IHME
Measuring what matters

Parsing the impact of Child Growth Failure on morbidity and mortality: an analysis of the Global Burden of Disease Study 2021

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I acknowledge and honor that this building stands on the unceded land of the Coast Salish peoples, land which touches the shared waters of all tribes and bands within the Duwamish, Suquamish, Tulalip and Muckleshoot nations.

Outline

- Percent attributable fractions (PAFs)
- Child Growth Failure
- Estimating Exposure
- Estimating Relative Risk
- Results
- Discussion
- Future Work

Percent attributable fraction (PAF)

For a risk-factor/outcome pair, if P_e is the percent of the population exposed to the risk and RR is the (increased) relative risk of the outcome for those exposed, the fraction of that outcome **attributable** to that risk is given as:

$$PAF = \frac{P_e(RR - 1)}{1 + P_e(RR - 1)}$$

For example, if smokers are **7 times** as likely to develop lung cancer than non-smokers, and in some population, **30%** of the population smokes, we have:

$$PAF = \frac{0.3(7 - 1)}{1 + 0.3(7 - 1)} = 64.3\%$$

Percent attributable fraction (PAF)

Different smokers smoke different amounts. We could further break down the increased relative risk of lung cancer for smokers by splitting “smokers” into ‘infrequent smokers’ and ‘daily smokers.’

We can still calculate an overall attributable fraction of lung cancer for all smokers if we know the relative risks for each group (RR_i and RR_d) and what fraction of the population falls into each category (P_i and P_d). For example, we might have:

$$PAF = \frac{P_i(RR_i - 1) + P_d(RR_d - 1)}{(1 - P_i - P_d) + P_i RR_i + P_d RR_D} = \frac{0.05(2-1) + 0.25(8-1)}{0.7 + 0.05 * 2 + 0.25 * 8} = 59.2\%$$

Percent attributable fraction (PAF)

Finally, we can further extend this calculation to account for changes in relative risks as exposure increases in a continuous manner:

$$PAF = \frac{\int_0^\infty RR(x)P(x)dx - 1}{\int_0^\infty RR(x)P(x)dx}$$

Now, we “just” need our continuous function of relative risk as exposure increases, $RR(x)$, and our pdf of exposure, $P(x)$.

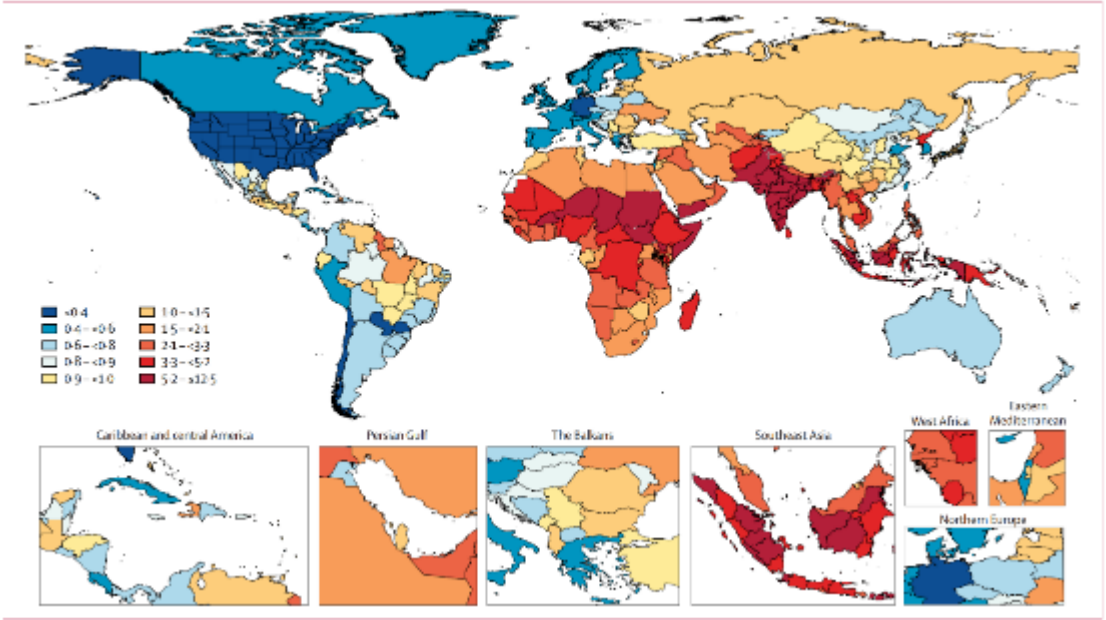
Child Growth Failure

Child growth failure (CGF) is (frequently) characterized by deficiencies in height-for-weight (HAZ; stunting), weight-for-height (WHZ; wasting), and weight-for-age (WAZ; underweight)

CGF is a risk factor for a number of under-5 diseases. In GBD 2019, these included diarrhea, lower respiratory infections, measles, and several neonatal disorders

According to GBD 2019, ~19% of all under-5 deaths are attributable to CGF.

The relative risks in these calculations were based on a single systematic review of 10 studies linking CGF with cause-specific death.



Estimating Exposure

Lead by Ryan Fitzgerald, the CGF team at IHME recast the estimation of exposure to consider a holistic, continuous approach.

By combining more than 1,700 data sources, Spatio-Temporal Gaussian Regression, and a novel ensembling approach to estimating continuous distributions, the team was able to estimate the entire distribution of exposure with unprecedented accuracy.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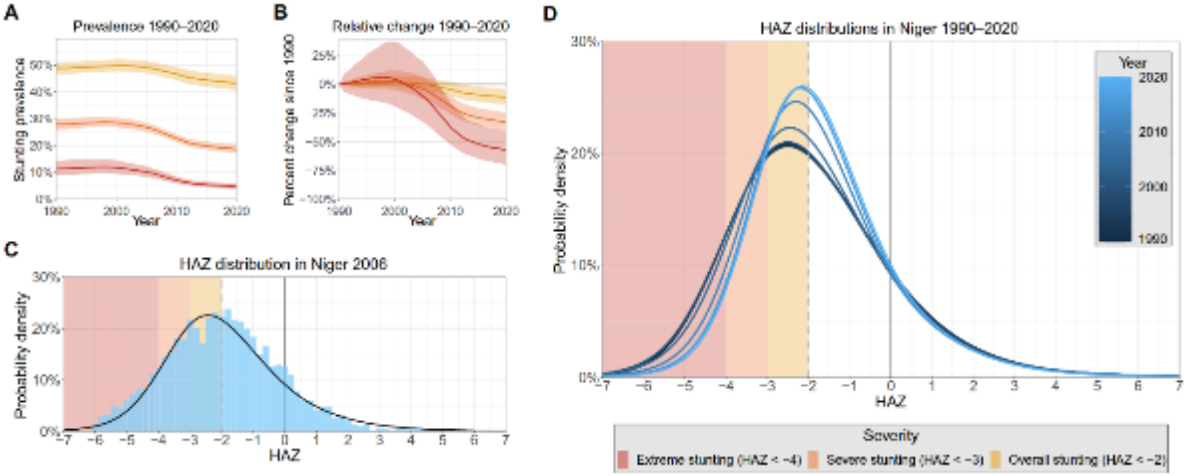
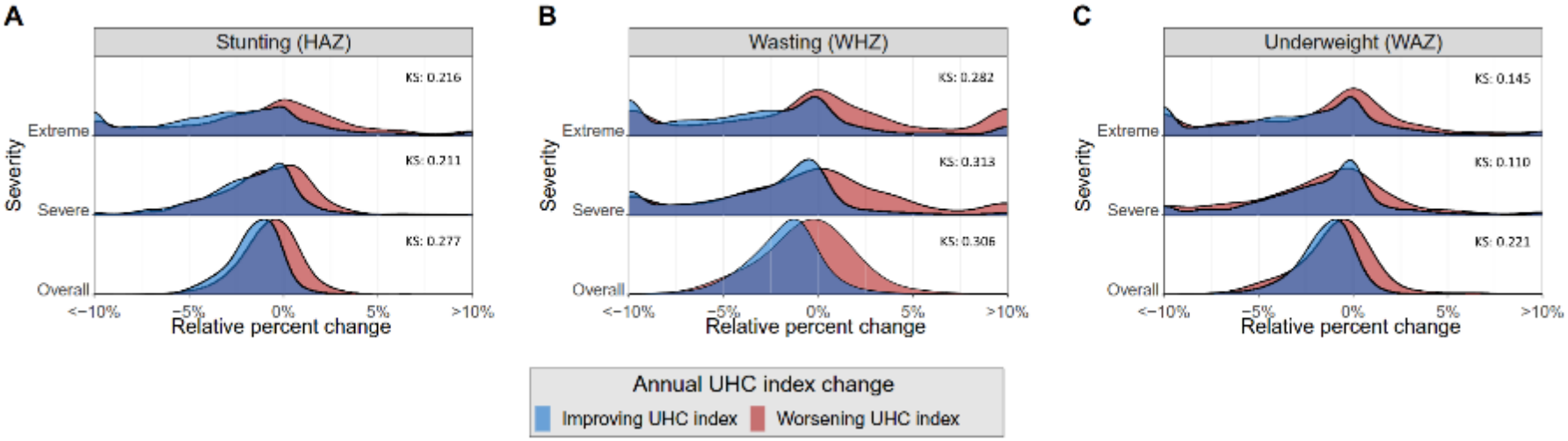
Current dichotomous metrics obscure trends in severe and extreme child growth failure



Estimating Exposure

By tracking changes in the distribution across time, more complex patterns in changes in severe CGF and drivers of these changes became apparent.



Estimating Exposure

- A new category of CGF, “extreme CGF” or $z < -4$ was identified (and confirmed to not be a data anomaly). In 2019, we estimated that across the world,
  - 20.3 (19.2 – 21.4) million children were extremely stunted
  - 1.32 (1.26 to 1.38) million children were extremely wasted
  - 9.51 (9.13 to 9.87) million children were extremely underweight

- Even with a “new” fifth exposure level, it became clear that “categories” of CGF were a poor measure of exposure, burden, and progress
  - A child who is 1.99 z-scores below expected levels is not equally poorly off as a child who is 1.01 z-scores below expected levels

- There was an immediate need for continuous relative risks that could be matched to these continuous exposure levels to more accurately understand the burden of CGF.

Estimating Relative Risk

Estimating relative risks associated with Child Growth Failure are inherently complicated. For example, a child may be wasted and then show up to the hospital with diarrhea because they have chronic diarrhea, not because they are wasted.

This cyclic causality makes cross-sectional data difficult to use in estimating relative risks.

The ideal data (and the data used in the previous systematic review) is from **longitudinal** studies as we need to match current disease outcomes to previous heath and anthropometric measurements.

Enter the Knowledge Integration (KI) database. The dataset contains millions of linked observations from longitudinal child health studies with disease outcomes (across the spectrum of severity) and anthropometric measurements.

Estimating Relative Risk

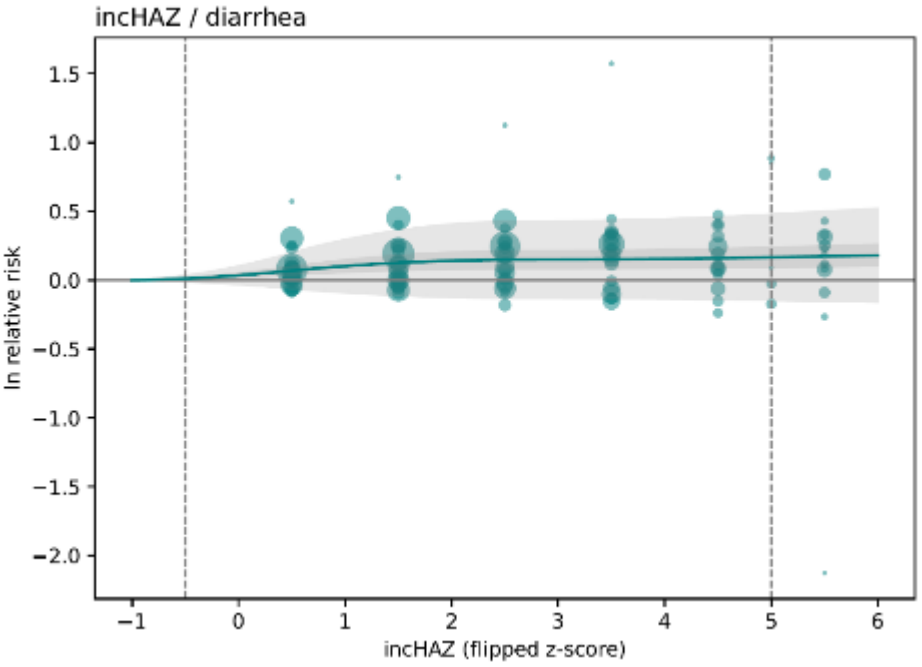
In work lead by Chris Troeger and Michael Arndt (with massive help from the IHME BoP team), the KI data was collapsed, relative risks were extracted and synthesized, and finally adjusted for simultaneous risk factor exposures.

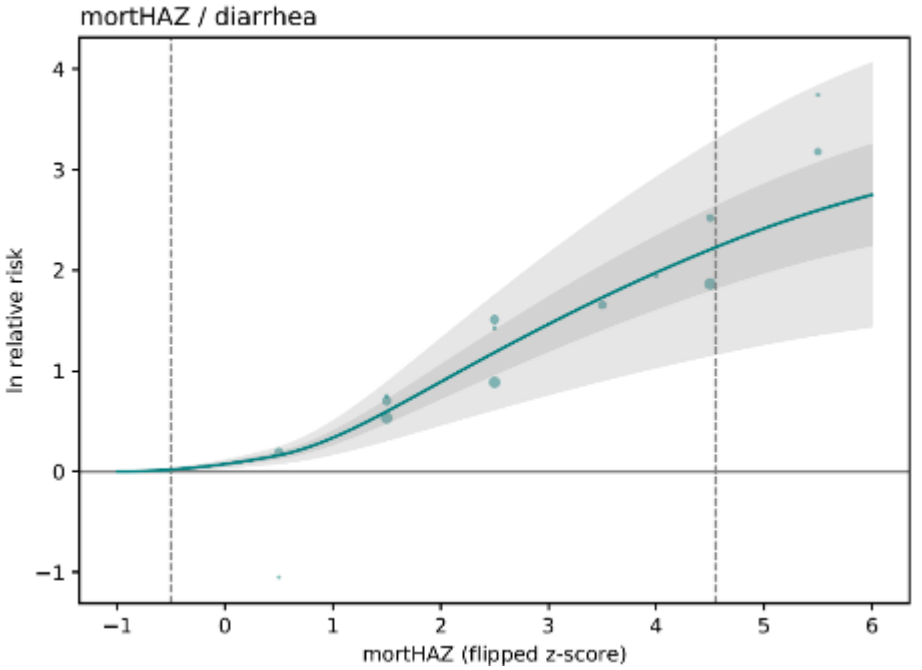
Previously, as is true for many relative risks in GBD, the relative risk for disease and death were assumed to be the same for CGF. For example, a severely stunted child was about twice as likely to have a diarrhea disease event and also twice as likely to die from diarrhea compared to a child who was not stunted.

The KI data allowed us to test the assumption of equal disease and death relative risks.

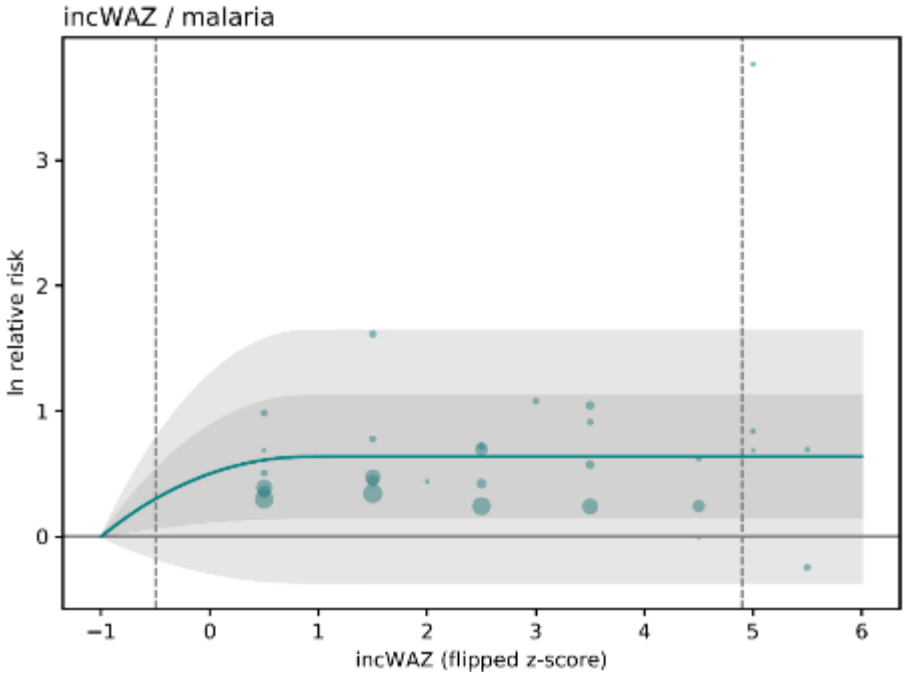
This assumption was very false.

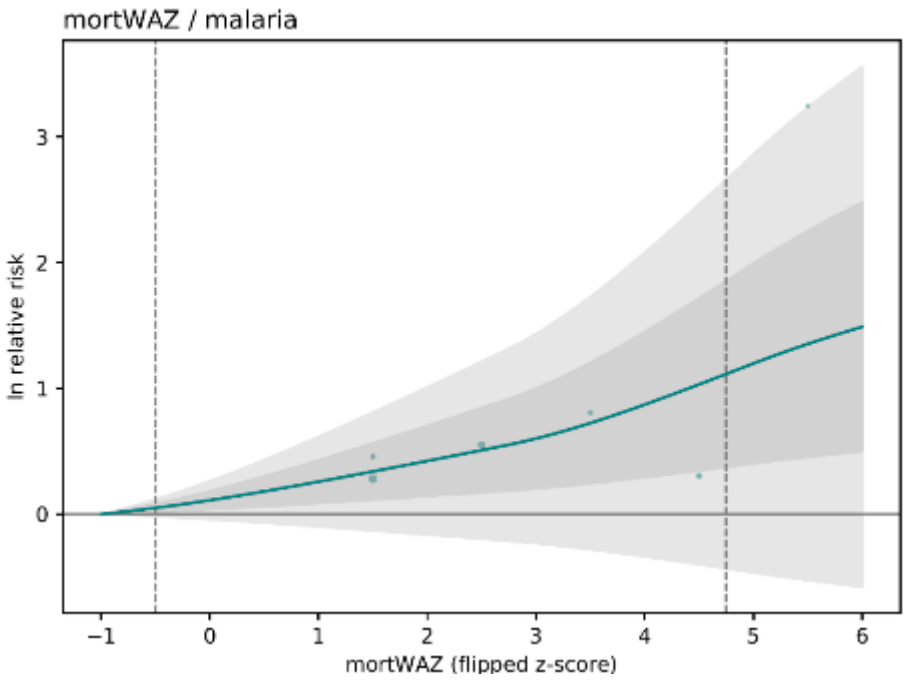
Estimating Relative Risk





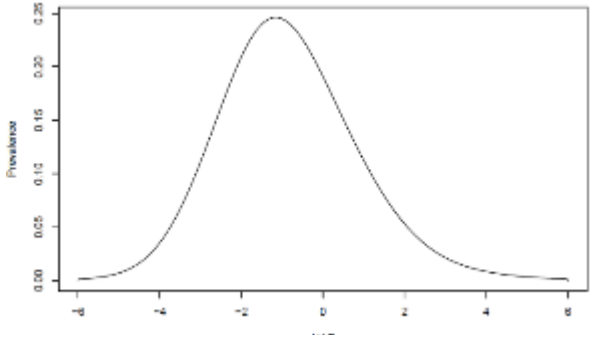
Estimating Relative Risk



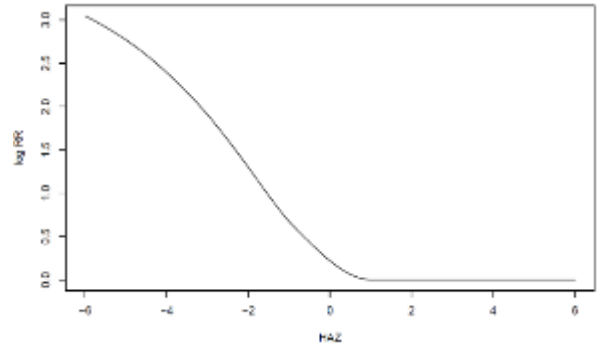


Estimating Relative Risk

Prevalence of HAZ

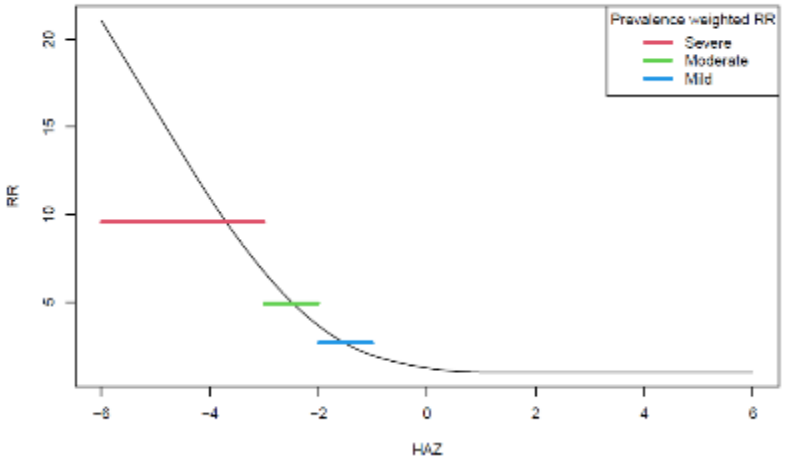


log RR of LRI Mortality for HAZ

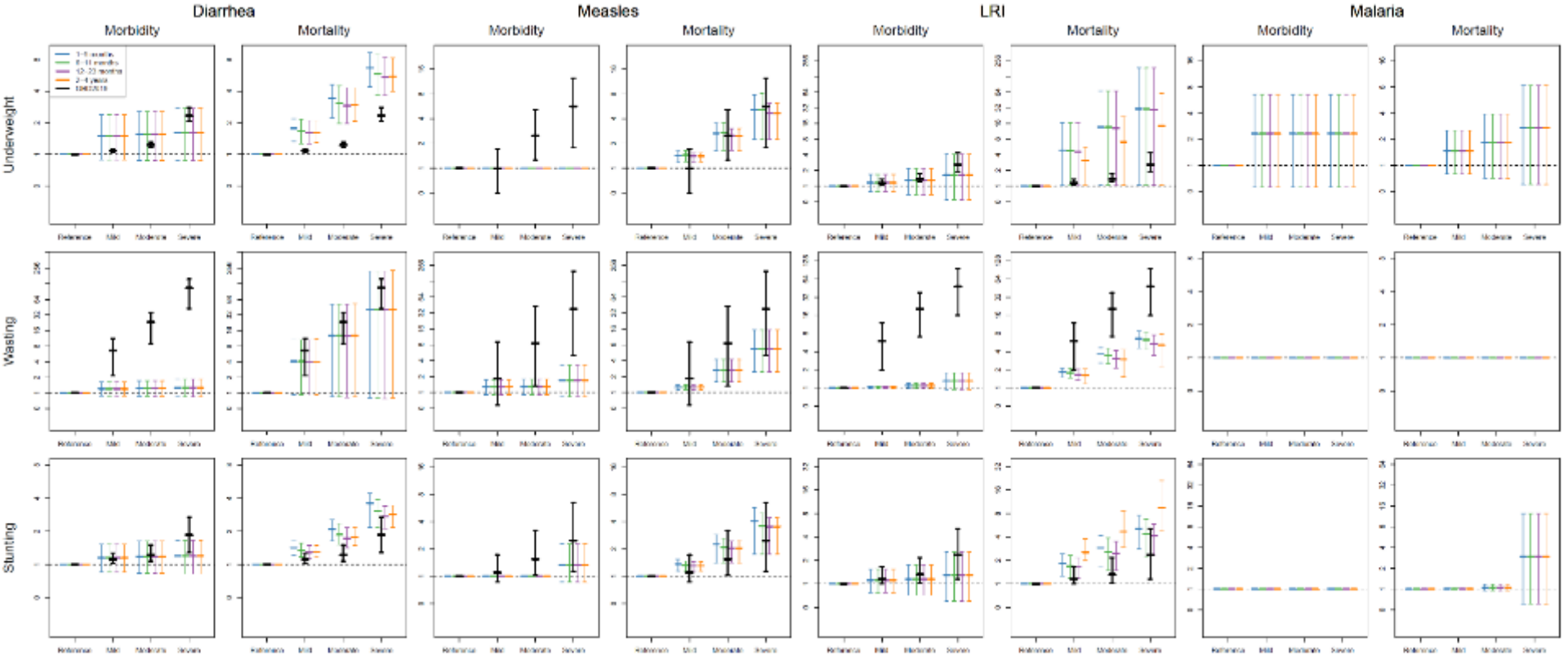


We then can combine our continuous relative risk with our continuous exposure curves!

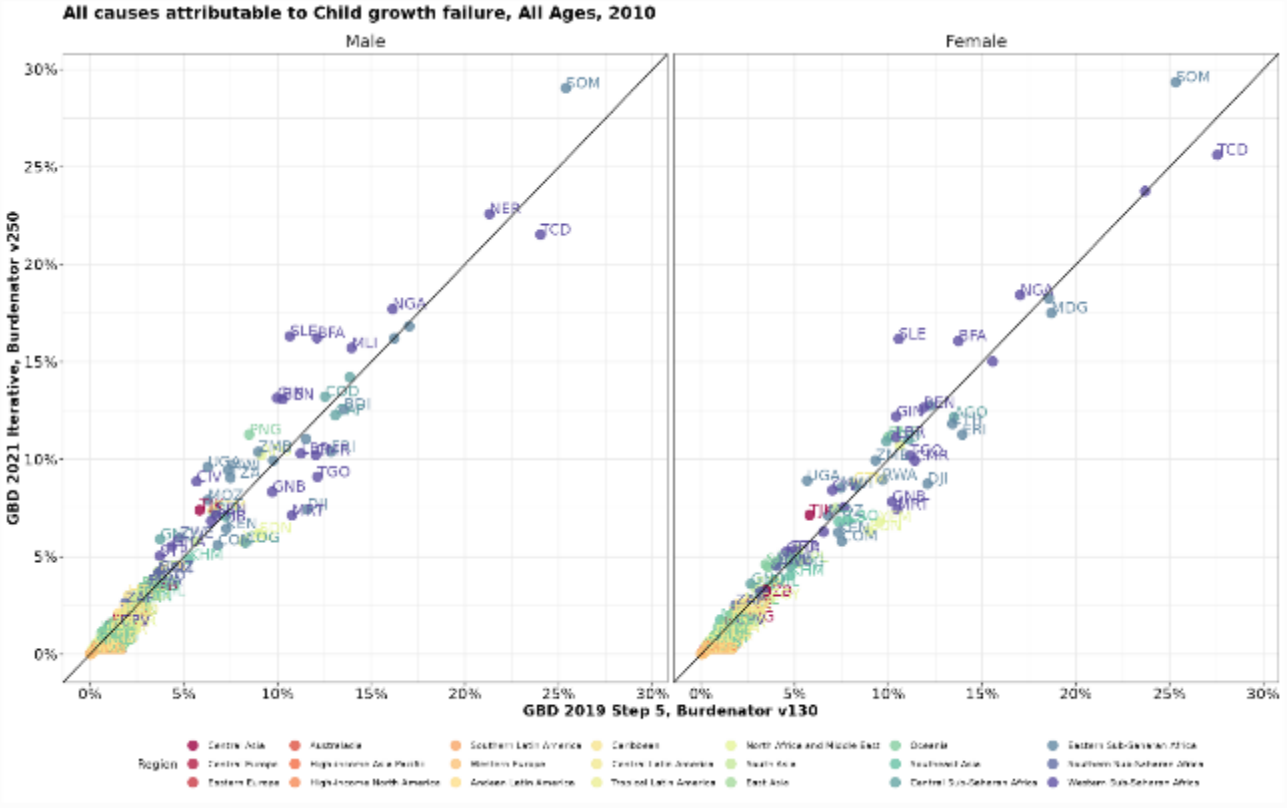
'New' RRs of LRI Mortality for HAZ



Estimating Relative Risk

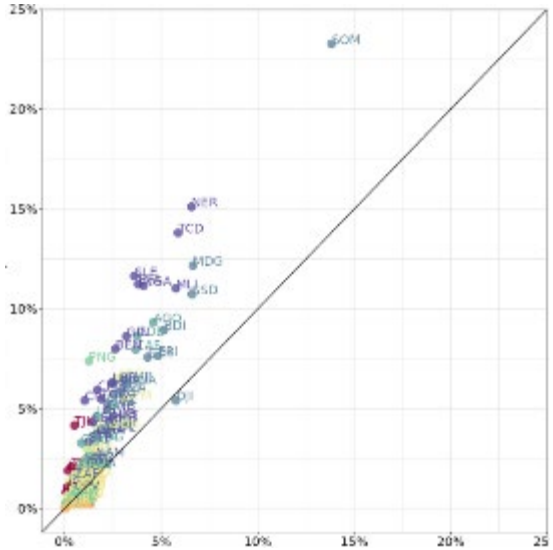


Results: CGF – Total & All Cause: Death

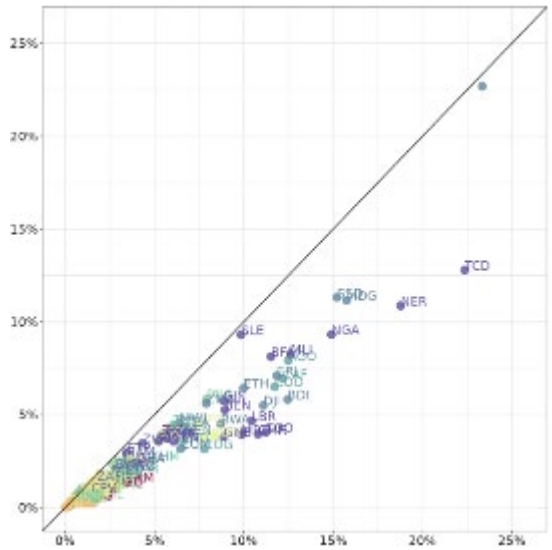


Results: CGF, All Cause, Death

Underweight

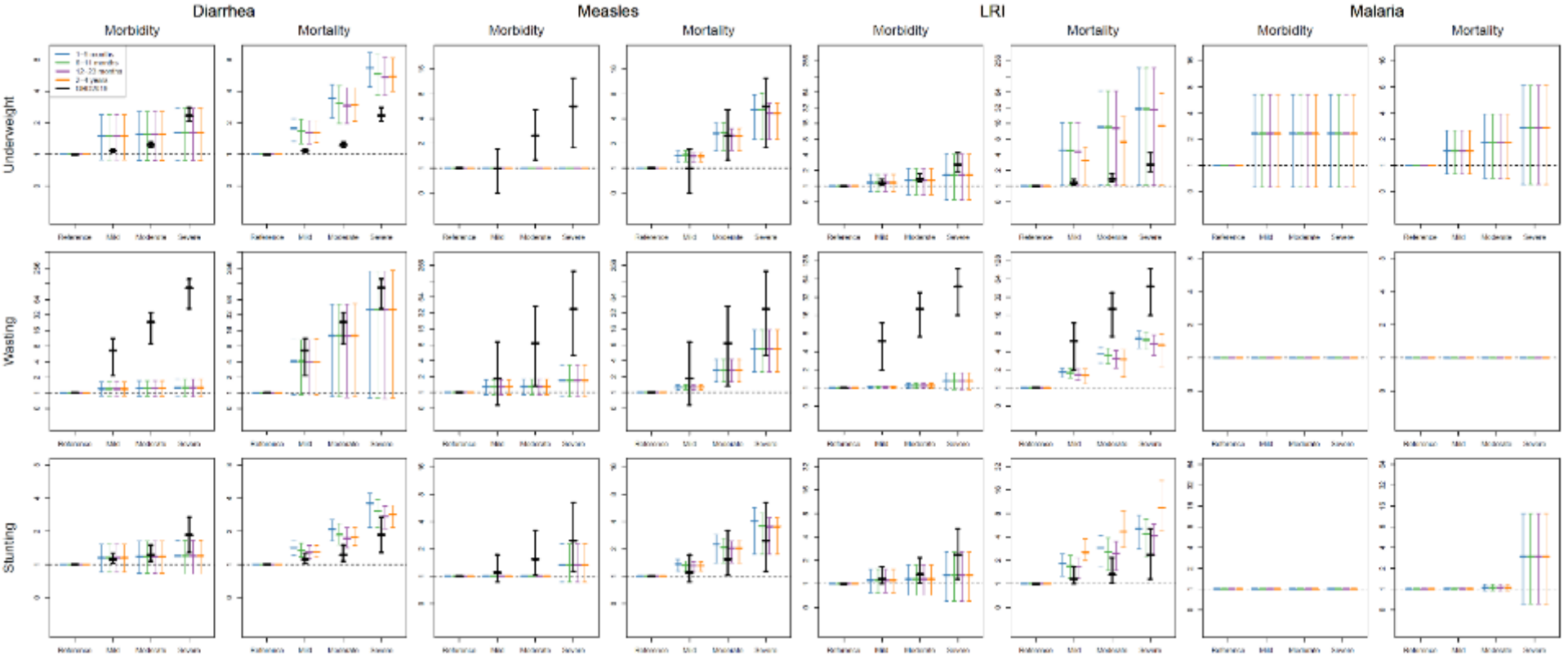


Wasting

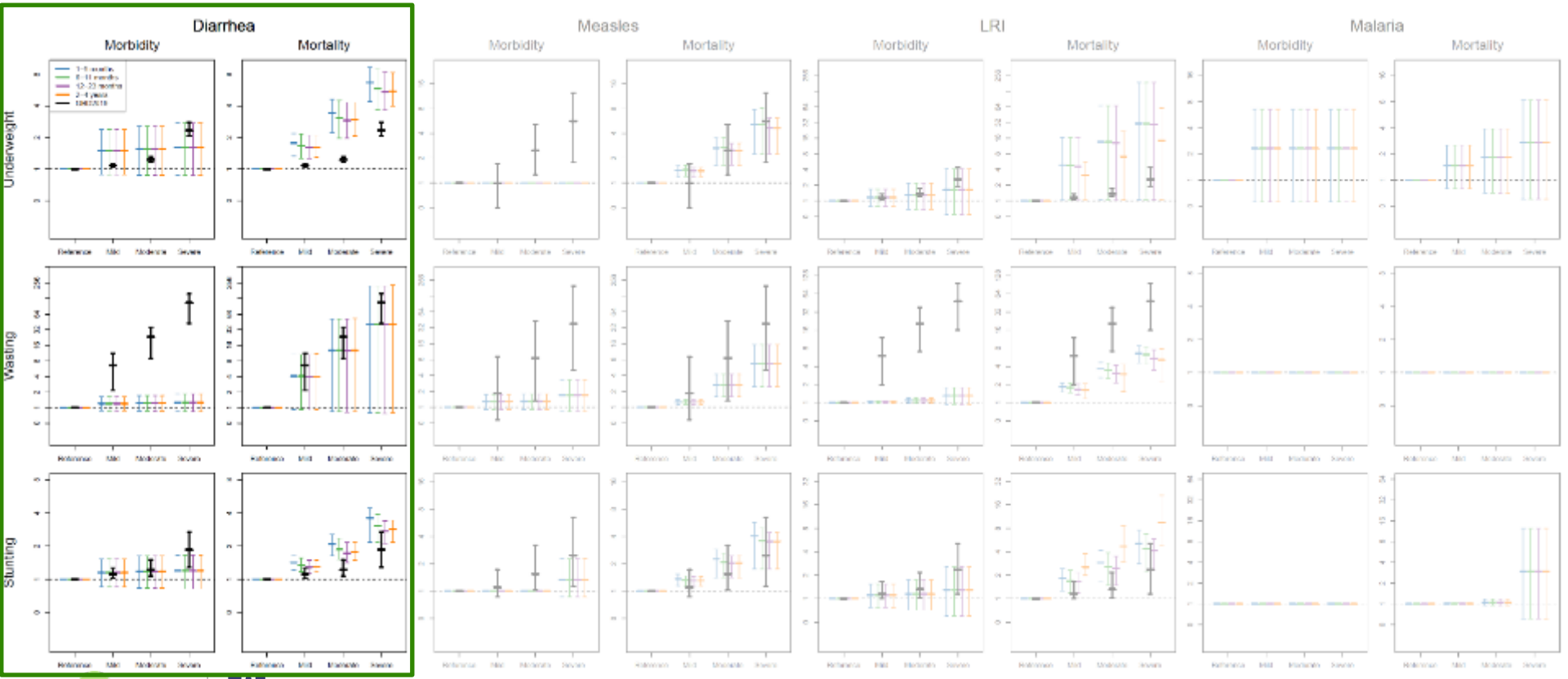


Underweight

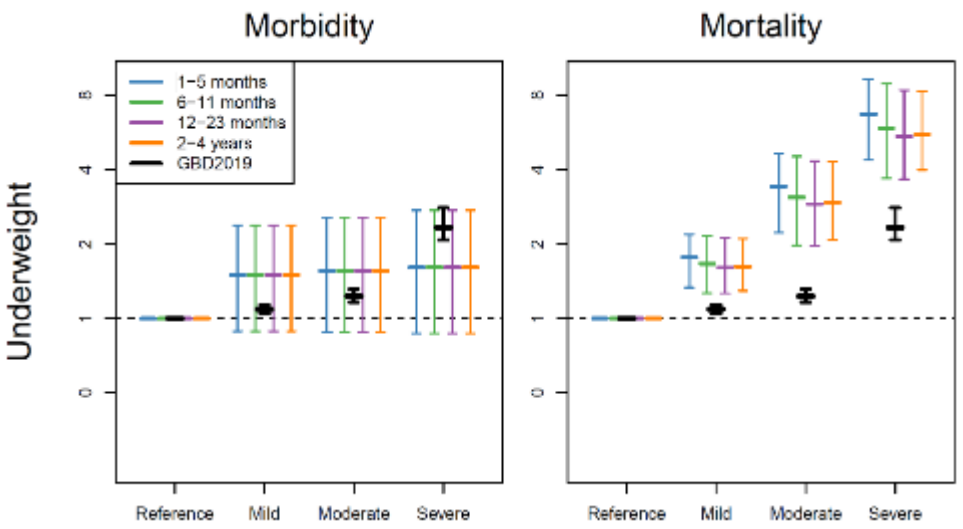
Results: RR Comparisons



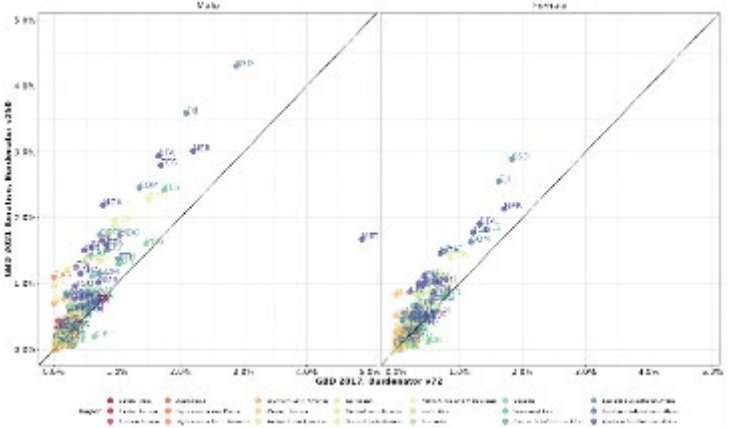
Results: RR Comparisons



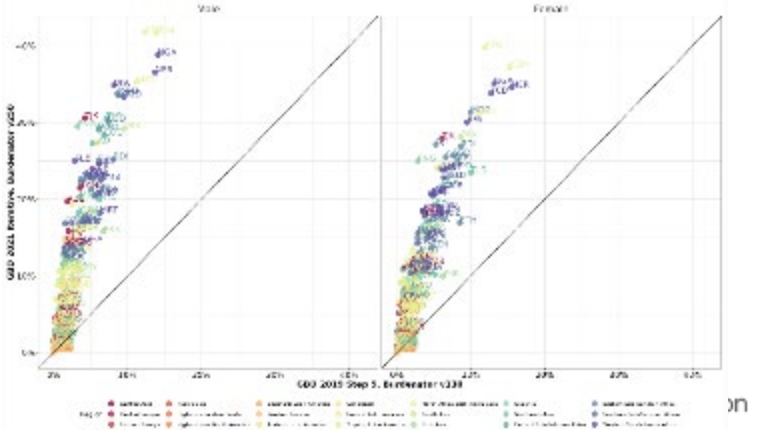
Results: Diarrhea



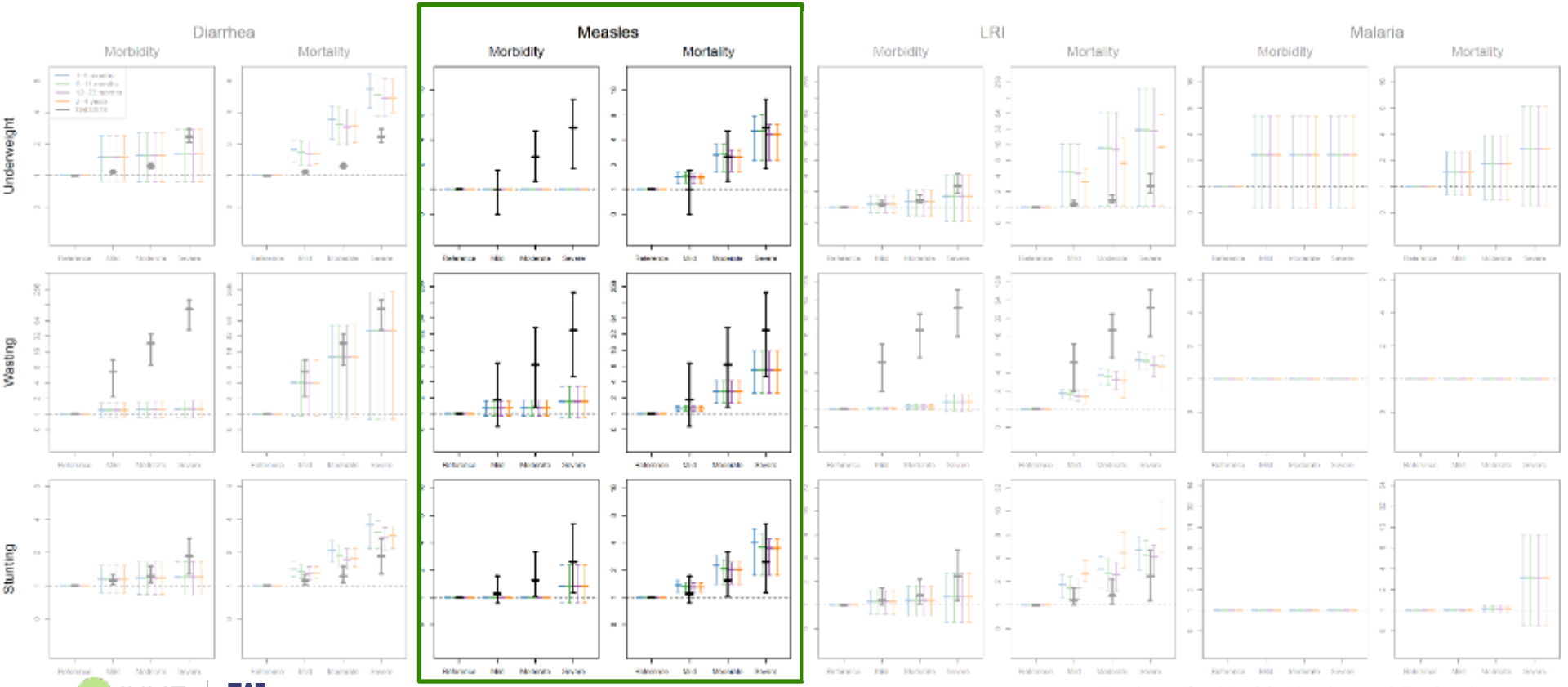
Diarrhea YLDs attributable to underweight



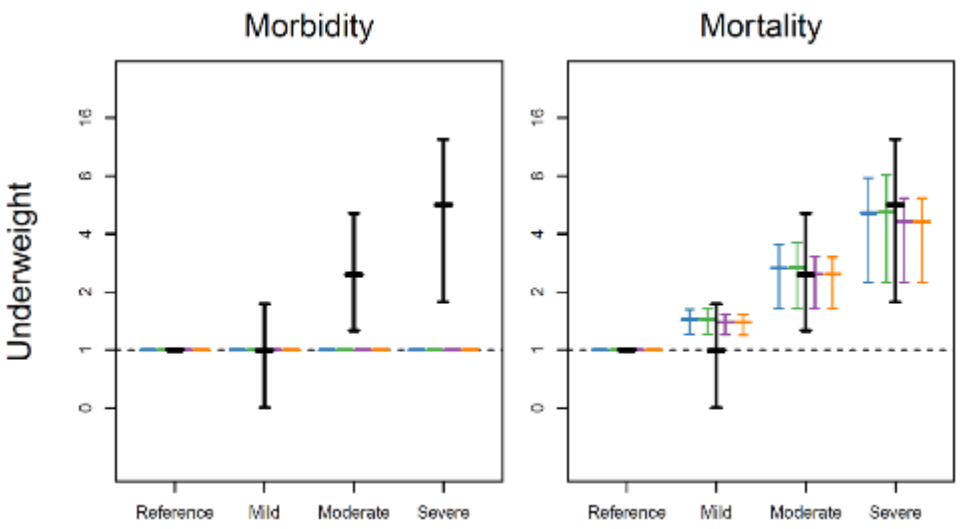
Diarrhea deaths attributable to underweight



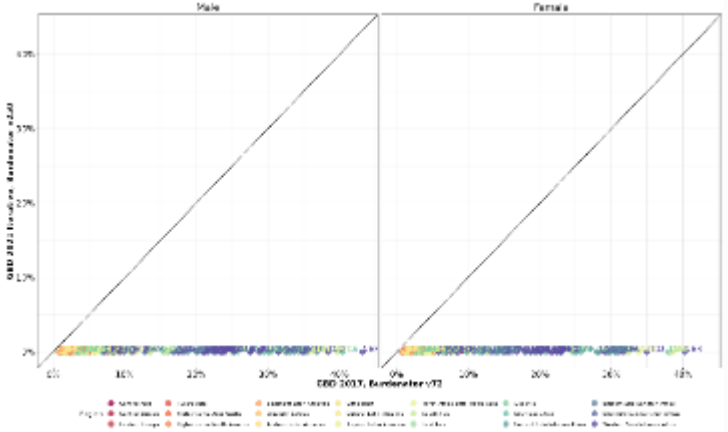
Results: RR Comparisons



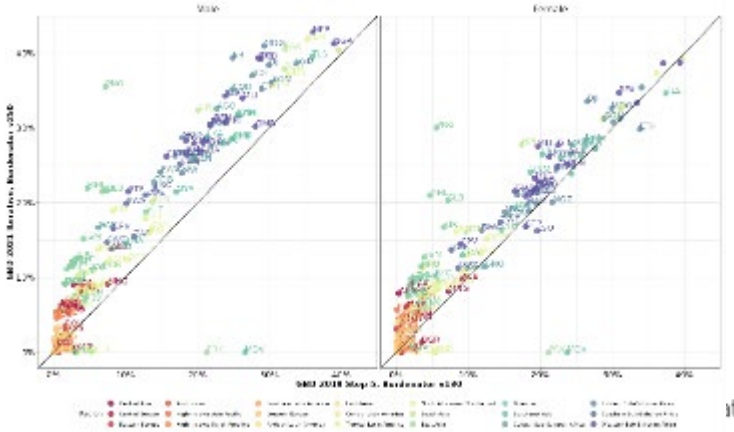
Results: Measles



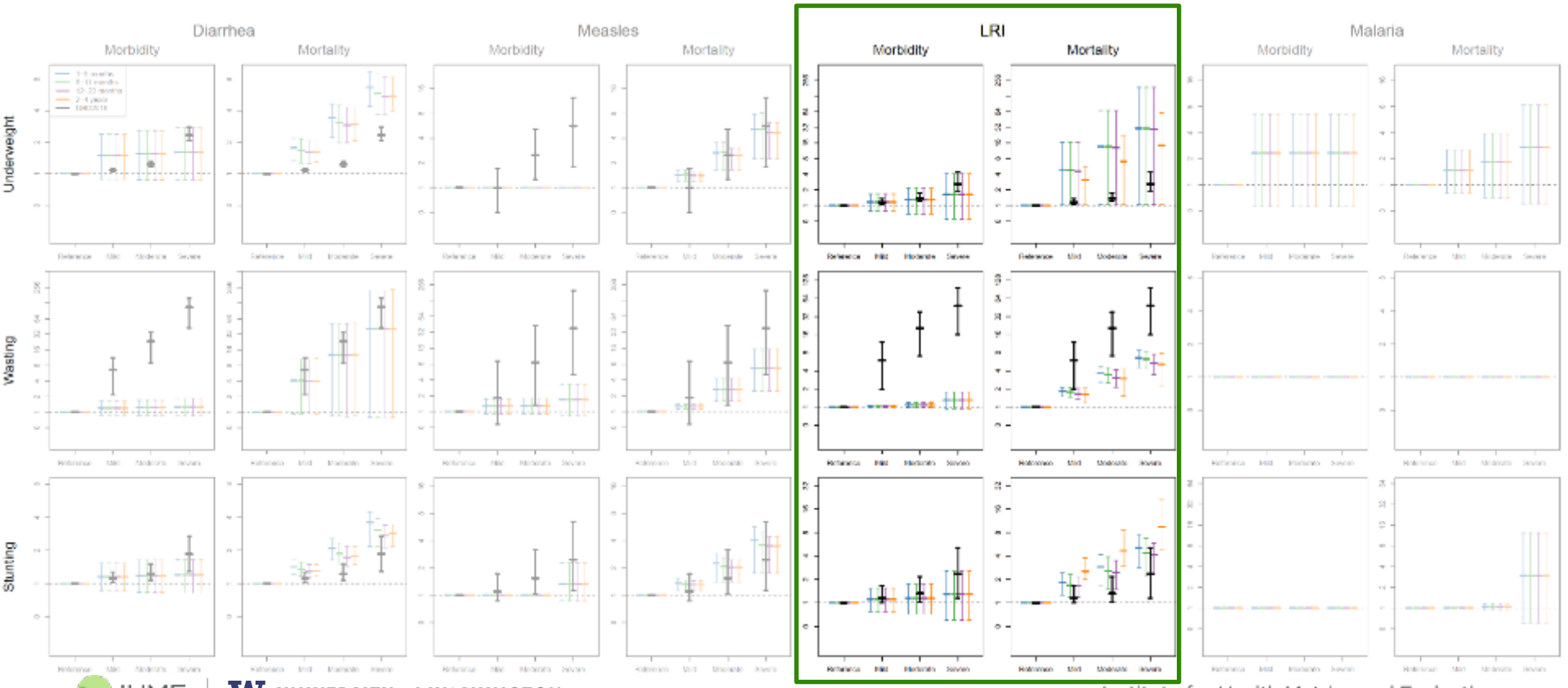
Measles YLDs attributable to underweight



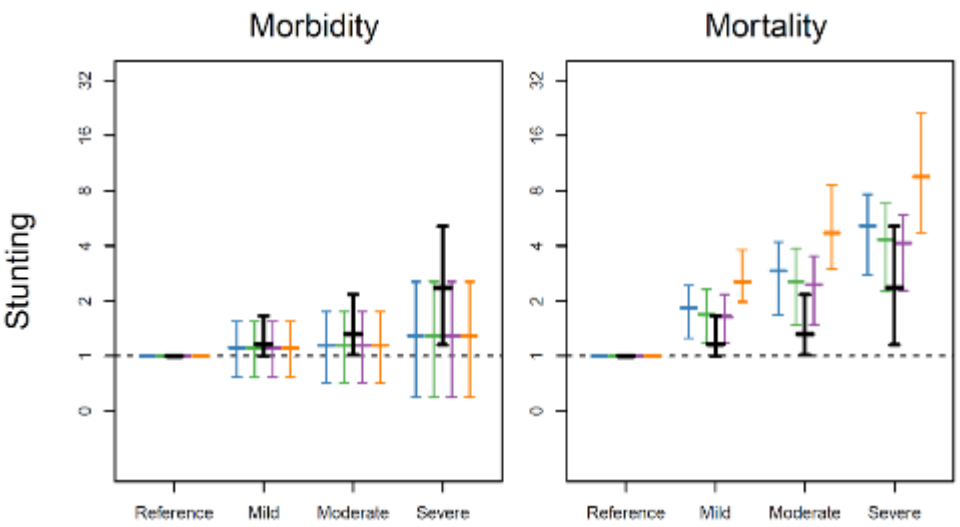
Measles deaths attributable to underweight



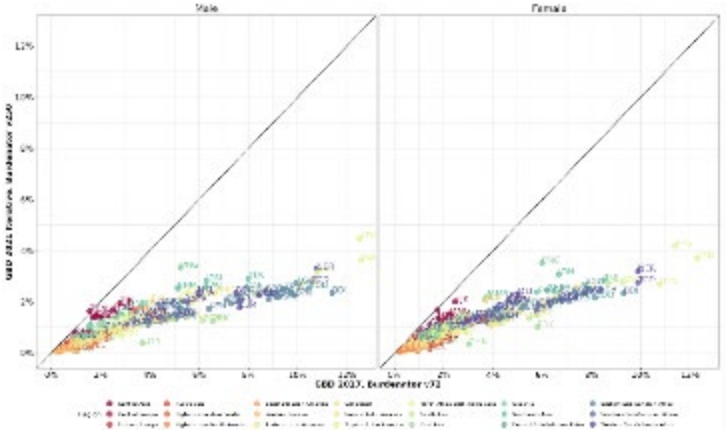
Results: Cause specific RR Comparisons



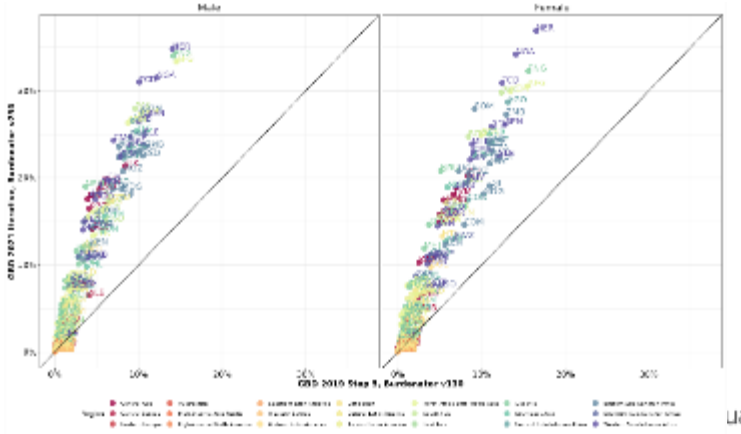
Results: LRI



LRI YLDs attributable to stunting



LRI deaths attributable to stunting



Discussion

- We have found significant differences between disease and death relative risks.

- Based on our estimates, while overall CGF burden remains comparable to previous estimates, the relative attribution of that burden has changed dramatically.

- Though the relative risks are low, there is evidence that CGF influences both malaria disease and death risk.

Future Work

There is no reason that stunting, wasting, and underweight should be modeled separately. Substantial evidence suggests that the underlying risk can be described by two variables not three.

A child's health and the relative risk of infection, disease, and death are determined by more than the child's anthropometric measurements a month in the past. Understanding the immediate relative risk as we have done here is only a (small) piece of the overall story.

We need to more carefully consider how a child's growth trajectory, health status at birth, and the health of the fetus and mother during pregnancy combine to alter the risk of disease events occurring (and the severity of those events).

Estimating these distal factors is critical to understand how to track progress, attribute burden, and design and evaluate optimal interventions to reduce under-5 disease burden.

Questions?