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Scientific Evidence for Personalized Nutrition: Ethical Implications of Methodological Limitations

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A Critical Appraisal of the Scientific Basis of Commercial Genomic Profiles Used To Assess Health Risks and Personalize Diet and Lifestyle Interventions

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Erasmus University Medical Center Rotterdam, Rotterdam, the Netherlands
Centers for Disease Control and Prevention, Atlanta GA, USA

EGAPP, February 2008, Atlanta GA

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Premature applications of genomic profiling

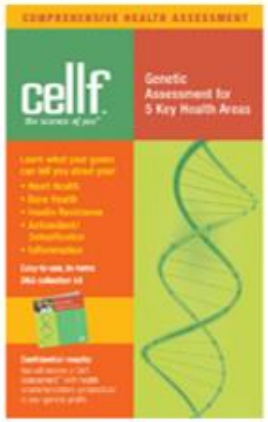
Sciona™ Optimal health through genetics™

GENOVATIONS™
Predictive Genomics for Personalized Medicine

genotrimsalugen™
DNA Customized Nutrition

SURACELL

genele



CELLF COMPREHENSIVE

A combined analysis of nineteen genes that may play an important role in how your body manages bone health, heart health, antioxidant and detoxification function, insulin sensitivity and inflammation. Perfect for those who want a complete snapshot of their overall health profile and recommendations for achieving optimal health without a specific disease focus.

Price: **$252.00**

Profiles

Disease-specific

- Heart health or cardiogenomic profile
- Bone health or osteogenomic profile
- Inflammation health
- Estrogenomic
- Immunogenomic

General

- Enhanced Basic Screening Panel
- Genoscore
- Nutritional Genetic Profile
- Personal DNA Analyses Starter Kit
- …

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ARTICLE

A Critical Appraisal of the Scientific Basis of Commercial Genomic Profiles Used to Assess Health Risks and Personalize Health Interventions

A. Cecile J.W. Janssens,[1,*] Marta Gwinn,[2] Linda A. Bradley,[2] Ben A. Oostra,[3] Cornelia M. van Duijn,[4] and Muin J. Khoury[2]

The American Journal of Human Genetics *82*, 593–599, March 2008 593

METHODS: Reviewing meta-analyses of genetic associations for the genetic variants included in the profiles

→ genetic associations to ANY disease

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Main findings

Companies tested 69 polymorphisms in 56 genes. We found:

- 24/56 genes: no meta-analyses
- 7/56 genes: no statistically significant association to ANY disease
- 25/56 genes were associated with 28 different diseases
- Minor effects, most ORs 0.75-1.5; few rare exceptions
- Cardiogenomic profiles: genes were more frequently associated with non-cardiovascular diseases than with vascular diseases
- Osteogenomic profiles: 2 of 5 genes were associated with disease. Yet, NOT with bone diseases, but with Alzheimer disease, asthma, non-Hodgkin's lymphoma, obesity, psoriasis, SLE

Janssens et al. *Am J Hum Genet 2008*

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VIEWPOINT

Uninformed consent in nutrigenomic research

A Cecile JW Janssens*[,1,2], Eline M Bunnik[3], Wylie Burke[4] and Maartje HN Schermer[3]

European Journal of Human Genetics (2017), 1–2

Informing also includes impact of tested genes on other diseases

Commentary reports about two studies

- Testing APOE gene to tailor recommendations saturated fat intake
- Forgot to disclose increased risk of Alzheimer's disease

Related ethical issues around informed consent, privacy, and data sharing

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OMICS A Journal of Integrative Biology
Volume 19, Number 9, 2015

DOI: 10.1089/omi.2015.0109

Original Articles

Meta-Analysis of Genes in Commercially Available Nutrigenomic Tests Denotes Lack of Association with Dietary Intake and Nutrient-Related Pathologies

Cristiana Pavlidis,[1] Zoi Lanara,[1,2] Angeliki Balasopoulou,[1] Jean-Christophe Nebel,[3] Theodora Katsila,[1] and George P. Patrinos[1]

Methods

A thorough search was conducted in the PubMed literature database for genotype–phenotype correlation studies on 38 genes using the following terms: ''nutrigenomics,'' ''gene name,'' and ''disease name'' (Table 1). The 38 genes of interest were chosen following research on commercially available nutrigenomics tests and their specifics. Our meta-analysis included 1170 entries published from 1995 to 2012.

Table 1. Search Criteria for Gene and Disease/Pathological Condition Association

Genes	*Disease/Pathological condition: investigation of possible association*
APOA1, APOA5, APOB, APOC3, APOE	Cardiovascular disease, Coronary heart disease, Coronary artery disease, Hypercholesterolemia
CETP	Cardiovascular disease, Coronary heart disease, Coronary artery disease, Hypercholesterolemia, Diabetes
GJA4 (CX37)	Atherosclerosis, Hypertension, Stroke, Coronary artery disease
HMGCR	Hepatic disease, Non- alcoholic fatty liver
LIPC	Hepatic disease, Hypercholesterolemia, Fatty acid metabolism
LPL	Dyslipidemia, CVD, Metabolic syndrome
PON1	Atherosclerosis, Diabetes, Metabolic syndrome
CAT	Diabetes, Hepatic diseases, Kidney diseases
GPX1	Various types of gastrointestinal cancer
GSTM1	Various types of gastrointestinal cancer, Various types of gastrointestinal disease, Coronary artery disease
GSTP1	Various types of gastrointestinal cancer, Various types of gastrointestinal disease, Coronary artery disease
GSTT1	Non-alcoholic fatty liver disease, Various types of gastrointestinal cancer, Various types of gastrointestinal disease, Coronary artery disease
MNSOD	Various types of gastrointestinal cancer, Coronary artery disease, Various types of gastrointestinal disease

controls) in a total of 1,170 entries were obtained. Conflicting findings indicated that there was a great incompatibility regarding the associations (or their absence) identified. No specific—and statistically significant—association was identified for any of the 38 genes of interest. In those cases, where a weak association was demonstrated, evidence was based on a limited number of studies. As solid scientific evidence is currently lacking, commercially available nutrigenomics tests cannot be presently recommended. Notwithstanding, the need for a thorough and continuous nutrigenomics research is evident as it is a highly promising tool towards

What professionals say

2014

FROM THE ACADEMY
Position Paper

Position of the Academy of Nutrition and Dietetics: Nutritional Genomics

health messages to more individualized dietary guidance. Although the discipline of nutritional genomics holds promise for tailoring diet to a person's genotype and influencing chronic disease development, the science is still developing. The knowledge gained from nutritional genomics requires an evidence-based approach to validate

Genes Nutr (2013) 8:373–381
DOI 10.1007/s12263-013-0338-6

2013

REVIEW

Do we know enough? A scientific and ethical analysis of the basis for genetic-based personalized nutrition

Ulf Görman · John C. Mathers · Keith A. Grimaldi · Jennie Ahlgren · Karin Nordström

Conclusion

There is convincing evidence that common diet-related diseases are influenced by genetic factors, but knowledge in this area is fragmentary and few relationships have been tested for causality. The evidence that genotype-based dietary advice will motivate appropriate behavior changes is also limited. However, traditional nutritional advice is not always based upon causality but also on observational epidemiological studies. In several specific cases of gene–diet interaction, it may be more beneficial for identifiable groups of individuals with specific genotypes to follow personalized nutritional advice rather than general dietary recommendations. From an ethical perspective, a precau-

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Now you can eat a healthy diet best suited to your genetic makeup, your metabolism, and your lifestyle. Turn DNA insights into easy-to-make food decisions for balanced meals that make your body happy.

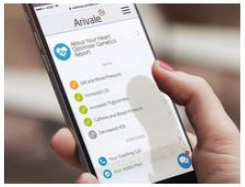
Calorie Mama: All-Access Premium
by Azumio

MealPlanner
by DNAFit

embodyDNA
by Lose It!

Metabolism+
by EverlyWell

Food Sensitivity+
by EverlyWell



Heart Optimizer: Genetics and Nutrition Coaching
by Arivale

Beat Your Genes: Weight Loss Coaching
by Arivale

Diet GENius
by Re:Point

GoalGetter
by InsideTracker

Nutrition

Calorie Mama: All-Access Premium
by Azumio

Lose weight the smart way with nutrition and workout plans customized to your DNA. Easily count calories by taking photos of your meals. Available exclusively on iOS.

Helix

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What companies promise

DNAFit
UNLOCK YOUR HUMAN POTENTIAL

Sign In

You're not the same as everybody else, so why follow everybody else's diet?

DNAFit
UNLOCK YOUR HUMAN POTENTIAL

Sign In

Now it's your turn - this is how it works

Take the guesswork out of dieting with a personalized nutrition plan based on your DNA

VITAGENE

Whether you're looking to slim down, maintain, or just want to eat a little healthier, your genetics contains valuable information to take control of your health and wellness in ways never before possible.

It's simple — your body is unique and your weight loss journey should be as well. Your DNA plays a large role in determining how your body interacts with food — from your preferences to your sensitivities and metabolism. This means that no generic diet is right for everyone.

People on a genetic-based diet lost 33% more weight on average than those on regular diet plans.

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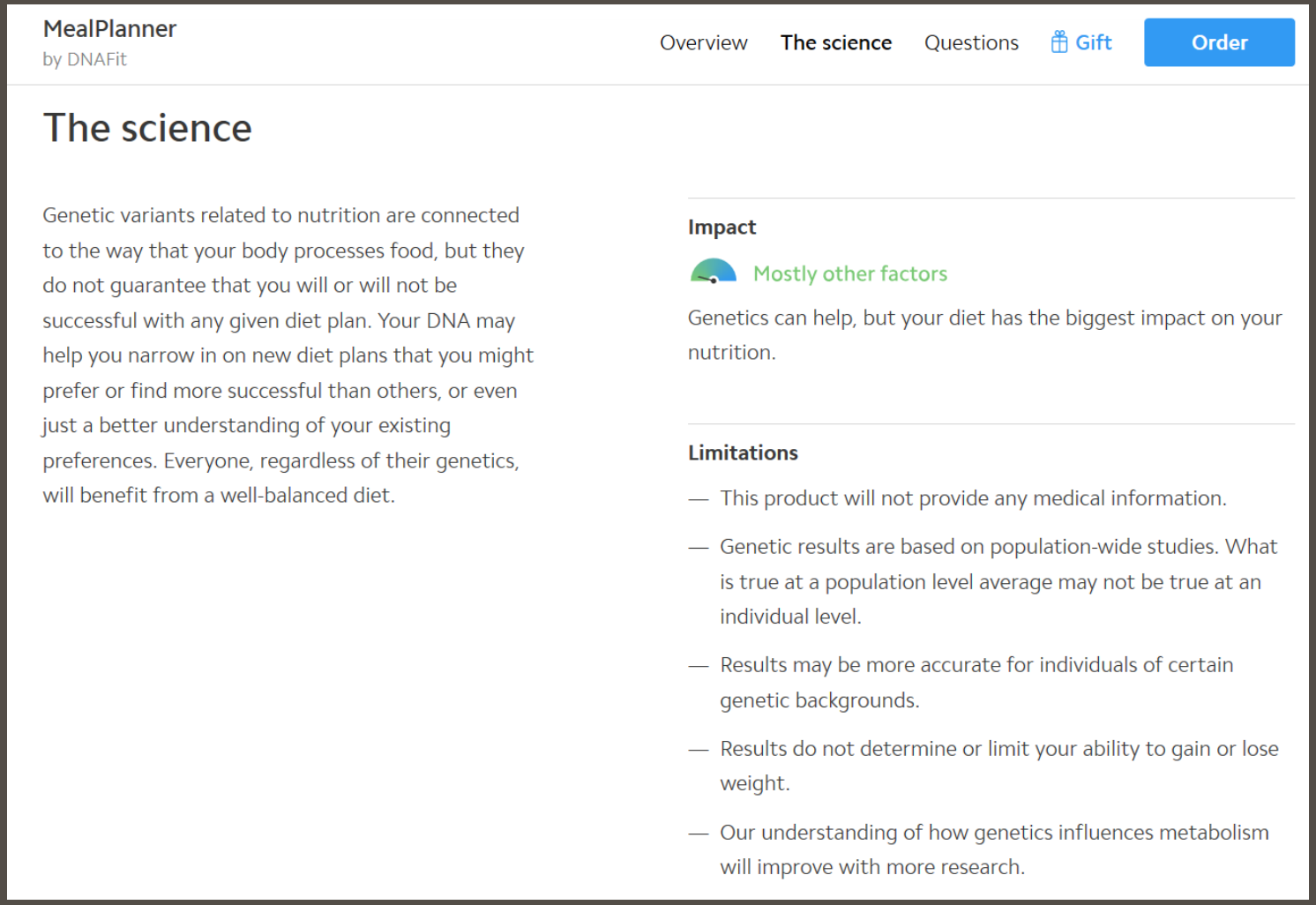
What their disclaimers reveal



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Ethical principles

Medicine

- Autonomy
- Beneficence
- Nonmaleficence
- Justice

Marketing (AMA)

Ethical norms:

- Do no harm
- Foster trust in marketing
- Embrace ethical values: Respect, Honesty, Responsibility, Transparency, Fairness, Citizenship

Beneficence

- Intent of doing good
- Developing and maintaining skills and knowledge, and continually update
- Consider individual circumstances of all patients

- Is the commercial offer in the interest of customers or the company?
- Do we have evidence on how to ‘compensate’ genetic effects with diet? (no)

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USPSTF Analytic Framework

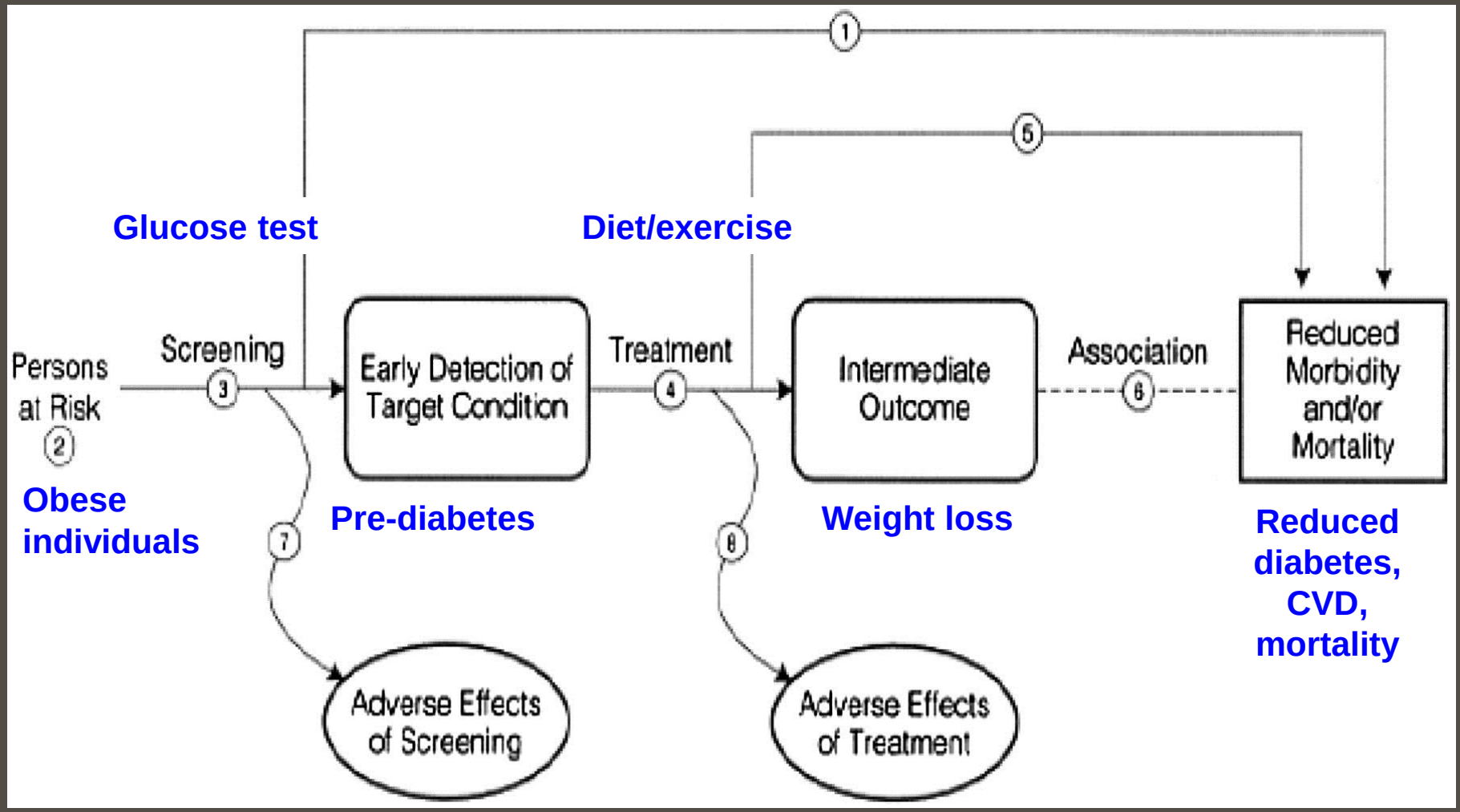

Figure taken from Melnyk et al. Pediatrics 2012;130:e399-e407

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USPSTF Analytic Framework

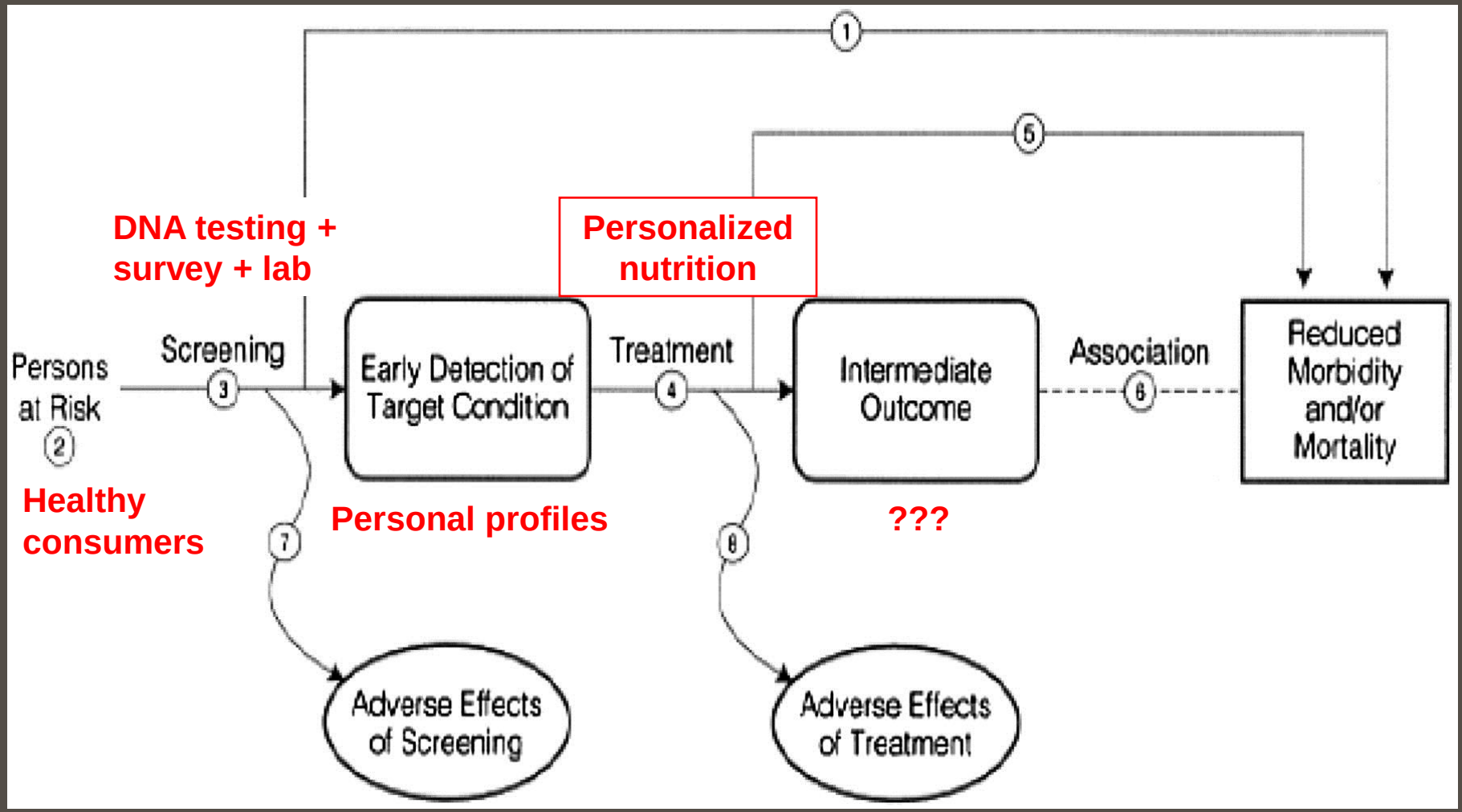

Figure taken from Melnyk et al. Pediatrics 2012;130:e399-e407

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Autonomy

- Customer should decide whether testing is useful for them → personal utility

- Needs information to make informed decision making

- Companies use proprietary algorithms give no insight in validity of recommendations

  Customers and scientists cannot verify validity

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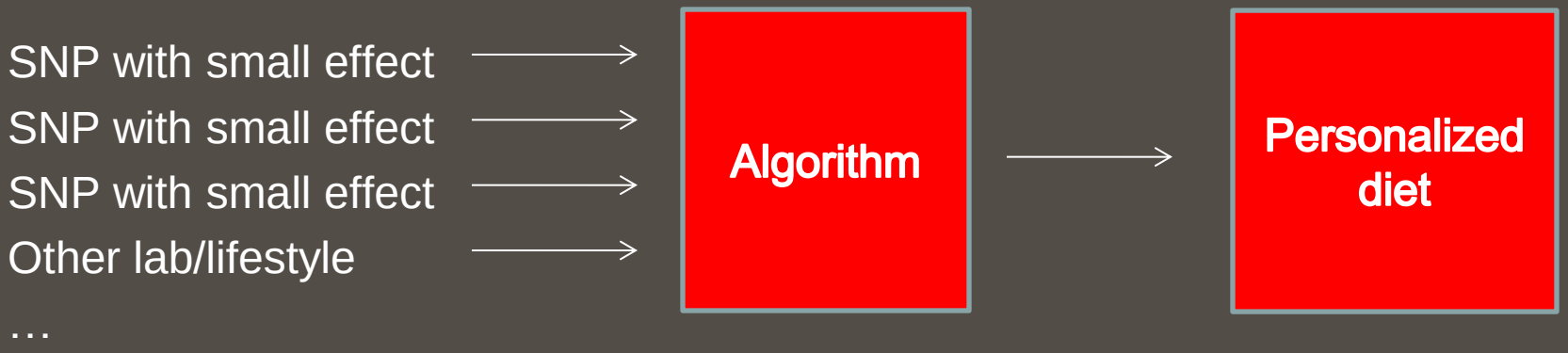
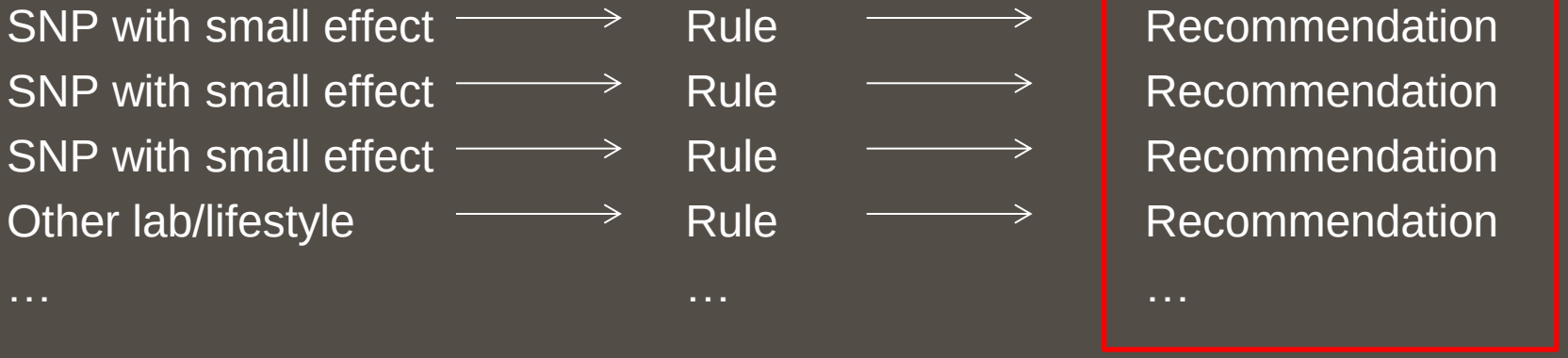
Proprietary algorithms: how advanced?





Personalized combination

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Table 3: Personalized recommendations given to the Nutrigenetic test patient group in addition to base diet.

Nutrient intervention group	% Receiving modified advice
Variation in *MTHFR, MTRR, MTR or CBS*: *Rationale*: Polymorphisms in genes involved in folic acid metabolism have been shown to influence this pathway affecting plasma homocysteine levels as well as the balance between DNA methylation and synthesis of nucleotides [14, 15]. *Recommendation*: Add supplement containing 800 mcg folic acid, 15 mg Vitamin B6 and 20 mcg B12	**98.6**
Variation in *GSTM1, GSTT1 or GSTP1*: *Rationale*: Patients with deletions in *GSTM1* which affect Phase II detoxification processes have been shown to have reduced levels of DNA adducts [16], and increased levels of GSTA1 circulating activity [17], when adequate levels of cruciferous vegetables have been consumed. Risk for lung cancer drops by up to 80% in individuals lacking *GSTM1* and/or *GSTT1* genes when consumption of cruciferous vegetables is high [18]. *Recommendation*: Ensure diet includes regular portions of cruciferous (5 times per week) and allium (daily) vegetables (suggestions and recipes provided to patient). Add broccoli extract and allium supplement if required.	**76.1**
Variation in *SOD2, SOD3, NOS3*: *Rationale*: superoxide dismutase enzymes are free radical scavengers that have important antioxidant activity which can be affected by genetic polymorphism [19] *Recommendation*: Add supplements containing antioxidants, Vit A (5,000 IU), Vit C (250 mg) and Vit E (200 IU).	**48.6**
Variation in *VDR, COL1A1*: *Rationale*: Several studies have shown that gene-diet interactions have a role to play in maintenance of bone condition. For example caffeine increased rate of bone loss but only in the presence of the *VDR taq1* variant [20]. Others have shown gene-diet effects involving calcium [21, 22] and vitamin D [23]. *Recommendation*: Keep caffeine below 2 cups coffee/day. Increase dairy component of diet (yoghurt, cheese and low fat milk). If required add supplement containing 800 IU vitamin D and 1,300 mg Calcium	**87.5**
Variation in *TNFα, IL6, NOS3*: *Rationale*: Variations in inflammation pathway genes *TNFα* and *IL6* have been shown to be pro-inflammatory and the effect can be modulated by increased levels of fish oil in the diet [24] *Recommendation*: Add supplement Omega 3 (700 – 1,400 mg). Make sure weekly diet contains portions of oily fish	**65.3**
Variation in *CETP, LPL, APOC3*: *Rationale*: Polymorphisms in genes involved in lipid metabolism and transport, in combination with dietary fat intake, have been shown to affect plasma cholesterol levels [25] *Recommendation*: The base low fat is already within the limits recommended for these variations so no further specific advice is given but current advice is reinforced and advice given to restrict consumption of dairy foods.	**79.2**
Variation in *ACE, PPARG*: *Rationale*: gene-diet and gene-exercise interactions have been reported to affect blood glucose and insulin levels [26, 27] *Recommendation*: The base low glycemic diet is already within the limits recommended for these variations so no further specific advice is given but current advice is reinforced. Extra exercise advised for this group	**80.6**

Arkadianos et al *Nutrition Journal* 2007

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My Home
Inbox (1)

My Health
Disease Risk
Carrier Status
Drug Response
Traits
Health Labs

My Ancestry
Maternal Line
Paternal Line
Relative Finder
Ancestry Painting
Global Similarity
Ancestry Labs

Sharing & Community
Compare Genes
Family Inheritance
23andMe Community
Genome Sharing

23andWe
Research Surveys (26)
Research Snippets

disease risk

Type 2 Diabetes ★★★★

share this

Established Research report on 9 reported markers, updated June 4th, 2009.

Your Data | How It Works | Timeline | MD's Perspective | Resources | Technical Report

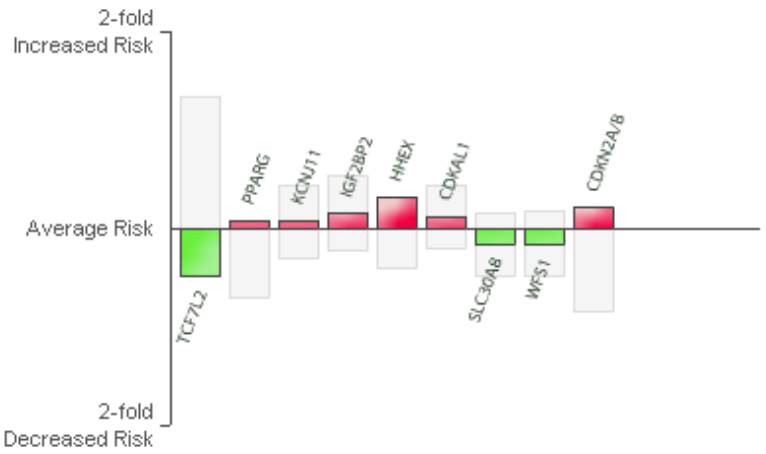
Next ▸ *Ulcerative Colitis*

About Type 2 Diabetes

Printable Version

The most common type of diabetes, type 2 diabetes mellitus occurs when chronically high blood sugar levels cause a breakdown of the body's natural response to eating sweets and starches. Left untreated, type 2 diabetes can result in kidney failure, blindness, and circulatory problems that increase the risk of heart attack or stroke. In the United States, almost 21 million children and adults have diabetes, but the rate of new diagnoses is increasing.

Learn more about the biology of Type 2 Diabetes...
Major discoveries in Type 2 Diabetes...

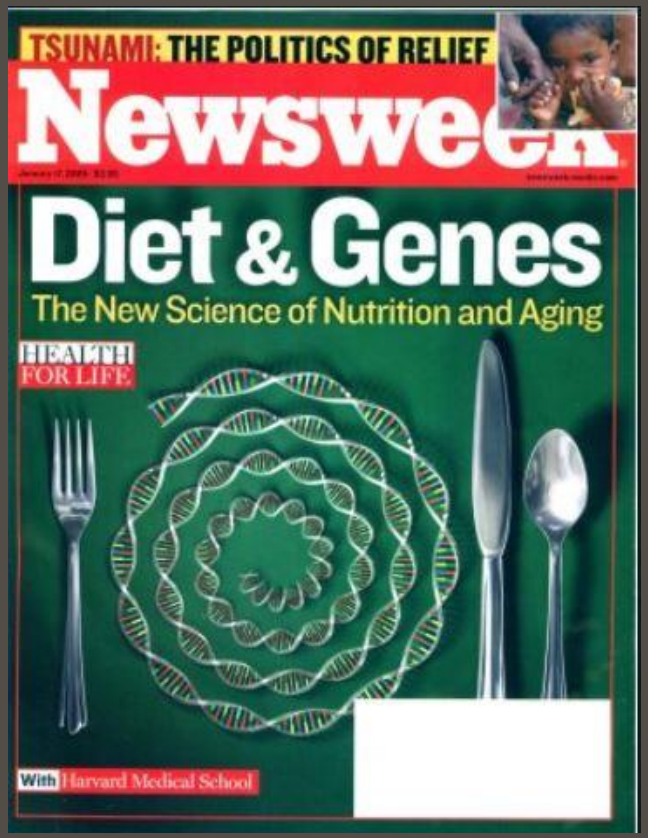


Your Genetic Data

Show information for Cecile Janssens assuming European ethnicity and an age range of 20-79

Where's mine?

Onward



2005

- Better and more relevant scientific studies
- More respectful conversation with consumers
  - Genetically personalized nutrition recommendations is still premature, largely lacking appropriate scientific basis
  - Just say it

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