Nutrition Epidemiology
Introduction and Background Concepts

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What is Nutritional Epidemiology?

• **Epidemiology** is the study of the determinants and the distribution of disease frequency in human populations

  – **Nutritional factors** may be one set of determinants of a disease and therefore…

• **Nutritional Epidemiology** is the study of the nutritional determinants of disease frequency in human populations

• **However, more broadly, it is also** the study of the distribution and determinants of nutritional status in human populations
Features of Nutritional Epidemiology

**Exposures**
- all people are exposed to varying degrees
- exposure is complex (repeated and variable) and not open to simple (or even direct) quantification
- core exposures are continuous in nature, mostly normal or transformable to normal, and not usually categorical
- effect sizes may be small but important, because of ubiquitous exposure
- latency period may be long or unknown: when doesn’t exposure matter?!
Features of nutritional epidemiology

- different levels of exposure may have different health effects in a population

- hard to separate out the effects of intakes of nutrients, variations in metabolism, effects due to other nutrients, etc.

- Last decade there has been an explosion in characterization of nutrition-related exposures related to health and well-being outcomes
  - Omics: proteomics, metabolomics, metabonomics
  - Food environment
  - The framing of a healthy diet (patterns, adherence, sustainability, level of processing)
Nutrient Intakes, the EAR and Disease

Figure 1. The black box between diet and disease in nutritional epidemiology

- Estimated intake
- True intake
- Absorbed amount
- Altered metabolism
- Risk factor change
- Preclinical disease
Study Design Issues

Evidence-building

- Case-control studies can face issues of temporality because a disease process can affect diet, metabolism and biomarkers making them less desirable/tricky
- Multiple ecological studies can be useful to understand a problem because dietary patterns and other environmental aspects can allow for greater variability in exposure
  - This greater variability can lead to heterogeneity of results across studies making the literature look inconsistent
- Cohort studies have built our knowledge base regarding nutrition and chronic disease, but are less preferred designs for causality
- Randomized controlled designs are preferred but may be impractical, yet they dominate evidence building for policies related to undernutrition and medical care (individual)
**Nutrition** is the **process** by which an organism uses food or anything ingested through digestion, absorption, transport, storage, metabolism and elimination for purpose of maintenance of life, growth, normal functioning of organs and the production of energy.

![Diagram of nutrient intake and utilization]

- Change in body nutrient pool
- Nutrient intake
- Nutrient utilized
Nutriture is the **physiological state** resulting from the balance between supply of nutrition and the expenditure of the organism (i.e., the nutrition process). Nutriture is unmeasurable.
Nutritional status is the expression of one (or more) aspect of the nutiture of an individual in a variable.

That variable is an **Indicator of Nutritional Status**.

Indicators usually:

- measure the stores/pools of nutrients
- measure dietary intake of the nutrient or "exposure" to the nutrient (biomarkers of dietary intake)
- measure one aspect of one physiological process that is dependent upon the nutrient of interest

The differences between and indicator of nutritional status and nutritional status itself is that indicators are affected by other non-nutritional factors, i.e., indicators are not specific to nutritional status.

- Immune status (sub-clinical infection)
- Genetic factors
- other
A. 24-hour recall method

- Interview of intake over previous 24-hr period by trained interviewer

- With multiple replicates you can estimate usual intake of individuals

- Recommended approach to estimating usual intake of populations
# 24-hour recall method

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
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<tbody>
<tr>
<td>• Inexpensive</td>
<td>• Likely to omit foods eaten infrequently</td>
</tr>
<tr>
<td>• Easy to do, quick</td>
<td>• Relies on memory, less recommended for children, elderly</td>
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<tr>
<td>• Low respondent burden</td>
<td>• Requires highly trained interviewers</td>
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<tr>
<td>• High compliance</td>
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<tr>
<td>• No literacy required</td>
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<tr>
<td>• People less likely to modify responses (social desirability)</td>
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<tr>
<td>• Recipes, brands, eating patterns</td>
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## Example of 24-hour recall form

<table>
<thead>
<tr>
<th>Time</th>
<th>Meal/Snack</th>
<th>Food/Drink Item</th>
<th>Quantity/Portion Size</th>
<th>Description/Recipe</th>
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Was this a typical day? _____  How so? ______________________
• 5-Step Multiple-Pass Approach
  – **Quick List** Collect a list of foods and beverages consumed the previous day.
  – **Forgotten Foods** Probe for foods forgotten during the Quick List.
  – **Time & Occasion** Collect time and eating occasion for each food.
  – **Detail Cycle** For each food, collect detailed description, amount, and additions. Review 24-hour day.
  – **Final Probe** Final probe for anything else consumed.

AMPM: Automated Multiple Pass Method
Assessing Usual Dietary Intake

B. Food record

– respondent keeps records of all foods eaten over specified period

– With multiple replicates you can estimate the usual intake of individuals

– Multiple records (or recalls) are considered the gold standard assessment of dietary intakes
Food Records

Advantages
- Can get recipes, brand names, eating patterns
- Doesn’t require methods development

Disadvantages
- Requires literacy
- Requires much cooperation
- Subjects may alter eating to facilitate record keeping
- Accuracy depends on motivation
- People over time shift to combination of record and recall
- Requires scales for weighed records
C. Food frequency questionnaires (FFQ)

- Structured questionnaire of food items
- Respondent is asked to summarize usual consumption of each item over a specified time period
- Number of food items: 60-150
- Qualitative or semi-quantitative if portion size is included
- Requires development for each use
Food frequency questionnaires

Advantages
- Fairly rapid (20-40 minutes)
- Low respondent burden
- Can ask about any period of exposure
- Can easily identify food patterns

Disadvantages
- Relies on respondent’s ability to summarize frequency and portion size
- Not as accurate as repeated sampling
- Has certain “black box” aspect to it
- Requires development and validation for use in each population
- Cognitive issues are paramount
- No recipes, brand names or meal pattern
- More prone to respondent modification (social desirability)
Over the past 12 months…..

117. How many glasses of **ICED tea**, caffeinated or decaffeinated, did you drink?

   O NONE (GO TO QUESTION 118)

   O Less than 1 glass per month
   O 1-3 glasses per month
   O 1 glass per week
   O 2-4 glasses per week
   O 5-6 glasses per week
   O 1 glass per day
   O 2-3 glasses per day
   O 4-5 glasses per day
   O 6 or more glasses per day

117a. How often was the iced tea you drank **decaffeinated or herbal tea**?

   O Almost never or never
   O About ¼ of the time
   O About ½ of the time
   O About ¾ of the time
   O Almost always or always
Food items on FFQ

- Food must be eaten reasonably often by significant number of respondents
- Food must contribute to nutrient intakes
- Variability in intake exists among respondents
What about in other settings?

- Low resource settings
- Infants and young children
  - Breast milk intake
  - Complementary foods
- Older children
Weighed intakes – food record

• Observer in household prospectively collecting information for food record
• Recording of recipes/mixed dishes
• Weighing of food/plate before/after meal
• Following the target individual
• Issues with common bowl settings
• Combine 12-hr weighed intake with 12-hr recall to obtain 24-hr intake
Assessment of breast milk intakes

• Test-weighing method
  – Observer with baby in household and where ever baby goes
  – Weigh baby before and after each feed
  – Baby sleeps with observer in order to weigh baby before night feeds
  – Obtain 12-hour weighed intakes and conduct sub-study on night time feeds and extrapolate to the rest of the study sample
  – This gives you volume or weight of breast milk consumed
  – No information about actual energy or nutrient intakes
• Gold standard for energy intake
Isotopic methods for the assessment of breast milk intakes

- Isotope: doubly-labeled water
- Small dose of water with deuterium and Oxygen-18, given either to infant or to the mother
- Collect urine or saliva at baseline and over 5-15 days in infant or both infant and mother
- Based on rates of disappearance, and correcting for changes in body composition, you can calculate the energy expenditure of infant over time
- Indirect method as it measures infant energy expenditure over time period
- No information on nutrient intakes other than energy
Breast milk nutrient content

• Variation over time (colostrum (first milk over the first few days), immature milk (until 14-21 days), mature milk)
• “Type of baby” matters (preterm/term)
• Within-mother variation is significant
  – within a feed
  – between feeds
  – first breast versus second breast
  – diurnal variation
• For some nutrients, content reflects maternal diet, for others no relation
• Variation between mothers is also high
Assessment of breast milk intakes

• Asking a set of “practice” questions in order to characterize dietary pattern is the principal method used to capture breast milk intakes of infants 0-6 months

• Reported breast-feeding behaviors that support optimal feeding/intakes
  – Put to the breast within one hour of birth
  – No pre-lacteal feeds
  – Breast feeding frequently and on-demand, day and night
  – Feed from both breasts at each feed
  – No additional liquids, not even water

• Exclusive, “full or almost exclusive “(addition of water), partial (other liquids/milks/foods) or token (< 25% energy from breast milk) (Labbok and Krasovec 1990)
Older infants and young children

• Query regarding the inclusion of typical foods in the diet over chosen time period ("practice" questions)
  – short food list adapted to setting (milks, cereals, legumes, fruits, vegetables, meats, other)
  – Time period (yesterday, past week, past 3 days)
  – Focus is on predominance of breastfeeding
  – Dietary diversity
• Ask additional general questions for "quantity"
  – Focus on principal grain/cereal pap or "weaning food"
  – "How many times did you child receive semi-solid or solid food?"
• Demographic and Health Surveys (DHS) are a good example of this method [https://www.icf.com/clients/dhs-program](https://www.icf.com/clients/dhs-program)
Issues in dietary assessment in children and adolescents

• Children, adolescents possess:
  – lower literacy skills
  – limited attention span, concept of time, memory
  – Limited knowledge of food preparation, food, measurement
  – Limited knowledge of portion size
  – Limited ability to assess frequency (of consumption)

• Because of this, most assessment is via 24-hr recall
• Active research involving technology to create interest
• Cognitive techniques to overcome memory issues
• Combine parent/child assessment techniques (5 years+)
• Children 10+ solo interview (maybe)
Anthropometric status/measures and change

• We often want a summary measure of an individual that reflects dietary and non-dietary inputs (morbidity, energy expenditure) to overall health
  – Anthropometric measures provide a useful and non-invasive and relatively burden-free tool for that purpose
  – Applications to all subjects (infants, children, adults, patients)
  – Measures include length/height, weight, circumferences, skinfold thicknesses and derived ratios/indices (waist-to-hip ratio, BMI)
• “Overall nutritional status”
Assessing size and growth in children

- Because children grow, and growth requires adequate nutrition, assessing attained size and/or growth is an indicator of the adequacy of the nutrition process in children
  - **Nutritional Status** is the current status of the child as reflected in weight, length/height or the relation between weight and length/height (related to age and sex)
  - When a child’s status falls outside an accepted range, he/she is **malnourished (wasted, stunted, overweight)**
  - **Growth** is the increase in these indicators of nutritional status over time
    - A child can be **malnourished** yet growing well or well-nourished yet growing poorly
- Compare the nutritional status or growth of children to **reference** or **standard** to interpret the data
“Growth Curves”: rather they are attained size charts or distance charts
Shows relation between distance curves and velocity curves

**FIG 5.** Alternative plots of theoretical serial weights at 1-mo intervals for girls A and B. Left panel, serial status values are plotted against NCHS reference data; right panel, 1-mo increments are plotted against the present reference curves. See text for details.
## Growth References and Standards

<table>
<thead>
<tr>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Represents normal variability in weight, height, and weight in relation to height that results when children grow up living in a nutritionally permissive environment, that is, an environment in which natural genetic variation in growth is allowed to be expressed</td>
</tr>
<tr>
<td>This growth chart shows us the likely distribution of heights and weights and average growth rates of healthy children</td>
</tr>
<tr>
<td>NCHS (2000)</td>
</tr>
<tr>
<td>Former International growth reference (NCHS 1977 or NCHS/WHO)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Standards</th>
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</thead>
<tbody>
<tr>
<td>Represents normal variability in weight, height and weight in relation to height that results when children grow up in a nutritionally permissive environment and within that context are fed “optimally” or according to scientific recommendations for optimal feeding/diet</td>
</tr>
<tr>
<td>This growth chart shows us the likely distribution of heights and weights and average growth rates of how children should grow</td>
</tr>
<tr>
<td>New WHO international standard (2006)</td>
</tr>
</tbody>
</table>

- Available at: [http://www.who.int/childgrowth/en/](http://www.who.int/childgrowth/en/)


- WHO (2007) produced reference for use with school-aged children
Recommendations for US pediatric population

In 2010, US/CDC adopted the WHO standard for assessing growth from birth to 2 years.

For assessing growth from 2-20 years, they recommend to continue with CDC Growth Curves (CDC, 2000).

See link for more information:
Z-score approach to nutritional status assessment

\[
Z \text{-score} = \frac{X_{\text{individual}} - X_{\text{median of reference}}}{SD_{\text{reference}}}
\]

(Reference for age and sex)

\(< -2 \text{ Z height-for-age}: \text{ stunted}\)

\(< -2 \text{ Z weight-for-height}: \text{ wasted}\)

\(< -2 \text{ Z weight-for-age}: \text{ underweight}\)
Figure 6. Z-score and corresponding percentile values of a normal distribution curve
Examples of Z-score calculations using the new Z-score Formula & 2000 Growth Charts

\[
Z = \frac{(X/M)^L - 1}{LS}
\]

- \(Z\) = Z-score
- \(X\) = Measurement (e.g., stature, weight, head circumference, or BMI value)
- \(M\) = Median
- \(L\) = Box-Cox transformation
- \(S\) = Standard Deviation
INTERGROWTH STUDY

• Ultrasound in the first trimester is used to date the pregnancy under the theory that the primary determinant of embryonic “size” is time since conception
• Ultrasound study of fetal growth to develop standards for assessing fetal growth through pregnancy
• Newborn size for gestational age reference
• Reference postnatal growth of preterm infants
Adolescent Assessment

- We assess size relative to chronological age, but maturational age is very relevant, affects interpretation.
- Maturational age refers to developmental age, like gestational age, but here it refers to sexual development or puberty.
- Puberty usually begins between 8-12 years for girls and 10-14 years for boys.
- Duration varies greatly, and initiation and duration are somewhat delayed/prolonged in settings with malnutrition.
- The transition between adolescent and adulthood is blurred.
Perhaps the first chart (1759-1777) showing height velocity in a male
US reference data for height velocity by sex (Kelly et al., 2014)

Figure 1. Reference curves for HV for males aged 5 to 18.5 years (A) and females aged 5 to 17.5 years (B). Shown are curves for the fifth, 10th, 25th, 50th, 75th, 90th, and 95th percentiles. The dots are the corresponding empirical percentiles smoothed with the Lowess method.
Variation in height velocity in US males and females depending on pubertal timing (Kelly et al., 2014)
WHO (2007) reference data for BMI-for-age (for girls)
### Definitions of under- and over-nutrition in children using BMI (CDC)

<table>
<thead>
<tr>
<th>BMI cut-point</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 5th percentile</td>
<td>Underweight</td>
</tr>
<tr>
<td>5th percentile to &lt; 85th percentile</td>
<td>Healthy weight</td>
</tr>
<tr>
<td>85th percentile to &lt; 95th percentile</td>
<td>Overweight</td>
</tr>
<tr>
<td>≥ 95th percentile</td>
<td>Obese</td>
</tr>
</tbody>
</table>

BMI in children is age and gender specific.
Assessment of nutritional status of adults is conceptually more complex than measuring that of children

1. There are racial/ethnic differences in adult stature and body composition that become apparent primarily during adolescence (not well documented)

2. Adults are no longer growing. Therefore, height is not a meaningful indicator of nutritional status yet must be measured in order to interpret weight differences across people and populations

3. There is no overriding measurable physiologic process occurring that can allow indication of function (like growth)

4. There is a greater normal variability in nutritional status across individuals, more willingness to regulate or adapt, perhaps
# Suggested cut-points of body mass index (BMI) for under- and over-nutrition among adults

<table>
<thead>
<tr>
<th>BMI cut-point</th>
<th>Classification</th>
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<tbody>
<tr>
<td><strong>Under-nutrition:</strong></td>
<td></td>
</tr>
<tr>
<td>&lt; 16.0</td>
<td>Severe under-nutrition</td>
</tr>
<tr>
<td>16.0 – 17.0</td>
<td>Moderate under-nutrition</td>
</tr>
<tr>
<td>17.1 – 18.4</td>
<td>Mild under-nutrition</td>
</tr>
<tr>
<td>&gt;= 18.5</td>
<td>Normal</td>
</tr>
<tr>
<td><strong>Over-nutrition:</strong></td>
<td></td>
</tr>
<tr>
<td>&lt; 18.5</td>
<td>Thin or under-weight</td>
</tr>
<tr>
<td>18.5 – 24.9</td>
<td>Average weight</td>
</tr>
<tr>
<td>25.0 – 29.9</td>
<td>Over-weight</td>
</tr>
<tr>
<td>30.0 – 34.9</td>
<td>Obesity Class I</td>
</tr>
<tr>
<td>35.0 – 39.9</td>
<td>Obesity Class II</td>
</tr>
<tr>
<td>&gt;= 40.0</td>
<td>Extreme Obesity</td>
</tr>
</tbody>
</table>

BMI = weight in kgs / height in m²
Multiple indices of relative weight

<table>
<thead>
<tr>
<th>Weight/height</th>
<th>Quetelet Index or BMI</th>
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<tbody>
<tr>
<td>Weight/height&lt;sup&gt;2&lt;/sup&gt; -</td>
<td>Rohrer’s Ponderal Index (newborns and more recently perhaps for adolescents (tri-ponderal mass index or TMI)</td>
</tr>
<tr>
<td>Weight/length&lt;sup&gt;3&lt;/sup&gt; -</td>
<td>Benn Index, where b is the slope of the line of weight (y) on height (x), (sample specific approach to index of weight independent of height)</td>
</tr>
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In adults, regardless of the index chosen, the correlation with more precise measures of fatness in adults is on the order of 0.7-0.8 (see Willet for discussion)