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 with 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 disproportionally 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?

**Americas:**
- Guatemala
- Peru

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

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

**Western Asia:**
- Iraq
- Turkey
- Yemen

**Southern Asia:**
- Afghanistan
- Bangladesh
- Cambodia
- India
- Nepal
- Pakistan

**Middle Africa:**
- Angola
- Cameroon
- DR Congo

**Southern Africa:**
- South Africa

**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\textit{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

<table>
<thead>
<tr>
<th>Typical CDISC</th>
<th>HBGDKi Usage</th>
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<tbody>
<tr>
<td>AE vs MH dichotomy</td>
<td>Using CE in all cases to avoid implying a pre/post distinction where one does not exist.</td>
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<td>RFSTDTC defines the study Baseline</td>
<td>Relative days important, but use DOB as the milestone. e.g., LBDY=1 is day of birth.</td>
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<tr>
<td>VISITNUM, VISIT reflect study design</td>
<td>Many observational studies still have visit schedules.</td>
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</tbody>
</table>
| 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 HBGDki

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)
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