



HEALTHY BIRTH, GROWTH & DEVELOPMENT

knowledge integration

USING CDISC TO SUPPORT THE HEALTHY BIRTH, GROWTH, & DEVELOPMENT KNOWLEDGE INTEGRATION

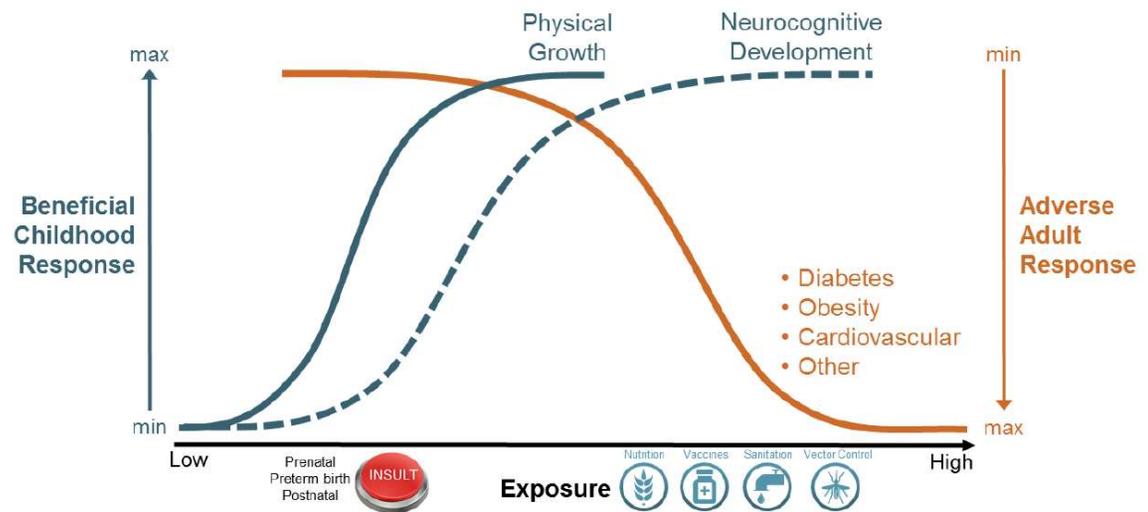
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■ STUNTING IN YOUNG CHILDREN

- Definition of stunting: height < 2 SDs below the median at a given age.
- World Health Organization goal: reduce stunting by 40%, from 165M to < 100M children by 2025.
- Stunting early in life: associated w/ reduced educational & economic achievement later in life.

But overtreatment is risky:

- Rapid catch-up after infancy may increase risk of metabolic & cardiovascular diseases in adulthood.
- We need improved understanding of relation between exposure and response.



OVERARCHING QUESTIONS: PATHWAY TO GOAL

1. Lifecycle:

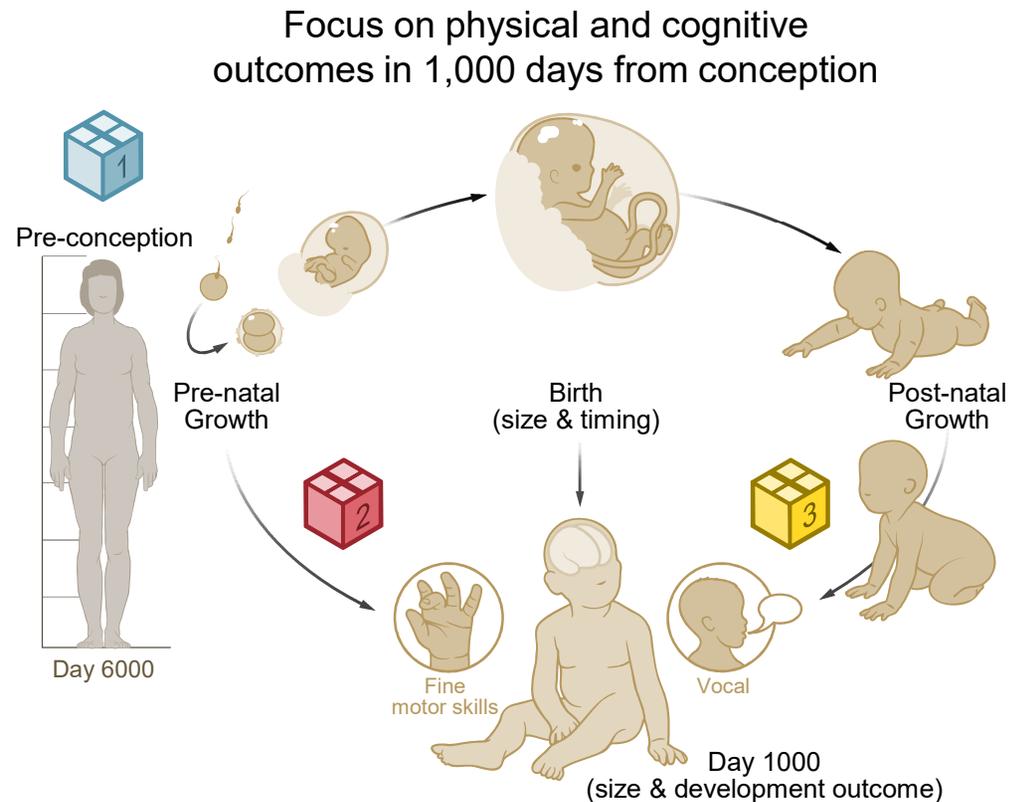
- To what extent is growth faltering explained by pre vs postnatal insults?
- What kind of recovery can we expect in infants born small for gestational age (SGA)?

2. Outcomes:

- Can we quantitatively characterize the relation and interaction between physical growth and neurocognitive development?

3. Pathways:

- Are there disproportionately large contributions on growth faltering from certain pathways, and can we rank-order risk factors?



■ 90% OF THE STUNTING BURDEN LIES IN 39 COUNTRIES

How do we deliver the right intervention(s), to the right child, at the right time, and at the right price?



Current estimates: 40.37% to 32.18% (20% reduction).
Source: The Lancet, Volume 382, Issue 9890, Pages 452 - 477, 3 August 2013

■ HEALTHY BIRTH, GROWTH, & DEVELOPMENT knowledge integration (HBGDki)

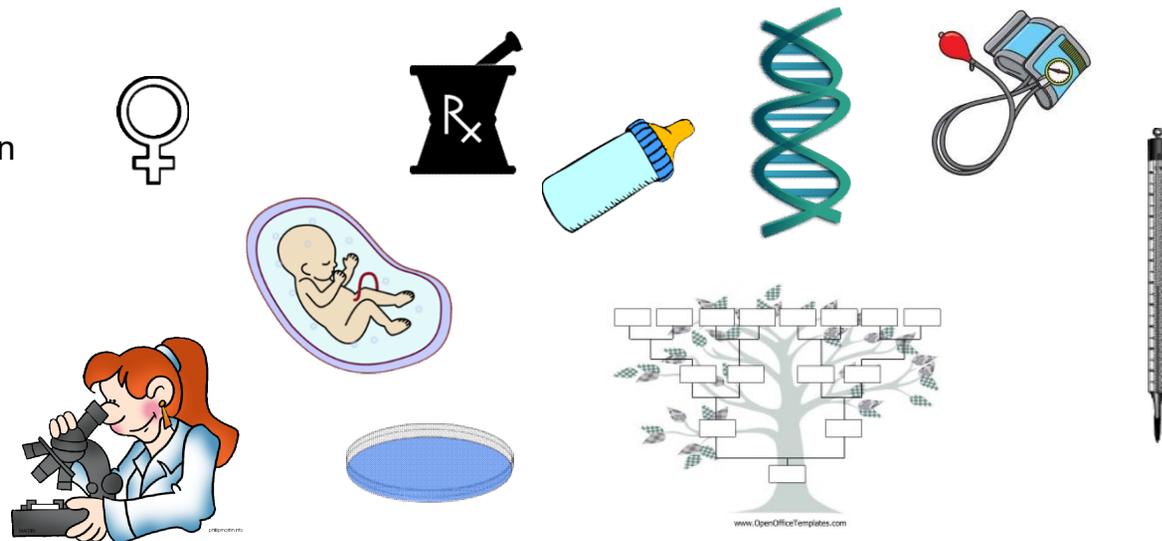
- Launched in 2013 by the Bill & Melinda Gates Foundation.
- Preterm birth, physical growth faltering, and impaired neurocognitive development:
 - Learn from currently available data.
 - Generate novel insights using modern data analytics.
 - Quantify effects of modifiable risk factors.
 - Generate predictive models to develop effective solutions.
- Multidisciplinary group of investigators contributed data from 130 studies (total, 9.8M children), including:
 - Observational studies:
 - Longitudinal growth and neurocognitive outcomes.
 - Longitudinal growth and fetal ultrasonograms.
 - Special populations (intergenerational, migrants, children of immigrants, high-risk pregnancies/births).
 - Interventional studies (nutrition, water, sanitation, hygiene, vaccine).

■ HOW DOES HBGD*ki* USE CDISC?

Healthy Birth, Growth, & Development knowledge integration

- Data curation process: intake; harmonize to common data standard (CDISC); prepare for analysis
- Facilitates combining data across studies, using standard tools, compiling detailed inventory
- Many common CDISC SDTM domains are used:

- Questionnaires
- Subject characteristics
- Clinical events & medication
- Reproductive system
- Associated persons
- Vital signs
- Morphology
- Laboratory findings
- Microbiology findings



■ SPECIAL CASES FOR OBSERVATIONAL STUDIES

Some CDISC definitions do not apply directly to studies without a treatment intervention

Typical CDISC	HBGD <i>ki</i> Usage
AE vs MH dichotomy	Using CE in all cases to avoid implying a pre/post distinction where one does not exist.
RFSTDTC defines the study Baseline	Relative days important, but use DOB as the milestone. e.g., LBDY=1 is day of birth.
VISITNUM, VISIT reflect study design	Many observational studies still have visit schedules.
Study epochs	Used to reflect pregnancy or developmental milestones rather than study design characteristics. <ul style="list-style-type: none"> • Prepregnancy, T1, T2, T3, intrapartum, postpartum. • In utero, delivery, neonatal, infancy, childhood.
Study arm describes randomization	Study arm describes different cohorts that were enrolled (e.g., case-control studies).

■ AD HOC DOMAINS IMPROVISED FOR HBGD*ki*

Interest in developing as CDISC special purpose domains?

Anthropometry & auxology

- Height, weight, BMI, head, waist, arm circumferences, and Z-scores for these
- Body composition estimates: fat mass, fat-free mass
- Bone and limb length measurements

Household variables

- Socioeconomic status, information about possessions, educational status of parents
- Physical quality of home including roof, wall, and floor materials
- Water, sanitation, and hygiene

Nutrition (currently under development as CDISC special-purpose domain)

■ CHALLENGES & LIMITATIONS

Diversity of datasets continues to increase in ways that are not anticipated

- Data domains that are unfamiliar to clinical trial experts
- Need to react to new data quickly (constant backlog of data to be integrated for first year of project).
- Should have anchored non-CDISC domains to an existing ontology

Study design characteristics

- Not currently using CDISC Study Design domains to full potential
- Need better tools to capture this metadata