HEALTHY BIRTH, GROWTH & DEVELOPMENT

knowledge integration

BILL & MELINDA GATES foundation

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

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80/20

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.
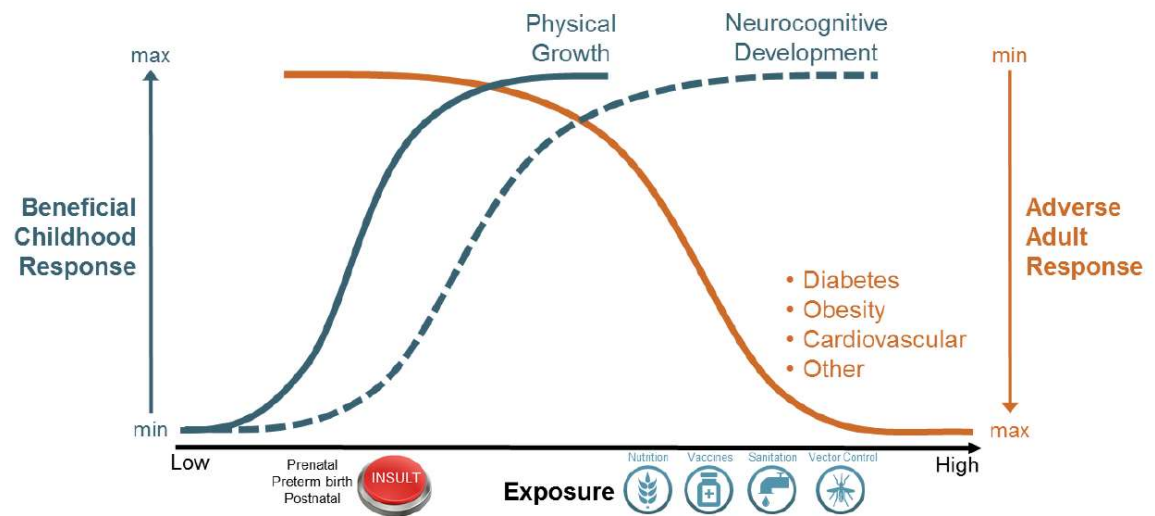
OVERARCHING QUESTIONS: PATHWAY TO GOAL
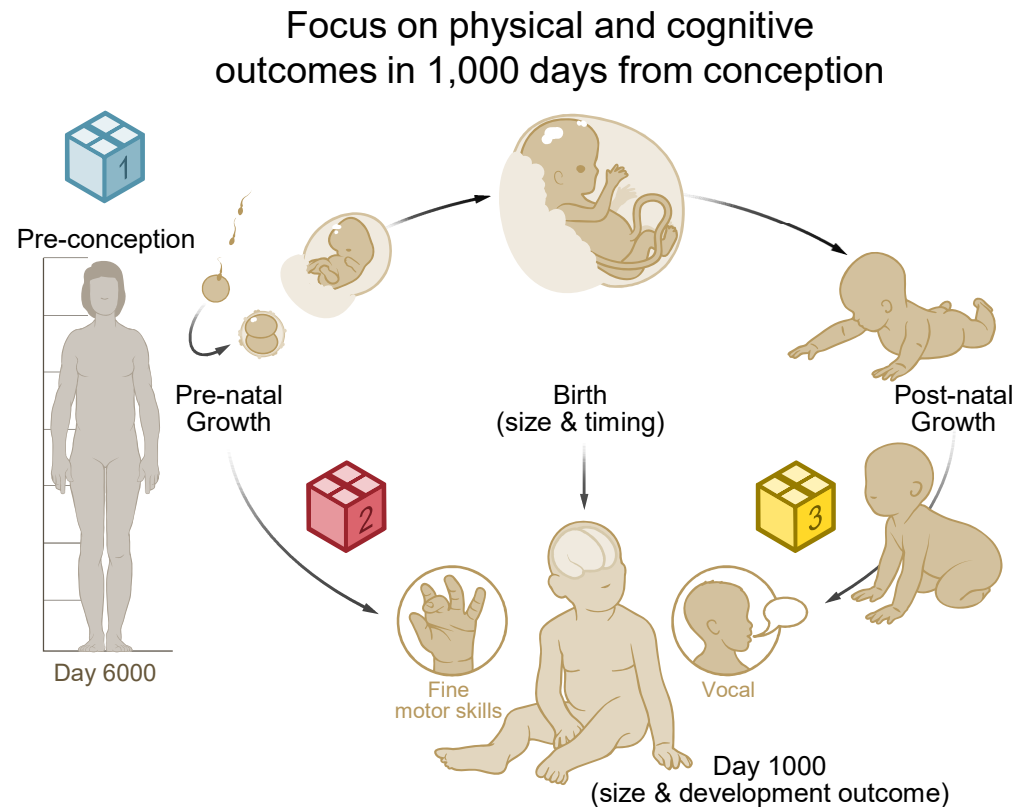
1. Lifecycle:
- To what extent is growth faltering explained by pre vs postnatal insults?
- What kind of recovery can we expect in infants born small for gestational age (SGA)?

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?

Focus on physical and cognitive outcomes in 1,000 days from conception

Pre-conception

Pre-natal Growth

Day 6000

Birth (size & timing)

Post-natal Growth

Fine motor skills

Vocal

Day 1000 (size & development outcome)

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?

Americas:
Guatemala
Peru

Northern Africa:
Chad
Egypt
Sudan
South Sudan

Western Africa:
Burkina Faso
Côte d'Ivoire
Ghana
Mali
Niger
Nigeria

Middle Africa:
Angola
Cameroon
DR Congo

Eastern Africa:
Burundi
Ethiopia
Kenya
Madagascar
Malawi
Mozambique
Rwanda
Uganda
United Republic of Tanzania
Zambia

Southern Africa:
South Africa

Western Asia:
Iraq
Turkey
Yemen

Southern Asia:
Afghanistan
Bangladesh
Cambodia
India
Nepal
Pakistan

South-Eastern Asia:
Indonesia
Myanmar
Philippines
Viet Nam

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

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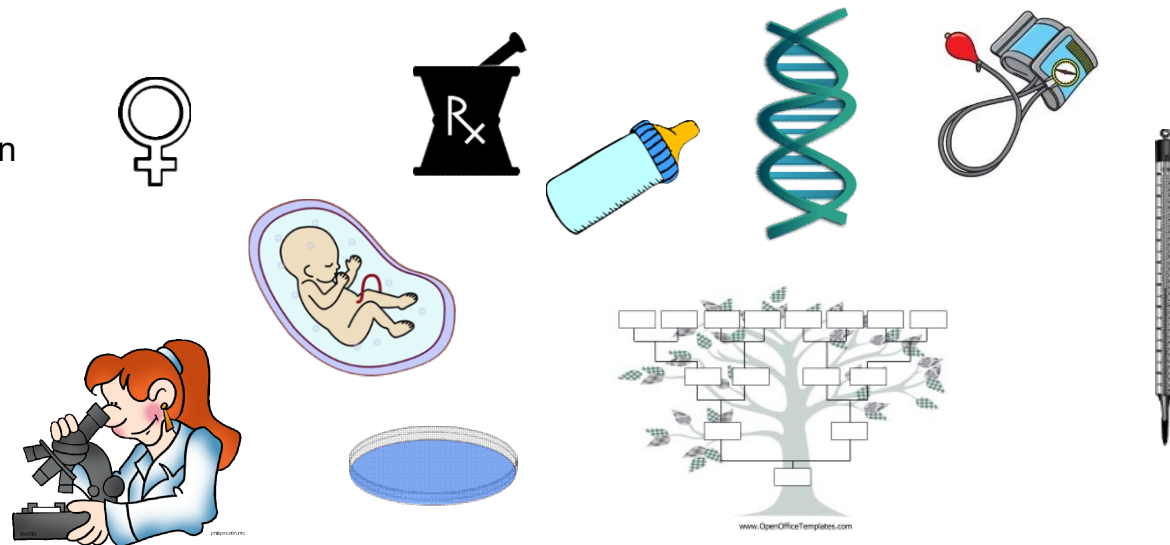
HBGD*ki*

SPECIAL CASES FOR OBSERVATIONAL STUDIES

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

Typical CDISC	HBGD*ki* 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. • 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)

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◼ 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