A Model of the Effects of GI Disease and Diet on Child Body Composition in Order to Improve Outcomes in Those Suffering from Malnutrition

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Objectives

(1) To develop a mathematical, physiological model[1] that describes effects of infection and nutritional status on nutrient absorption and metabolizable energy dynamics in individual children.

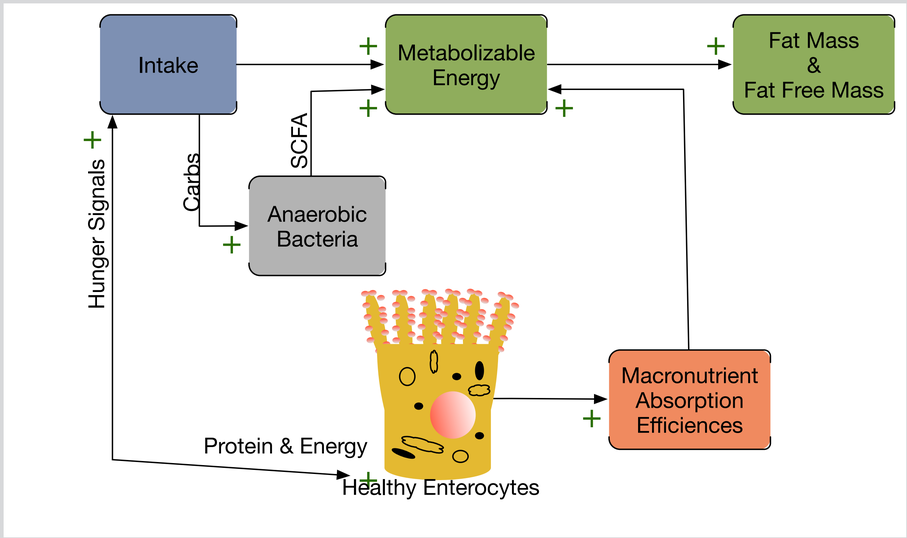
(2) To use the model to help explain how malnourishment coupled with pathogenic insults result in changes in fat mass (FM) and fat free mass (FFM) profiles seen in the literature.

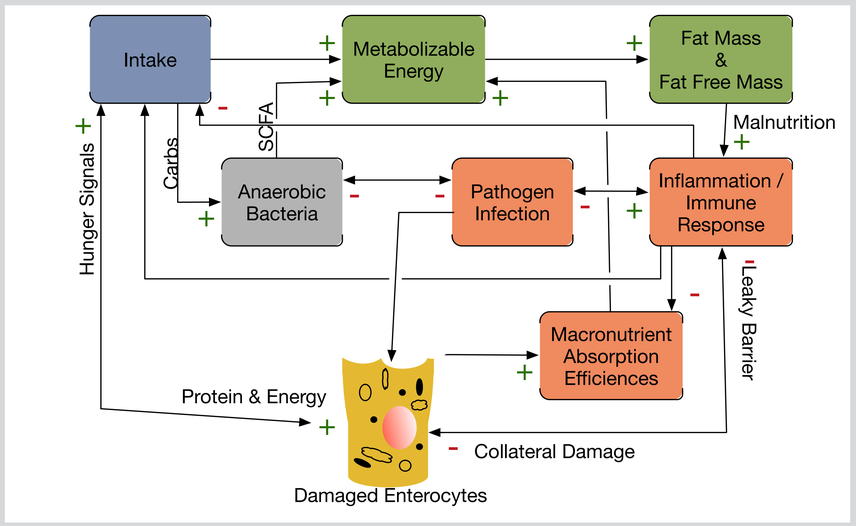
(3) To deploy a Shiny App to explore how child-rearing patterns, weaning, nutritional status and timing of pathogen inoculation impact healthy growth through simulation.

(4) To apply the model to predict effective interventions for growth faltering in children in low- and middle-income countries.

Methods

(1) Physiologic parameters were defined, based on wide array of literature data[2] ⟶





(2) The model was calibrated with different absorption efficiencies in response to nutrient content, phenotypes and pathogenic insults to undernutrition ⟵

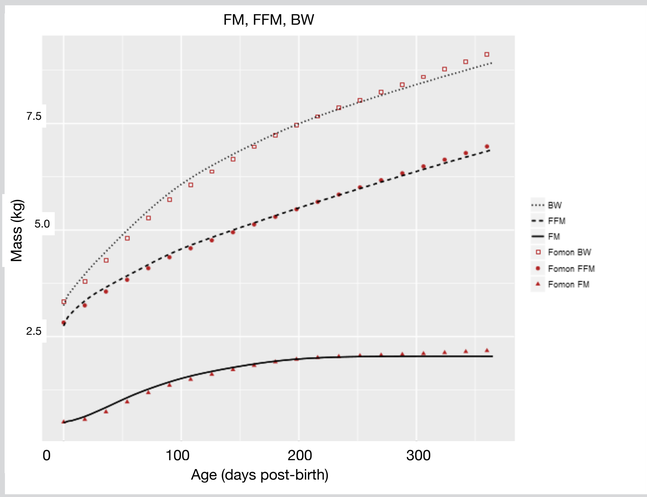
(3) The model was validated with external data, and used to run simulations of a 'recovery phase'

Conclusions

- Model implies that depending on the degree of malnutrition and an individual's phenotype, the growth trajectories can vary in ways that are sometimes non-intuitive. The model was able to produce some unusual phenotypes seen in infants at risk of malnutrition[3] whereby FM is increased despite energy intakes generally smaller than age-appropriate requirements, by imposing repeated cycles of weight loss and gain due to infections.
- The model demonstrates significant impact of pathogen exposure on nutrient absorption. This highlights the importance of hygiene and sanitation in addition to nutritional intervention in children at risk for malnutrition.
- Real-time simulations using the Shiny App allow users to explore the cause of growth stunting in individuals exposed to various pathogens on a background of various child rearing and weaning patterns.

Presented at American Pediatrics 2018; Copies available at: metrumrg.com/publications
Access Shiny App at https://www.metrumrg.com/interactive-apps-decision-making/

Results (Output from Shiny App)



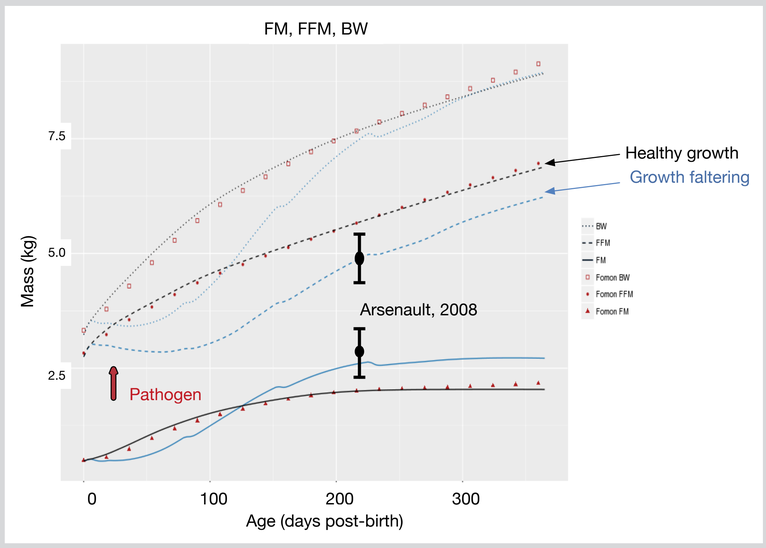
Energy available in the model for growth was derived from intake of macronutrients from the diet. Metabolizable energy is then deposited into FM or FFM.

Biological inputs such as sex, birthweight and duration of exclusive breastfeeding were also used to calibrate model outputs to 'healthy' growth (WHO) standards from birth to 2 years.

Output from the Shiny App (user interface) demonstrates how biological inputs effect growth outcomes in healthy children.

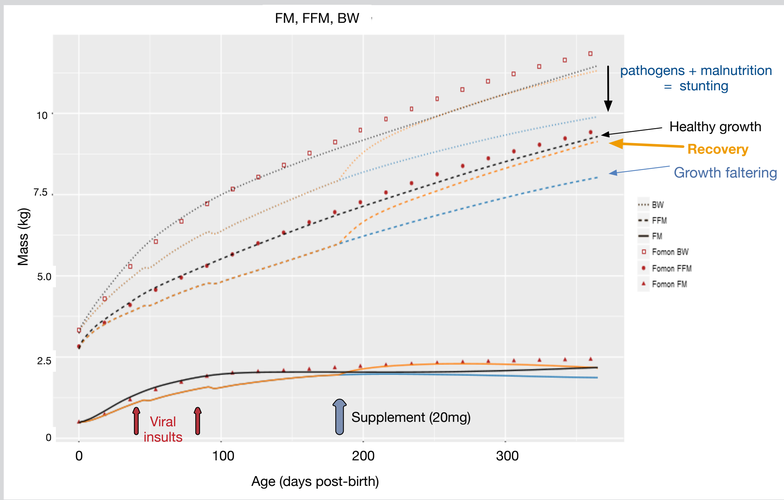
As a **validation step**, moderate malnutrition and cycles of pathogen inoculation were simulated and compared to 'new' data (literature data not used in calibration)[3].

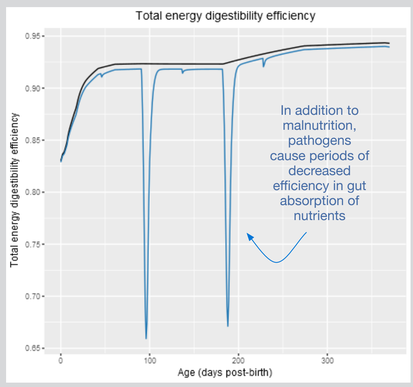
A recovery phase was simulated.



Simulation settings: no excl. bf, nonbm diet : rel. tot. eng intake = 0.91, prot. eng intake =0.91, pathogen = yes, # inf/yr = 5, Inoculation start/end = 6/250,bacteria=1, virus=1-4

Some energy loss can be attributed to malabsorption in the gut (damaged enterocytes) under scenarios of underfeeding or infection. To fit real-world data representing these scenarios, the model was expanded to include macronutrient absorption efficiencies, dynamics of severe bacterial and viral infections and effects of malnutrition on GI/immune function.





Simulation settings: rel bf req. = 0.85, age weaned = 548, non-bm diet = rel. tot. eng intake = 0.85, prot. eng intake =0.91, pathogen = yes, bacteria=1,3,5, virus=2,4

References

1.) Hall KD, Butte NF, Swinburn BA CC. Dynamics of childhood growth and obesity: development and validation of a quantitative mathematical model. Lancet Diabetes Endocrinol 2013;1(2):97105.
2.) Bill & Melinda Gates Foundation Healthy birth, growth and development knowledge integration (HBGDki) project provided access to data and also funded this work.
3.) Arsenault JE, Lpez de Romaa D, Penny ME, Van Loan MD, Brown KH. Additional zinc delivered in a liquid supplement, but not in a fortified porridge, increased fat-free mass accrual among young Peruvian children with mild-to-moderate stunting. J Nutr [Internet] 2008;138(1):108-114. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18156412