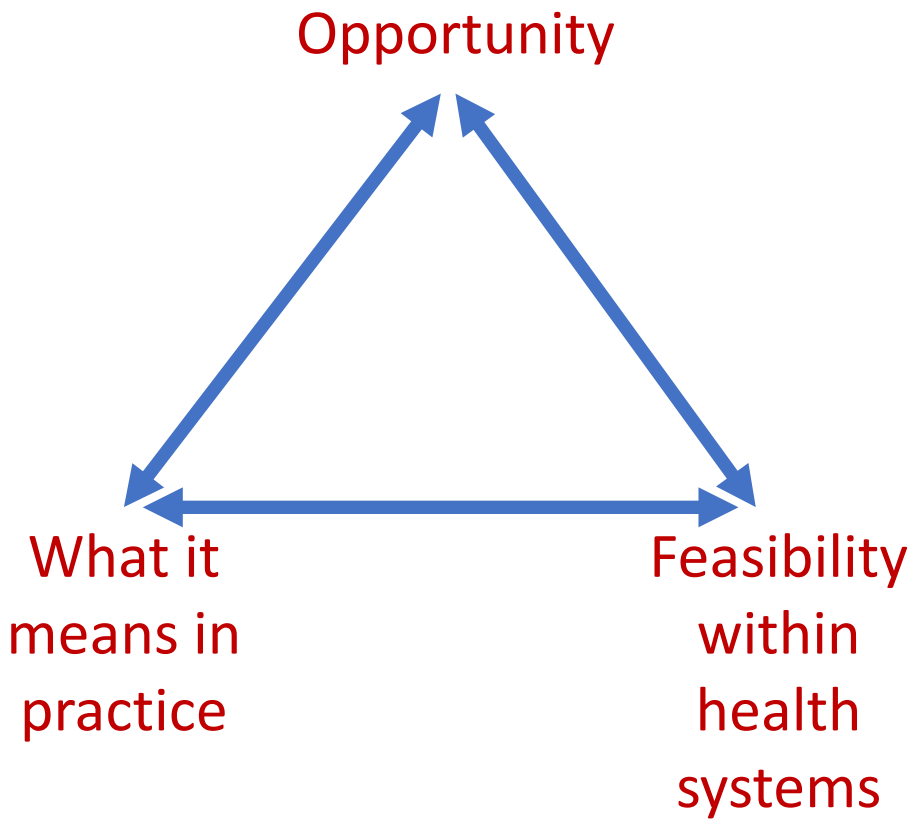
What would be needed for health systems to de-escalate care for low risk children?

- This is complicated!!
- Health professionals and health systems tend to be risk averse
- At the same time, they recognise that children may be admitted who could be managed – sometimes more safely – at home
- Need evidence to inform appropriate and acceptable clinical and social criteria for determining ‘low risk’
- Difficult to conduct research as safety and mortality would require very large sample sizes of ‘low’ risk children ….. but is needed

➔ Catch 22

Next steps

- Explore health systems opportunities
  - Incorporate risk assessments into routine clinic assessments and how targeted additional care can be provided --------- **but keep it as simple as possible**
  - Identifying low risk infants/children and consider views/feasibility of de-escalating care



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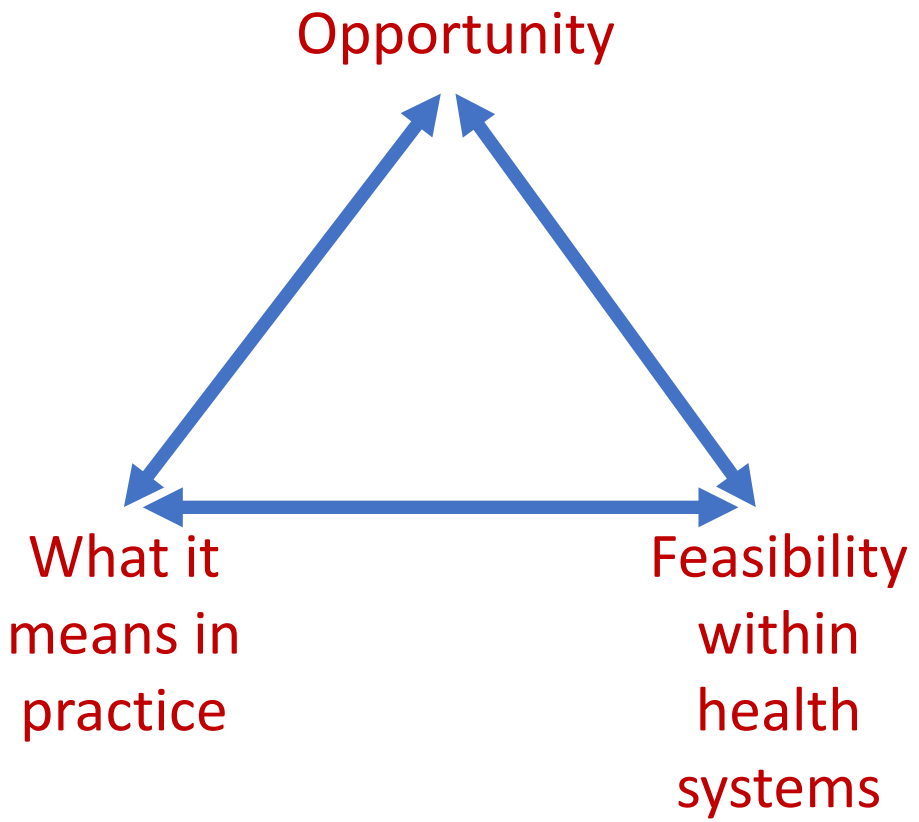
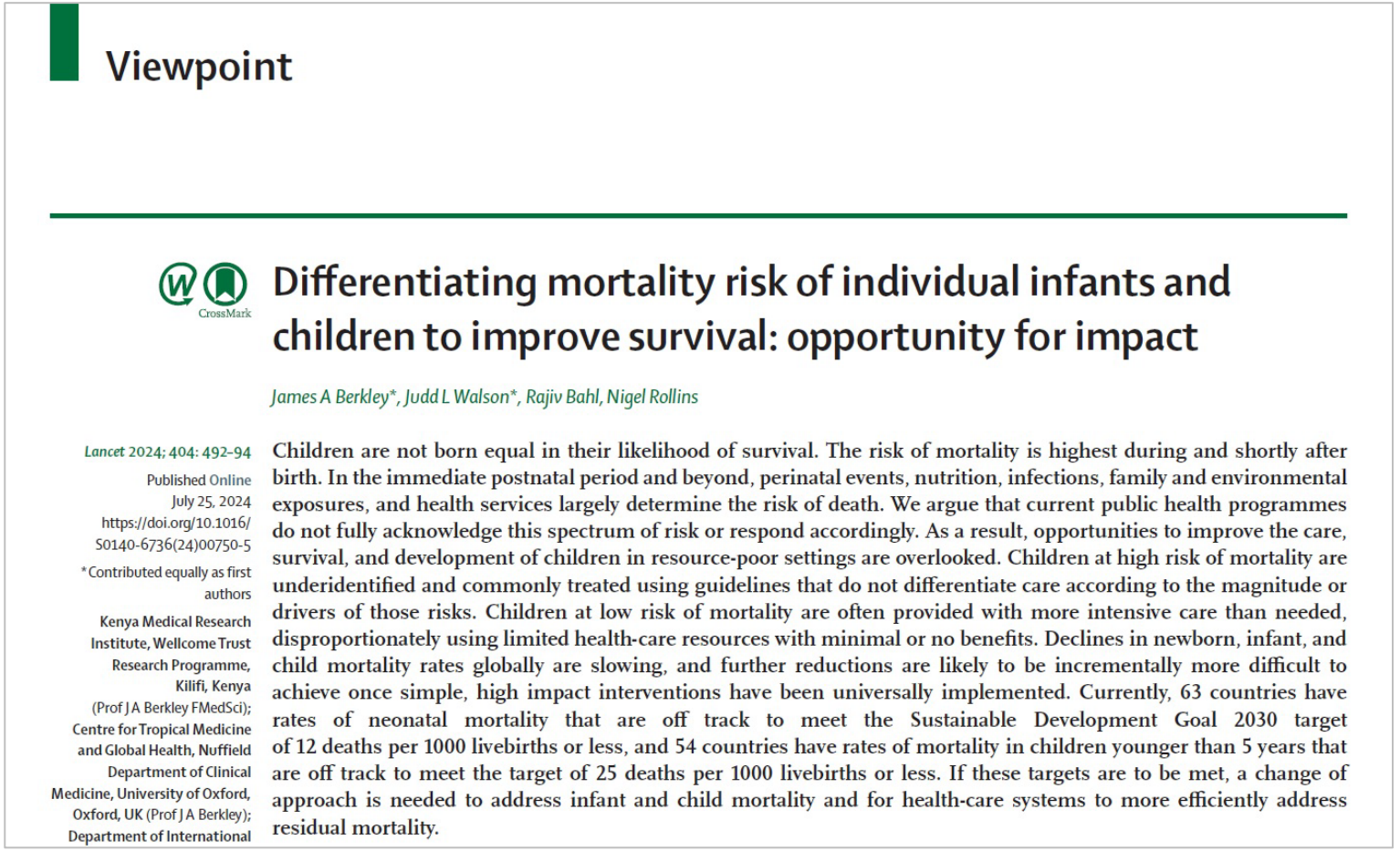
  - Incorporate risk assessments into routine clinic assessments and how targeted additional care can be provided --------- **but keep it as simple as possible**
  - Identifying low risk infants/children and consider views/feasibility of de-escalating care
- Consider other risk predictors e.g. is the mother the main caregiver/is the mother alive
- Predictive performance of different anthropometric combinations and thresholds
- Similar predictive analyses to identify other ‘at-risk’ individuals e.g. pregnant women



Thank you

Infant- and child-level predictors of mortality in low-resource settings: the WHO Child Mortality Risk Stratification Multi-Country Pooled Cohort. medRxiv 2024. (preprint)

https://doi.org/10.1101/2024.07.06.24309988



Viewpoint

Differentiating mortality risk of individual infants and children to improve survival: opportunity for impact

James A Berkley*, Judd L Walson*, Rajiv Bahl, Nigel Rollins

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Children are not born equal in their likelihood of survival. The risk of mortality is highest during and shortly after birth. In the immediate postnatal period and beyond, perinatal events, nutrition, infections, family and environmental exposures, and health services largely determine the risk of death. We argue that current public health programmes do not fully acknowledge this spectrum of risk or respond accordingly. As a result, opportunities to improve the care, survival, and development of children in resource-poor settings are overlooked. Children at high risk of mortality are underidentified and commonly treated using guidelines that do not differentiate care according to the magnitude or drivers of those risks. Children at low risk of mortality are often provided with more intensive care than needed, disproportionately using limited health-care resources with minimal or no benefits. Declines in newborn, infant, and child mortality rates globally are slowing, and further reductions are likely to be incrementally more difficult to achieve once simple, high impact interventions have been universally implemented. Currently, 63 countries have rates of neonatal mortality that are off track to meet the Sustainable Development Goal 2030 target of 12 deaths per 1000 livebirths or less, and 54 countries have rates of mortality in children younger than 5 years that are off track to meet the target of 25 deaths per 1000 livebirths or less. If these targets are to be met, a change of approach is needed to address infant and child mortality and for health-care systems to more efficiently address residual mortality.

https://www.thelancet.com/article/S0140-6736(24)00750-5/abstract