How to use genetic information for nutritional guidance

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## Disclosures

<table>
<thead>
<tr>
<th>AFFILIATION/FINANCIAL INTERESTS (prior 12 months)</th>
<th>CORPORATE ORGANIZATION</th>
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Objectives

After this presentation you will be able to

- explain how to assess the utility of a nutrigenetic variant

- minimize adverse consequences of genetic information

- use at least 5 high-utility nutrigenetic variants in practice
Evaluation of genetic information

Before a genetic test can be generally accepted in clinical practice, data must be collected to demonstrate the benefits and risks that accrue from both positive and negative results.

Final Report of the Task Force on Genetic Testing: 
Promoting Safe and Effective Genetic Testing in the United States
National Institutes of Health-Department of Energy Working Group on Ethical, Legal and Social Implications of Human Genome Research, September 2007
Evaluation of genetic information

- Analytical validity
- Clinical validity
- Clinical utility
- Ethical, legal and social implications

Foundation for Blood Research/CDC, 2004
Clinical utility of genetic information

- Clinical utility takes into account the impact and usefulness of the test results to the individual, the family, and society.
- The benefits and risks to be considered include the psychological, social, and economic consequences of testing as well as the implications for health outcomes.

Secretary’s Advisory Committee on Genetic Testing, 2008
Clinical utility of genetic information

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- The benefits and risks to be considered include the psychological, social, and economic consequences of testing as well as the implications for health outcomes.

Secretary’s Advisory Committee on Genetic Testing, 2008

Clinical utility = “net benefit”
Utility of genetic information

In how many cases is the outcome better with the information than without it?
Utility of genetic information

In how many cases is the outcome better with the information than without it?

Outcome is the balance of benefits and harms
A brief digression about nutrigenetic harms
A brief digression about nutrigenetic harms

Such harms are mostly related to

- Expenditures and opportunity costs
- Misguided use of risky therapies
- Psychological and social burdens
- Insurance and employment risks
How to reduce harms

By eliminating exposure to genetic information
How to reduce harms

By eliminating exposure to genetic information

Patients and clients need nutrition guidance, not DNA sequence data!
Using anonymized information in practice

→ by working with a healthcare professional
  ▪ who provides guidance
  ▪ without disclosing the information

→ with an online meal planning tool that is
  ▪ self-administered
  ▪ fully anonymized (double masking)
Utility of genetic information

In how many cases is the outcome better with the information than without it?
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Outcome is the balance of

benefits and harms
Utility of genetic information

In how many cases is the outcome better with the information than without it?

Outcome is the balance of

benefits and harms

The balance is better with fewer harms
How then can we assess clinical utility?

By estimating the net benefit of genetic information
Case Study: Folate intake and homocysteine

Homocysteine (µmol/L)

Dietary Folate Equivalents (µg/day)

RDA
Case Study: Folate intake and homocysteine

- **MTHFR 677TT**
- **MTHFR 677CC**

- **Homocysteine (µmol/L)**
  - RDA
  - 2xRDA

- **Dietary Folate Equivalents (µg/day)**
Case Study: Folate intake and homocysteine

- **Homocysteine (µmol/L)**
  - MTHFR 677TT
  - MTHFR 677CC

- **Dietary Folate Equivalents (µg/day)**
  - RDA
  - 2xRDA

- **∆ Hcys**
  - 3.04 µmol/L: -15 %
  - 0.64 µmol/L: -3 %

- **∆ MI risk stroke risk**
  - -24 %
  - -5%
Case Study: Folate intake and homocysteine

Dietary Folate Equivalents (µg/day)

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<th>Homocysteine (µmol/L)</th>
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<th>2xRDA</th>
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<td>MTHFR 677TT</td>
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<tr>
<td>MTHFR 677CC</td>
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</table>

Δ Hcys  Δ MI risk  stroke risk
3.04 µmol/L  -15 %  -24 %
0.64 µmol/L  -3 %   -5 %

Prevention potential:
Screen 10,000 middle-aged men, adapt recommendation for 1000, to prevent about 1-2 events per year. Additional benefits are likely.
Case Study: Folate intake and homocysteine

What you want to do in practice:
Guide individuals with two MTHFR 677 T alleles (rs1801133 TT) to get at least 600 µg dietary folate equivalents.
Case Study: Folic acid and breast cancer

- **DHFR 19del+/+**: 52% increase in breast cancer risk
- **DHFR 19del-/-**: 5% decrease in breast cancer risk

**Prevention potential:**
Screen 1000 women, adapt recommendation for 200, prevent breast cancer in 6-7.

Based on data from Xu et al. AJCN 2007;85:1098-1102
Case Study: Folic acid and breast cancer

What you want to do in practice:
Guide women with a DHFR 19 bp del allele to get generous amounts of folate from plant sources and avoid supplements and fortified foods with folic acid.
Case Study: Calcium and bone health

Absorbed calcium, mg (estimated)

Calcium intake (mg/day)

RDA
1.5 * RDA
∆ absorbed calcium

Data from Dawson-Hughes et al. J Clin Endocrinol Metab 1995;80:3657-3661

Prevention potential: Too small for meaningful estimate.
Case Study: Calcium and bone health

Data from Krall et al. J Bone Min Res 1995;10:978-984

Prevention potential:
Outcome different only when well below current intake recommendation.
Case Study: Calcium and bone health

What you want to do in practice:
Do not use the VDR B allele (rs1544410 A) to suggest higher vitamin D intake to carriers.
Case Study: Calcium and colorectal cancer

Based on data from Dai et al. AJCN 2007;86:743-751
Case Study: Calcium and colorectal cancer

Based on data from Dai et al. AJCN 2007;86:743-751
Case Study: Calcium and colorectal cancer

Based on data from Dai et al. AJCN 2007;86:743-751

Potentially a 82% decrease in CR cancer risk
Case Study: Minerals and colorectal cancer

*What you want to do in practice:*
Guide carriers of a TRPM7 A allele (rs8042919 A) to keep their Ca/Mg ratio below 2.5
Case Study: Coffee and myocardial infarction

Data from Cordelis et al. JAMA 2006;295:1135-1141

Prevention potential:
Screen 2200 middle-aged men, adapt recommendation for 1000, to prevent 2-4 MI per year. Additional benefits are possible.
Case Study: Coffee and myocardial infarction

*What you want to do in practice:*
Guide men with a CYP1A2*1F allele (rs762551 C) to caffeine intakes of less than 200 mg/day
Case Study: PUFA and cardiovascular health

Prevention potential:
Equal benefits at RDA level intake?
Higher than average risk for variant carriers who don’t eat fish.

100 g (3.5 oz) salmon/week provides about 40-50 mg/1000 kcal

Data from Dwyer et al.
Case Study: PUFA and cardiovascular health

Reducing daily meat intake by 4 oz or eating one egg less typically reduces AA intake by about 20-30 mg/1000 kcal.

Prevention potential:
The effect on artery thickness of decreasing AA intake from high to average may be comparable to that of smoking cessation or curing diabetes.

Data from Dwyer et al.
Case Study: PUFA and cardiovascular health

What you want to do in practice:
Guide carriers of an ALOX5 indel variant to limit arachidonic acid intake (meat/eggs) to less than 65 mg/day (4 oz meat or one large egg contain 20-30 mg arachidonic acid)
Case Study: Saturated fat and obesity

Prevention potential:
Screen 1,000 people, adapt recommendation for 150, prevent 12-14 pounds weight gain in more than half of them.

Case Study: Saturated fat and obesity

What you want to do in practice:
Guide carriers of two APOA2 alleles C (rs5082 CC) to limit their saturated fat intake to less than 12 g/day
Case Study: Choline and organ dysfunction

Response to choline intake

% of men developing signs of organ dysfunction

Daily choline intake (mg/kg)

Data from Kohlmeier et al. PNAS 2005;102:16025-16030
Case Study: Choline and organ dysfunction

*What you want to do in practice:*
Guide men with an MTHFD1 A allele (rs2236225 A) to get about 800 mg choline per day
### Some genes for tailoring nutrition guidance

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Final comments

Intervention effects in genetic subgroups are easily obscured by the lack of significant response of the majority.

Many dietary interventions are only effective, if they are targeted to genetically susceptible individuals.

The likely effect size of some genotype-specific interventions is as large as that of medical treatments.
9th Annual Congress of the
International Society for Nutrigenetics and Nutrigenomics
Chapel Hill, May 17-19, 2015

Register soon, space is limited!  http://isnn2015.org