Nutrigenomics and the Future of Nutrition

Setting the Stage: Introduction & Overview

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Disclosures

• Member, NAREEE Advisory Board & Chair, REE Scientific Advisory Council

• Member, Planning Committee for Vitamin D Standardization Program

• Visiting Scientist, NIH Office of Dietary Supplements, 2016-2017

• NIH funding (Vitamin D Metabolism in Pregnancy)
Objectives

• Overview Population-based Dietary Guidance
  – Food-based Dietary Guidelines
  – Dietary Requirements
    • Nutritional Kinetics and Dynamics Relative to Population-based Dietary Requirements

• Nutrigenomics and Transition to Individually-based Dietary Guidance
  – Personalized Nutrition

• Complexities for Transition Ahead
Decision-Making Steps: Health Outcome

1. Hazard (Health Outcome) Identification (Literature Review)

2. Hazard Characterization (Dose-Response Assessment → Ref. Value)

based on nutrient risk assessment models (WHO, 2006)
Synthesizing the Evidence

– Food-based Dietary Guidance
  • European Food Safety Authority (EFSA)

– Nutrient Requirements
  • Dietary Reference Intakes (DRI)
  • EURRECA, SCAN & EFSA
EFSA Scientific Opinion Establishing Food-Based Dietary Guidelines

• Integrate scientific knowledge about nutrients, foods & health in order to identify dietary patterns that facilitate achievement of desirable food and nutrient intakes
• Focus: diet-disease relationships of particular relevance to the specific population
• Use step-wise approach to identify
  • diet-health relationships (review evidence)
  • country specific diet-related health problems
  • nutrients of public health importance
  • foods relevant for food-based dietary guidelines
  • food consumption patterns

**Target Population**
Children and adults (2y+), healthy and at risk for chronic disease

Key Definitions:
*Dietary patterns:* The quantities, proportions, variety, or combination of different foods, drinks, and nutrients (when available) in diets, and the frequency with which they are habitually consumed.

**Intervention/Exposure**
Adherence to a dietary pattern (e.g., a priori patterns (indices/scores), data driven patterns (factor or cluster analysis), reduced rank regression, or patterns derived from other methods (DASH, vegetarian))

**Comparator**
Different levels of adherence to a dietary pattern; Adherence to a different dietary pattern

**Endpoint Health Outcomes**
- Incidence of breast cancer
- Incidence of colorectal cancer
- Incidence of prostate cancer
- Incidence of lung cancer

Potential Confounders:
- Total energy intake
- BMI
- Sex
- Age
- Smoking
- Alcohol intake
- Physical activity
- SES
- Race/ethnicity
- Family history
- Genetics
- ERT
- Cx screening
DRI: Distribution of Requirement Frequency & Risk of Adverse Outcome in Generally Healthy Population

% Healthy Population
At RISK of Adverse Health Outcome

High

Low

50%

97.5%

Ear

RDA

UL

INTAKE
Proposed Chronic Disease DRI: Range of Effect

[Diagram showing intake-response curves and the range of beneficial intakes for decreased and increased intakes.]
Population Approach Reflects Individual Uncertainty
DRI: Distribution of Requirement in Healthy Population

Why This Variability in Requirement or Response?
# Nutritional Kinetics, Dynamics & Requirements

<table>
<thead>
<tr>
<th>Nutrient Intake</th>
<th>Kinetics</th>
<th>Nutrient Concentration @ Site of Action</th>
<th>Dynamics</th>
<th>Nutrient Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absorption</td>
<td></td>
<td>Individual Variation</td>
<td>Actions of nutrient</td>
<td></td>
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<tr>
<td>Digestion</td>
<td></td>
<td>Genetics</td>
<td>D-R at site of action &amp; effect</td>
<td></td>
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<tr>
<td>Bioavailability</td>
<td></td>
<td>Epigenetics</td>
<td>Maximal efficacy</td>
<td></td>
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<tr>
<td>Distribution</td>
<td></td>
<td>Nutrient – Gene Interactions</td>
<td>Temporal response</td>
<td></td>
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<tr>
<td>Volume</td>
<td></td>
<td>Age</td>
<td>Adverse or beneficial effect</td>
<td></td>
</tr>
<tr>
<td>Compartments</td>
<td></td>
<td>Sex</td>
<td>D-R at site of action</td>
<td></td>
</tr>
<tr>
<td>Body composition</td>
<td></td>
<td>Physiological State</td>
<td>Deficiency</td>
<td></td>
</tr>
<tr>
<td>Metabolism</td>
<td></td>
<td>(Growing, Pregnant)</td>
<td>Toxicity</td>
<td></td>
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<tr>
<td>Excretion</td>
<td></td>
<td>Lactating, Stress, Disease, etc.)</td>
<td>Range</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nutrient-Diet Interactions</td>
<td>Temporal response</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Nutrient-Environment Interactions</td>
<td>Inflammatory response</td>
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<tr>
<td></td>
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<td>Drug-nutrient interactions</td>
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</tr>
</tbody>
</table>

- Individual Variation
- Genetics
- Epigenetics
- Nutrient – Gene Interactions
- Age
- Sex
- Physiological State (Growing, Pregnant Lactating, Stress, Disease, etc.)
- Nutrient-Diet Interactions
- Nutrient-Environment Interactions
- Drug-nutrient interactions
- Actions of nutrient
- D-R at site of action & effect
- Maximal efficacy
- Temporal response
- Adverse or beneficial effect
- D-R at site of action
- Deficiency
- Toxicity
- Range
- Temporal response
- Inflammatory response
Nutrigenomics  Personalized Nutrition

Genome of Individual

Nutrients  Diet  Foods  Food Components

Health
Complexities of Nutrigenomics & Chronic Disease Endpoints: CVD

DIET

I. Nutrients
II. Food
III. Food Groups
IV. Dietary patterns
V. Interventions with diets or foods

GENETIC COMPONENT

SNPs
GRSs
NGS

Gene-diet interactions

CVD PHENOTYPES

Intermediate and final cardiovascular disease (CVD) phenotypes:
Multiple gene-diet interactions in determining different CVD

Phenotype 1
Phenotype 2
Phenotype 3
Phenotype 4
Phenotype 5
Phenotype 6
Phenotype 7
Phenotype 8
Phenotype 9
Phenotype 10
Phenotype 11
Phenotype 12

Consumer & Food Behaviors

• Health not only driving force
• TASTE often primary force
• Behavior change neither easy nor understood fully
• Barraged by conflicting information
Integrating Population-based & Personalized Dietary Guidance?

• 43 nutrients
  – Variable amounts in foods
  – Necessary dietary pattern must provide even less abundant
• Other bioactive food components
• Nutrigenomics incomplete
Nutrigenomics & Future of Nutrition: Complexities & Opportunities

• Interrelationship of diet, genomics & health (disease prevention): Session 1
• Application of nutrigenomics to diet tailored to individual: Session 2
• Policy & ethical implications: Session 3
  – Nature & strength of evidence
  – Consumer perspective & behavior
• Opportunities: Session 4