Global epidemic of type 2 diabetes: The roles of diet, lifestyle, and genes

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Harvard School of Public Health
Professor of Medicine
Harvard Medical School
The global burden

- 366 million people have diabetes in 2011; by 2030 this will have risen to 552 million
- 80% of people with diabetes live in low- and middle-income countries
- 183 million people (50%) with diabetes are undiagnosed
- Diabetes caused 4.6 million deaths in 2011
- Diabetes caused at least USD 465 billion dollars in healthcare expenditures in 2011; 11% of total healthcare expenditures in adults (20-79 years)
Escalating diabetes Epidemic in China

Pan et al. Diabetes Care 1994; Gu et al. Diabetologia 2003; Yang et al. NEJM 2010
Characteristics of Type 2 Diabetes in Asia

- Asians tend to develop diabetes at lower BMI levels.
- The burden of disease in Asia is disproportionately high in the young to middle aged people.
- Rapid nutrition transition has left many countries facing coexisting problems of over- and under-nutrition (in utero exposure to poor nutrition and over-nutrition in later life).
- High prevalence of gestational diabetes in Asian women contributes to the vicious cycle of ‘diabetes begetting diabetes’

Chan et al. JAMA 2009
Global Causes of Obesity

- Genetics: Some groups are more prone to overweight and obesity than others. FTO is the strongest obesity gene, but it does not explain population differences in obesity rates.

- Nutrition Transition: From traditional diet and lifestyle to Westernized diet/lifestyle

- Epidemiologic Transition: From malnutrition and infection to chronic degenerative diseases, but in utero undernutrition co-exists with overnutrition in later life.

- Demographic Transition: High fertility and mortality to low fertility and mortality
Fast Food Nation
Sugar-Sweetened Beverages and Genetic Risk of Obesity


Sugar-Sweetened Beverages and Genetic Obesity Risk
September 21, 2012 | Qi and Others
(DOI: 10.1056/NEJMoa1203039)

Sugar-free Drinks in Normal-Weight Children
September 21, 2012 | J.C. de Ruyter and Others
(DOI: 10.1056/NEJMoa1203034)

EDITORIAL

Calories from Soft Drinks — Do They Matter?
September 21, 2012 | S. Caprio
(DOI: 10.1056/NEJMMe1209884)

Sugar-Sweetened Beverages and Adolescent Weight
September 21, 2012 | C.B. Ebbeling and Others
(DOI: 10.1056/NEJMoa1203388)
Genetic Susceptibility

Genetic risk score

32 obesity genes

1 unit = 1 risk allele

FTO  MC4R  GIPR  TMEM160  TMEM18  SH2B1  GPC5B  MAP2K5  NRXN3  PRKD1  MTIF3  FAIM2  MTCH2  BDNF  SH2B1  TMEM18  FAIM2  LRRN6C  GNPDA2  PCSK1  RPL27A

Genetic Predisposition Score
<table>
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<tr>
<th>Cohort</th>
<th>Relative Risk</th>
<th>P Value for Interaction</th>
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<tbody>
<tr>
<td>NHS and HPFS</td>
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<td>0.02</td>
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<tr>
<td>&lt;1 serving/mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–4 servings/mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2–6 servings/wk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 servings/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WGHS</td>
<td></td>
<td>0.007</td>
</tr>
<tr>
<td>&lt;1 serving/mo</td>
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<td></td>
</tr>
<tr>
<td>1–4 servings/mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2–6 servings/wk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥1 servings/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pooled</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&lt;1 serving/mo</td>
<td></td>
<td></td>
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<td>1–4 servings/mo</td>
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<td>2–6 servings/wk</td>
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<td></td>
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<tr>
<td>≥1 servings/day</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1.** Relative Risk of the Development of Obesity per Increment of 10 Risk Alleles, According to Intake of Sugar-Sweetened Beverages.
Genomics and proteomics tell you what **might** happen, but **metabolomics** tells you what actually **did** happen!

*Bill Lasley, University of California, Davis*
Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease

Zeneng Wang¹,², Elizabeth Klipfell¹,², Brian J. Bennett³, Robert Koeth¹, Bruce S. Levison¹,², Brandon DuGar¹, Ariel E. Feldstein¹,², Earl B. Britt¹,², Xiaoming Fu¹,², Yoon-Mi Chung¹,², Yuping Wu⁴, Phil Schauer⁵, Jonathan D. Smith¹,⁶, Hooman Aillarye⁷, W. H. Wilson Tang¹,²,⁶, Joseph A. DiDonato¹,², Aldons J. Lusis³ & Stanley L. Hazen¹,²,⁶

Figure 6 | Gut-flora-dependent metabolism of dietary PC and atherosclerosis. Schematic summary illustrating newly discovered pathway for gut-flora-mediated generation of pro-atherosclerotic metabolite from dietary PC.
Meta-analysis of red meat intake and T2 diabetes

Pan et al., AJCN 2011
Diet rapidly and reproducibly alters the human gut microbiome

The animal-based diet increased the abundance of bile-tolerant microorganisms (*Alistipes, Bilophila* and *Bacteroides*) and decreased the levels of Firmicutes that metabolize dietary plant polysaccharides (*Roseburia, Eubacterium rectale* and *Ruminococcus bromii*).

Microbial activity mirrored differences between herbivorous and carnivorous mammals.
Association of Dietary, Circulating, and Supplement Fatty Acids With Coronary Risk
A Systematic Review and Meta-analysis

Rajiv Chowdhury, MD, PhD; Samantha Wamakula, MPhil*; Setor Kunutsor, MD, MST*; Francesca Crowe, PhD; Heather A. Ward, PhD; Laura Johnson, PhD; Oscar H. Franco, MD, PhD; Adam S. Butterworth, PhD; Nita G. Forouhi, MRCP, PhD; Simon G. Thompson, FMedSci; Kay-Tee Khaw, FMedSci; Dariush Mozaffarian, MD, DrPH; John Danesh, FRCP*; and Emanuele Di Angelantonio, MD, PhD*
FATS

Classification by number (and location) of double bonds and carbon chain length

Saturated

Monounsaturated

(One double bond)

Polyunsaturated

(Many double bonds)
Types of Fat and Incidence of CHD
(Nurses’ Health Study)

% Change in CHD

-40 -20 0 20 40 60 80 100

1%E 2%E 3%E 4%E 5%E

Trans

Refined Carbs

Saturated

Mono

Poly

Total fat = NO RELATIONSHIP

### Nuts and Mortality (Ying et al. NEJM 2013)

<table>
<thead>
<tr>
<th>Cause of Death and Type of Nut</th>
<th>Women</th>
<th>Men</th>
<th>Pooled</th>
<th>Hazard Ratio (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>All causes</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any nut</td>
<td></td>
<td></td>
<td></td>
<td>0.86 (0.82–0.89)</td>
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<tr>
<td>Peanut</td>
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<td></td>
<td></td>
<td>0.88 (0.84–0.93)</td>
</tr>
<tr>
<td>Tree nut</td>
<td></td>
<td></td>
<td></td>
<td>0.83 (0.79–0.88)</td>
</tr>
<tr>
<td>Cancer</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any nut</td>
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<td></td>
<td></td>
<td>0.91 (0.85–0.97)</td>
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<tr>
<td>Peanut</td>
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<td></td>
<td></td>
<td>0.94 (0.88–1.02)</td>
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<tr>
<td>Tree nut</td>
<td></td>
<td></td>
<td></td>
<td>0.83 (0.76–0.90)</td>
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<tr>
<td>Heart disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any nut</td>
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<td></td>
<td></td>
<td>0.74 (0.68–0.81)</td>
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<tr>
<td>Peanut</td>
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<td></td>
<td></td>
<td>0.76 (0.68–0.84)</td>
</tr>
<tr>
<td>Tree nut</td>
<td></td>
<td></td>
<td></td>
<td>0.76 (0.67–0.85)</td>
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</tbody>
</table>
Sugars

Natural Sugars

Added Sugars

Added during preparation or processing
# Added Sugar in the American Diet

22 teaspoons per day

350 calories!

~50% of added sugar from beverages

## TOP SOURCES

<table>
<thead>
<tr>
<th>Rank</th>
<th>Food Types</th>
<th>%</th>
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<tbody>
<tr>
<td>1</td>
<td>Sugar-sweetened beverages</td>
<td>37.1</td>
</tr>
<tr>
<td>2</td>
<td>Grain-based desserts</td>
<td>13.7</td>
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<td>3</td>
<td>Fruit drinks</td>
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<td>4</td>
<td>Dairy desserts</td>
<td>6.1</td>
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<tr>
<td>5</td>
<td>Candy</td>
<td>5.8</td>
</tr>
<tr>
<td>6</td>
<td>Sugars/honey</td>
<td>4.2</td>
</tr>
<tr>
<td>7</td>
<td>Tea</td>
<td>4.0</td>
</tr>
<tr>
<td>8</td>
<td>Ready-to-eat cereals</td>
<td>2.9</td>
</tr>
<tr>
<td>9</td>
<td>Yeast breads</td>
<td>2.2</td>
</tr>
<tr>
<td>10</td>
<td>Syrups/toppings</td>
<td>1.5</td>
</tr>
</tbody>
</table>

NCI: Sources of Calories from Added Sugars among the US Population, 2005–06.  
http://appliedresearch.cancer.gov/diet/foodsources/added_sugars
Ingredients list: By weight

*Using different types of added sugar can bury “sugar” lower down in the list

CREAM, SKIM MILK, LIQUID SUGAR (SUGAR, WATER), WATER, CORN SYRUP, SUGAR, EGG YOLKS, COCONUT OIL, WHEAT FLOUR, BUTTER (CREAM, SALT), COCOA, MILK, VANILLA EXTRACT, MILK FAT, GUAR GUM, SOYBEAN OIL, NATURAL FLAVORS, SALT, SOY LECITHIN, CARRAGEEENAN, SODIUM BICARBONATE

Doesn’t distinguish added vs. natural sugars

Weight gain
Higher risk of obesity
Higher risk of Type 2 Diabetes
Higher risk of high blood pressure
High cholesterol
Cardiovascular disease

HSPH Nutrition Source
Risk of CVD Mortality
According to % Calories from Added Sugar

NHANES 1988-2006

* Adjusted for age, sex, race/ethnicity, education, smoking status, alcohol consumption, BMI, physical activity, family history of CVD, Healthy Eating Index, antihypertensive medication use, systolic blood pressure, total cholesterol, and total calorie intake

Yang et al. JAMA Internal Medicine, 2014
Exporting Our Health Problems?

- Highly caloric (~150 calories/12 oz. can)
- Less satiating
- No redeeming nutrition
- Not real food

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**Global Trends**

*Change in Total Volume of Carbonated Soft Drinks Consumed Between 2002 and 2007*

- US
- Australasia
- Western Europe
- Asia Pacific
- Middle East and Africa
- Latin America
- Eastern Europe

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Spread virtual happiness.
Type a name to create your own custom bottle.
Coffee, Decaffeinated Coffee, and Tea Consumption in Relation to Incident Type 2 Diabetes Mellitus

A Systematic Review With Meta-analysis

Rachel Huxley, DPhil; Crystal Man Ying Lee, PhD; Federica Barzi, PhD; Leif Timmermeister; Sebastien Czernichow, MD, PhD; Vlado Perkovic, MD, PhD; Diederick E. Grobbee, MD, PhD; David Batty, PhD; Mark Woodward, PhD

Figure 2. The relationship between coffee consumption and subsequent type 2 diabetes mellitus in different categories of coffee consumption. The center of each black square is placed at the summary point estimate; the area of the square is proportional to the statistical size; and each vertical line shows the 95% confidence interval about the summary estimate.
Coffee
Primary Prevention of Cardiovascular Disease with a Mediterranean Diet

Ramón Estruch, M.D., Ph.D., Emilio Ros, M.D., Ph.D., Jordi Salas-Salvadó, M.D., Ph.D., Maria-Isabel Covas, D.Pharm., Ph.D., Dolores Corella, D.Pharm., Ph.D., Fernando Arós, M.D., Ph.D., Enrique Gómez-Gracia, M.D., Ph.D., Valentina Ruiz-Gutiérrez, Ph.D., Miquel Fiol, M.D., Ph.D., José Lapetra, M.D., Ph.D., Rosa María Lamuela-Raventos, D.Pharm., Ph.D., Lluís Serra-Majem, M.D., Ph.D., Xavier Pintó, M.D., Ph.D., Josep Basora, M.D., Ph.D., Miguel Angel Muñoz, M.D., Ph.D., José V. Sorlí, M.D., Ph.D., José Alfredo Martínez, D.Pharm, M.D., Ph.D., and Miguel Angel Martínez-González, M.D., Ph.D., for the PREDIMED Study Investigators*
Primary end-point (MI, stroke or death from CV causes)

Hazard Ratios (95% CI)*
- EVOO: 0.70 (0.53-0.91), P=0.009
- Nuts: 0.70 (0.53-0.94), P=0.016

Control diet
- Med diet, nuts
- Med diet, EVOO

Number at risk
- Control group: 2450
- Med Diet+EVOO: 2543
- Med Diet+Nuts: 2454

Years

<table>
<thead>
<tr>
<th>Years</th>
<th>Control group</th>
<th>MeDiet+EVOO</th>
<th>MeDiet+Nuts</th>
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<tbody>
<tr>
<td>0</td>
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<td>2543</td>
<td>2454</td>
</tr>
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<td>1</td>
<td>2268</td>
<td>2486</td>
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<td>2093</td>
</tr>
<tr>
<td>3</td>
<td>1583</td>
<td>1987</td>
<td>1657</td>
</tr>
<tr>
<td>4</td>
<td>1268</td>
<td>1687</td>
<td>1389</td>
</tr>
<tr>
<td>5</td>
<td>946</td>
<td>1310</td>
<td>1031</td>
</tr>
</tbody>
</table>
What is the Mediterranean diet?
At Least 7 Glasses of Wine Each Week

FEB 25 2013, 2:56 PM ET 120

Pivotal research in the New England Journal of Medicine today confirmed well-worn notions that the Mediterranean diet -- including produce, olive oil, nuts, etc. -- significantly reduced rates of heart attacks and strokes, as compared to a low-fat diet. Now, to make these foods as accessible as corn sugar
Prevention and management of type 2 diabetes: dietary components and nutritional strategies

The Lancet, 2014
Overall diet quality: Key to Diabetes Prevention and Management

Ley et al. Lancet 2014
Global Perspective

• Concerted worldwide efforts and policies are warranted to improve food environment and system
  – nutrition and agricultural policies that favor the production and distribution of healthy food
  – increasing taxes on unhealthy products can reduce consumption of these foods
  – improving and standardization of front-of-package and nutrition facts labels

• Sound agricultural and nutrition policies in conjunction with public health campaigns could reshape the trajectory of nutrition transition and global food supply

Ley et al. Lancet 2014