Metrics of Food Aid Effectiveness: Beyond Z-scores

June 28th, 2018
Food Assistance for Nutrition Evidence Summit
Washington D.C.
Please cite this presentation as:

Nutritional Assessment
Defining Expectations

Integrating Nutrition into
Basic and Clinical Research and Care

Daniel J. Raiten, Ph.D.
Program Director- Nutrition
Context and Conceptual Framework
Complex Health Context:
It’s Not Just About *Too Much* or *Too Little*!

- Under-nutrition
- Nutrition Transition
- Malnutrition (over/under)
- Infectious Diseases
- Microbiome Inflammation
- Non-communicable Disease

(DOHaD)

Birth ————> Death
Nutrition: Working Definition

The sum of all processes involved in the taking in and utilizing food substances by which growth, repair and maintenance of normal functions of the body as a whole or in any of its parts.

Because nutritional status can affect or be affected by any/all of these processes, each must be considered in determining nutritional needs, standards of care, or the roles of diet/nutrition in health and/or disease.
Tools and Approaches for Nutritional Assessment
Objectives of Nutritional Assessment

Determine the best types and amounts of evidence that fully integrate and address the roles of diet and nutrition in all aspects of health promotion, disease prevention and treatment in order to:

1. Support the safe and effective application of existing standards of clinical care, or to establish new standards;

2. Develop and evaluate programs, policies and guidance; and

3. Ensure the validity and reliability of research data and its appropriate translation.
Components of Nutritional Assessment

- Measurement of dietary intake/consumption patterns
- Inferences from anthropometry
- Measurement of biochemical indices / biomarkers of nutrient status
- Consideration of health context and factors that might impact on ingestion, digestion, absorption, metabolism, transport or utilization of nutrients
- Measure of responses to nutritional intervention

Because health context matters and because nutrition involves more than what we consume, it’s difficult to rely on single measures to draw conclusions about functional roles of diet/nutrition. *Think diabetes!*
The ability to answer core questions about the role of nutrition in health or disease is contingent on the tools needed to address:

**Exposure**: what has been consumed, including bioavailability

**Status**: where an individual/population stands relative to accepted cut-offs, e.g., adequate, marginal, deficient;

**Function**: reflecting the role of a nutrient within a relevant biological system; and

**Effect**: impact of a given status or intervention on relevant functional outcome(s).

**Users**: bench/clinical researchers, care providers, program developers and implementers, M&E, policymakers
How Do We Understand Effect?

Effect of interventions and/or status can be measured by assessing:
• Direct Impact on specific nutrient dependent system: e.g. transketolase (vit B₁); EGPT (vit B₆)
• Indirectly via assessment of non-specific changes in function: e.g., changes in growth, immune function, neurodevelopment

What are the roles of:
• Outcomes that reflect some aspect of function or effect, but independently are not sensitive/specific measures of particular nutrient relationships (e.g., neurodevelopment)?

• Measures traditionally used for program development and evaluation, but may not be sensitive/specific to nutrition in other contexts (e.g., growth, anemia, DALYs)?
Definitions and Expectations

**Biomarkers**
- Sensitive and specific measures of nutrient exposure, status and function
- With the exception of exposure (where valid), measure of function must be of use clinically or programmatically

**Bio-indicators**
- Sentinel measures of functional change due to nutritional status, disease or intervention
  - > Lacks sensitivity and specificity as sole measures of nutrition, but have value when used with biomarkers of particular nutrients

**Public Health Indicators**
- Non-specific and non-sensitive with regard to nutrition and health
- Reflection of “system” responses and/or shifts in response to population manipulation
Phase 1: Lessons learned

Need for more complete view of the biology of nutrition via better understanding of:

• Nutrient interactions within biological systems:
  ➢ Fundamental understanding of nutrient biology/physiology
  ➢ Understanding bi-directional relationships: e.g.,

Nutrition ↔ Inflammation

• Ability to detect differences between nutritional need/response and physiology (e.g. iron)

Each will improve discovery, development and implementation (including interpretation) of biomarkers.
Nutrition and Inflammation: Why Does it Matter?

• Inflammation shares a bi-directional relationship with nutrition - each affects the other in ways that we are just beginning to appreciate.

• Inflammation can directly affect nutrient intake, absorption and homeostasis.

• Without accounting for inflammation, interpretation of some of the most common biomarkers of nutrient status is compromised:
  ➢ Both acute and chronic inflammation can directly affect the selection, use and interpretation of biomarkers of nutrient status, function or effect.

Reponses: INSPIRE and BRINDA
Summary and Conclusions

• Food ≠ Nutrition

• Context matters as it has implications for nutritional assessment and interpretation of measures.

• We need to be able to distinguish between dietary need and physiological response

• We need to be clear about expectations in terms of our interpretation of results.

• What are we really measuring and what does it mean?
Body Composition

Susan B. Roberts, PhD
Director, Energy Metabolism Laboratory
Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University
Professor of Nutrition, Tufts University
Professor of Psychiatry & Scientific Staff Member in Pediatrics, Tufts Medical School

The Challenge:

• Lean tissue (protein) vs. fat accretion likely important for recovery and long-term health

• But differences between treatments expected to be small

• Most body comp methods have serious limitations (precision and/or accuracy) that render them invalid in undernourished children
What about gold standard DXA?

- Gold standard imaging to separate fat from lean soft tissue and bone
- Best potential method, but edematous vs. normally-hydrated tissue not distinguished
- Could potentially be converted to portable scanner for e.g. mid upper arm
What about gold standard $^{2}$H$_2$O dilution?

• Give dose deuterated water & measure concentration in urine/blood, calculate dilution to determine total body water

• Lots of measurement error!

• Two assumptions are necessary, both likely invalid for undernourished children:
  - Deuterium ‘space’ assumed to be 3% greater than total body water but can vary with body protein content (2-7%)
  - Hydration of lean tissue assumed to be 73% but likely influenced by diet composition (e.g. 68-78%)

• Example: malnourished infant weighing 5.0 kg on admission, gains 15% weight
  - Diet A gain $\Delta$ lean 525 g if hydration is 73%
    493 g if hydration is 78%
  - Diet B gain $\Delta$ lean 450 g if hydration is 73%
    484 g if hydration is 68%

• Assumptions make it impossible to distinguish 60% vs 70% lean tissue in weight gain
What about field multi-compartment: MUAC + skinfolds?

- Multi-compartment fewer assumptions
- Field equivalent of imaging
- Major limitation is field quality control

Lean tissue = 
MUAC Area - Adipose Area

Summary

• Important measurement but no perfect method

• Multiple-compartment MUAC + skinfolds least susceptible to bias currently, provided there is adequate field QC

• Functional measures, e.g. cognition, strength also important
BIOELECTRICAL IMPEDANCE AND MALNUTRITION

Carlos S. Grijalva-Eternod
June 2018
BIOELECTRICAL IMPEDANCE AND MALNUTRITION
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Reactance ($X_c$, $\bigcirc$)

Impedance ($Z$)

Phase angle ($\theta$)

Resistance ($R$, $\blacklozenge$)

Healthy
BIOELECTRICAL IMPEDANCE AND MALNUTRITION

Reactance ($X_c$, $\Theta$) vs. Resistance ($R$, $\Theta$)

- Healthy
- SAM
  - no oedema
BIOELECTRICAL IMPEDANCE AND MALNUTRITION

- **Reactance** ($X_c$)
- **Resistance** ($R$)
- **Phase angle** ($\phi$)
- **Impedance** ($Z$)

**Healthy**
- SAM no oedema
- SAM with oedema
BIOELECTRICAL IMPEDANCE AND MALNUTRITION

The diagram illustrates the relationship between resistance (R), phase angle (\( \Phi \)), and reactance (Xc) in the context of bioelectrical impedance analysis. The graph shows different categories of biological states:

- **Healthy**
- **SAM with oedema**
- **SAM no oedema**

The axes represent:

- Resistance (R, \( \Omega \))
- Phase angle (\( \Phi \))
- Reactance (Xc, \( \Phi \))

The vector migration graph on the right side of the diagram provides additional insights into the relationship between impedance and malnutrition stages.
BIOELECTRICAL IMPEDANCE AND MALNUTRITION
• Segmental BIVA is more reproducible (comparing two readings)
BIOELECTRICAL IMPEDANCE AND MALNUTRITION

Calm

Agitated

Unrestrained

Restrained
Thank you
Metrics of Food Aid Effectiveness for Nutrition: Beyond Z-scores
Neurocognitive Assessment in Nutrition Research – Why & How

June 28, 2018
Food Assistance for Nutrition Evidence Summit
Washington D.C.
Mark Manary, MD
Malnourished children experience cognitive deficits upon recovery from malnutrition and later in life

**Malawi – 2017**
Cognition upon recovery from severe acute malnutrition

<table>
<thead>
<tr>
<th>Neurocognitive Measure</th>
<th>Z score</th>
<th>% with a delay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross motor</td>
<td>-3.1</td>
<td>80</td>
</tr>
<tr>
<td>Fine motor</td>
<td>-2.9</td>
<td>73</td>
</tr>
<tr>
<td>Language</td>
<td>-1.6</td>
<td>48</td>
</tr>
<tr>
<td>Social</td>
<td>-2.8</td>
<td>69</td>
</tr>
</tbody>
</table>


**Barbados - 2012**
Adults with previous MAM or SAM under 12 months scored lower on cognitive tests 40 years later, regardless of IQ or childhood standard of living.

<table>
<thead>
<tr>
<th>Neurocognitive Measure</th>
<th>Malnutrition effect adjusted for childhood standard of living</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAARS</td>
<td></td>
</tr>
<tr>
<td>Inattentive symptoms</td>
<td>0.10** 0.03</td>
</tr>
<tr>
<td>Hyperactive symptoms</td>
<td>0.06 0.03</td>
</tr>
<tr>
<td>DSM-IV ADHD symptoms</td>
<td>0.10** 0.03</td>
</tr>
<tr>
<td>ADHD index</td>
<td>0.09** 0.03</td>
</tr>
<tr>
<td>CPT</td>
<td></td>
</tr>
<tr>
<td>Commission errors</td>
<td>0.09* 0.04</td>
</tr>
<tr>
<td>Omission errors</td>
<td>0.12** 0.04</td>
</tr>
<tr>
<td>Reaction time</td>
<td>0.03 0.04</td>
</tr>
<tr>
<td>Reaction time SE</td>
<td>0.11* 0.05</td>
</tr>
</tbody>
</table>

Malnourished children experience cognitive deficits later in life

Ethiopia, 2017
(Woldehanna T, Berhman J, Araya M)

Children stunted at age 5 scored lower on every cognitive test than non-stunted children both at age 5 and age 8.

<table>
<thead>
<tr>
<th></th>
<th>All children (N=1883)</th>
<th>Stunted at age 5 (n=587)</th>
<th>Non-stunted at age 5 (n=1296)</th>
<th>Mean Difference(a)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standardized core of PPVT test at age 5 (out of 204)</td>
<td>67.54</td>
<td>63.25</td>
<td>69.44</td>
<td>-6.19 ***</td>
</tr>
<tr>
<td>Standardized core of PPVT test at age 8 (out of 204)</td>
<td>78.51</td>
<td>69.99</td>
<td>82.36</td>
<td>-12.37 ***</td>
</tr>
<tr>
<td>% Standardized core of PPVT test at age 5</td>
<td>33.11</td>
<td>31.00</td>
<td>34.04</td>
<td>-3.04 ***</td>
</tr>
<tr>
<td>% Standardized core of PPVT test at age 8</td>
<td>38.48</td>
<td>34.31</td>
<td>40.37</td>
<td>-6.06 ***</td>
</tr>
<tr>
<td># of correctly answered Q-CDA test at age 5 (out of 15)</td>
<td>8.21</td>
<td>7.74</td>
<td>8.43</td>
<td>-0.69 ***</td>
</tr>
<tr>
<td># of correctly answered Q-CDA test at age 8 (out of 29)</td>
<td>6.34</td>
<td>4.62</td>
<td>7.12</td>
<td>-2.49 ***</td>
</tr>
<tr>
<td>% of math questions correctly answered at age 5</td>
<td>54.76</td>
<td>51.60</td>
<td>56.18</td>
<td>-4.58 ***</td>
</tr>
<tr>
<td>% of math questions correctly answered at age 8</td>
<td>21.87</td>
<td>15.94</td>
<td>24.55</td>
<td>-8.60 ***</td>
</tr>
<tr>
<td>Dummy variable for a child begun formal school at 7</td>
<td>0.77</td>
<td>0.64</td>
<td>0.84</td>
<td>-0.20 ***</td>
</tr>
<tr>
<td>Grade completed at the age 8</td>
<td>0.79</td>
<td>0.59</td>
<td>0.88</td>
<td>-0.30 ***</td>
</tr>
</tbody>
</table>

*** p<0.01
Measuring Cognition

1. IQ
2. Bayley’s Scale of Infant Development (BSID)
3. Griffith’s Developmental Quotient (GDQ)
4. Infant Problem Solving
5. Infant Eye Tracking
6. CANTAB (IED Test)
7. MDAT
Milk protein improves cognition in Ghana: CANTAB

The following tests were used to examine visual memory pattern, recognition memory, comprehension, rule acquisition, and attention set shifting:

- Motor Screening Task (MOT)
- Paired-Associated Learning (PAL)
- Pattern Recognition Memory (PRM)
- Big/Little Circle (BLC)
- Intra/Extradimensional Set Shift (IED)
Children with SAM in Malawi consuming RUTF with optimized fatty acid profiles are currently being tested using Infant Problem Solving in the first year of age, and the MDAT at age 3.

1. Reach for covered toy
2. Uncover toy
3. Reach for toy
4. Successfully retrieve toy
Metrics of Food Aid Effectiveness for Nutrition: Field-friendly neurocognitive tests

June 28, 2018
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Washington D.C.
Jukka Leppänen
Infrared eye tracking

What is eye tracking?
– tracking of eye movements by measuring light reflections from the cornea and pupil
– a method to assess visual, attentional, and neurocognitive function
– non-invasive: data can be collected remotely during a brief period of screen viewing
– applicable across ages

Why eye tracking?
– an accessible indicator of brain function
  • a network of brain areas controls human eye movements and supports vital cognitive functions (e.g., attentional orienting and holding)¹-²
  • Neurodevelopmental problems alter this network and result in measurable changes in eye-movement metrics³-⁵
– automated, objective, and standardized⁶-⁷
– high temporal and spatial resolution

Relevance for malnutrition
– malnutrition compromises the development and function of multiple organ systems, including the brain
– evaluation of treatment protocols should not be confined to anthropometric indicators, but should also include measures of neurocognitive, emotional, and social function⁸
– e.g., deprivation of LC-PUFAs in malnutrition⁹ may affect brain networks (caudate nucleus, superior colliculus, prefrontal areas) that are relevant for sensory function¹⁰-¹² and response control¹³-¹⁴
Saccades
- Latency
- Amplitude (accuracy)
- Duration, velocity

Fixations
- Duration
- Spatial distribution
A case-control study (4:1) comparing children with MAM and well-nourished, age-matched controls (7-11 months)

Measurements at baseline and after 5 weeks of treatment (MAM)
• eye tracking (a mobile, battery-powered lab)
• observational tests of neuropsychological function (visual reception)

Test success rates after piloting:
• 1st test: 90%
• 2nd test 90%
• 1st & 2nd: 87%

Reproducibility (test-retest correlations):
• same day: .74
• 1-wk interval: .77
• 4-wk interval: .65

Sensitivity to age-related changes
• 7 vs. 18 months (p < .001)
References


