Tooth Decay and Liver Decay: The Nexus Between Doctors and Dentists

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NOHC, Cincinnati, OH, April 18, 2016
• No disclosures
(except I wrote a book)
Tooth Decay
Dentists were the first anti-sugar advocates
"The worst mistake in the history of the human race" (Jared Diamond)

Virtually no evidence of caries in the human fossil record until 10-12k ya (i.e., after the invention of Agriculture)

5 million BCE  

10,000 years
Prevalence of Dental Caries in European Populations

Kean, 1980
March 27, 1934
Hotel Pennsylvania, New York City

Conservative theory — Clean teeth do not decay:
Dr. Thaddeus P. Hyatt, Metropolitan Life and New York University
Dr. Alfred Walker, New York University
Dr. Maurice William, Oral Hygiene Committee of Greater New York

Nutritional dentistry — Caries are a manifestation of your internal metabolic milieu:
Dr. Elmer V. McCollum, Johns Hopkins University
Dr. Arthur H. Merritt, American Academy of Periodontics
Dr. Weston A. Price, Dental Research Laboratories, Cleveland, OH.
The pathogenesis of caries 1934

Keyes and Jordan, 1963
Current mouth flora

The Modern Rise of Strep. Mutans

Figure 3: Changes in the diversity and composition of oral microbiota. (a) For the V3 region sequences, we estimated the phylogenetic diversity of the archaeological dental calculus samples (n = 34) and compared them to modern calculus (n = 6) and plaque (n = 13). We estimated phylogenetic diversity from only classified, Gram-positive bacterial sequences to minimize the influence of taphonomic bias. Diversity was calculated at a depth of 34 sequences and bootstrapped to assess the robustness of the pattern. Error bars represent bootstrapped diversity values generated by sampling 255 replicates without replacement. BP, years before the present. (b) Specific primers were used to amplify sequences unique to the oral pathogens S. mutans and P. gingivalis. Error bars represent bootstrapped frequencies generated by sampling 255 replicates without replacement.
The pathogenesis of caries 1934

Keyes and Jordan, 1963
More sugar + older teeth = More caries

Figure 1 Three-dimensional model of the cumulative numbers of caries in upper central incisor teeth. Data were plotted on a log scale, by post-eruptive tooth age up to 8 years, and related to the average annual sugar consumption per head in Japan from 1935 to 1957 (Takeuchi et al. [14], with permission).

Sheiham and James, BMC Public Health 14:863, 2014
Log-linear relationship between sugar and caries

Figure 2 Relationship between annual per capita sugar consumption and annual caries incidence in lower first molars. Data based on 10,553 Japanese children whose individual teeth were monitored yearly from the age of 6 to 11 years of age. Data plotted on a log scale. (Adapted from Koike [18]).

Sheiham and James, BMC Public Health 14:863, 2014
Stephan Curve

pH changes in plaque following application of different carbohydrate solutions

- sorbitol
- starch, raw
- starch, cooked
- lactose
- glucose
- fructose
- sucrose
Starch vs. sucrose vs. both

Epidemiologic data:
Starch + low sugar → low incidence of caries
Starch + high sugar → high incidence of caries

Epidemiologic data:
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---

**Table 1.** Biomass (dry-weight), total amount of protein, and EPS in *Streptococcus mutans* UA159 biofilms formed in the presence of starch and sucrose, alone or in combinations

<table>
<thead>
<tr>
<th>Experimental groups</th>
<th>Dry-weight (mg)</th>
<th>Total amount of protein (mg)</th>
<th>Total amount of EPS (µg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starch</td>
<td>0.75 (0.27)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.1 (0.08)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>88.98 (17.84)&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Starch + sucrose</td>
<td>6.25 (0.69)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>1.3 (0.12)&lt;sup&gt;2&lt;/sup&gt;</td>
<td>1747.99 (146.62)&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Sucrose</td>
<td>5.50 (0.45)&lt;sup&gt;3&lt;/sup&gt;</td>
<td>1.5 (0.32)&lt;sup&gt;3&lt;/sup&gt;</td>
<td>1411.28 (256.45)&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Starch + glucose + fructose</td>
<td>1.25 (0.42)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>0.2 (0.12)&lt;sup&gt;1&lt;/sup&gt;</td>
<td>126.37 (16.58)&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Sucrose + glucose</td>
<td>3.92 (0.92)&lt;sup&gt;4&lt;/sup&gt;</td>
<td>1.4 (0.21)&lt;sup&gt;4&lt;/sup&gt;</td>
<td>850.31 (190.79)&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Values (SD, n = 12) in the same column followed by the same superscript numbers are not significantly different from each other (P > 0.05, ANOVA, comparison for all pairs using Tukey test).

Starch vs. sucrose vs. both

Epidemiologic data:
- Starch + low sugar: low incidence of caries
- Starch + high sugar: high incidence of caries


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**Table 4. Analysis of dental enamel according to treatment**

<table>
<thead>
<tr>
<th>Treatment*</th>
<th>Water</th>
<th>Starch</th>
<th>Sucrose</th>
<th>Starch + Sucrose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mineral loss</td>
<td>447-9</td>
<td>189-0</td>
<td>420-0</td>
<td>160-1</td>
</tr>
<tr>
<td>10µm</td>
<td></td>
<td></td>
<td>956-6</td>
<td>543-6</td>
</tr>
<tr>
<td>20µm</td>
<td>1421-8</td>
<td>653-8</td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

* T1, H2O; T2, 2% starch; T3, 10% sucrose; T4, 2% starch + 10% sucrose.

a,b Mean values with unlike superscript letters were significantly different (P<0.05).


Ribeiro et al., Br J Nutr 94:44, 2005
"It seems that were we to turn to a low sugar, high fat type of diet, such as is prescribed for diabetic patients, we might expect a prompt and marked reduction in caries susceptibility. This type of diet is practicable in many countries, but fats are in many regions considerably more expensive to produce than are starches and sugars. At any rate, we now know how to produce good teeth as respects structure and how to preserve them in considerable measure from decay. “

Elmer V. McCollum, Newer Knowledge of Nutrition, 1939
SIP ALL DAY
GET DECAY
"We realize very well, however, that if sugar is the great offender in the cause of dental caries, as seems to be the case, we have a very difficult task ahead in making much progress in its control by the reduction of sugar intake so far as the mass of people is concerned. **Most people would prefer some decay rather than to eliminate the sweets…** We should keep up the admonition and give the evidence as to its harmful effect on teeth. At the same time, let us hope our research workers discover a more practical means of controlling or preventing dental decay."
The pathogenesis of caries 1947

Keyes and Jordan, 1963
The pathogenesis of caries 1947

Keyes and Jordan, 1963
Mechanisms of action of fluoride

**Fig. 1.** Caries attack in the absence of fluoride (a) and in the presence of fluoride (b). In the presence of fluoride, the risk period (red area) is smaller than in the absence of fluoride as a result of a lower critical pH (pH 5.0 vs. 5.5). During remineralization, fluoridated hydroxyapatite is formed which is less soluble than the hydroxyapatite formed in the absence of fluoride.

Amaechi and van Loveren, Monogr Oral Sci, Karger 2013, pp. 15-26
In 1945, Grand Rapids became the first city in the world to fluoridate its drinking water... During the 15-year project, researchers monitored the rate of tooth decay among Grand Rapids' almost 30,000 schoolchildren. After just 11 years, [Dr. H. Trendley] Dean - who was now director of the NIDR-announced an amazing finding. The caries rate among Grand Rapids children born after fluoride was added to the water supply dropped more than 60 percent. This finding, considering the thousands of participants in the study, amounted to a giant scientific breakthrough that promised to revolutionize dental care, making tooth decay for the first time in history a preventable disease for most people.
Fluoride in water or toothpaste cuts cavities

But we’ve reached an equilibrium – no further reduction in prevalence in caries

Dye et al. NCHS, Vital and Health Statistics, National Health Survey, 2007
AAPD Leadership Perspective on the AAPD Foundation's Collaboration with the Coca-Cola Foundation (March 4, 2003)

A Brief Summary of Actions from AAPD Foundation President Joel H. Berg

...This commitment from the Coke Foundation is a large, unrestricted gift to the AAPD Foundation’s endowment to fund independent research. Universities or other independent university-related entities selected by the AAPD (after a competitive process using an RFP-type protocol) will conduct the research. The gift does not involve endorsements, sponsorships or other relationships or affiliations. The Coca-Cola Foundation distributes millions of dollars annually to non-profit entities, including large grants to Habitat for Humanity and the Boys and Girls Clubs of America. We hope to leverage this interest on the part of the Coca-Cola Company and its Foundation in the oral health of children.

A Position Statement from AAPD Executive Director John S. Rutkauskas

The AAPD and AAPDF leadership firmly believes that this collaboration is in the best interest of children. Both AAPD members and parents should be assured that we have never and will never – endorse any consumer product from any corporate sponsor. That would not be in the best interests of the AAPD, parents or the children we serve. The Foundation’s research topics and protocol and its choice of consumer education messages have always been chosen by its Board, comprised primarily of pediatric dentists. This is a donation from Coca-Cola’s Foundation to our Foundation. We genuinely believe that we can make a big difference in promoting responsible choices for parents regarding their children’s dental health and overall health.
The Sugar Industry Shaped Government Advice On Cavities, Report Finds

Alexandra Sifferlin

March 10, 2015

Internal sugar industry documents reveal how it influenced national research priorities for tooth decay

A new report reveals that the sugar industry heavily influenced federal research—as well as the guidelines that resulted from that research.

Tooth decay remains a

Sugar Industry Influence on the Scientific Agenda of the National Institute of Dental Research’s 1971 National Caries Program: A Historical Analysis of Internal Documents

Cristin E. Kearns1,2,3, Stanton A. Glantz1,2,4,5,6, Laura A. Schmidt1,2,6,7
Portland, OR says “no” to fluoride

May 22, 2013
Guideline Summary

Guideline Title


Bibliographic Source(s)


<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Diagnostics</th>
<th>Interventions</th>
<th>Fluorides</th>
<th>Diet</th>
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<tr>
<td>Low risk</td>
<td>Recall every 6-12 months</td>
<td>Twice daily brushing</td>
<td>Counseling</td>
<td></td>
<td>Surveillance</td>
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<td>Recall every 6 months</td>
<td>Twice daily brushing with fluoride toothpaste</td>
<td>Counseling</td>
<td></td>
<td>Active surveillance of incipient lesions</td>
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<td>Moderate risk parent not engaged</td>
<td>Recall every 6 months</td>
<td>Twice daily brushing with fluoride toothpaste</td>
<td>Counseling, with limited expectations</td>
<td></td>
<td>Active surveillance of incipient lesions</td>
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<tr>
<td>High risk parent engaged</td>
<td>Recall every 3 months</td>
<td>Twice daily brushing with fluoride toothpaste</td>
<td>Counseling</td>
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*Guideline on caries-risk assessment and management for infants, children and adolescents.*

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No dietary advice for any age group
IS HIGH SUGAR INTAKE AFFECTING YOUR ORAL HEALTH?
March 14, 2014

The World Health Organization may cut their recommended daily sugar intake in half. Should you follow their advice?

What Kind of Sugars Are You Consuming?

How Often Do You Indulge?

How Often Do You Brush?

“To sum up, while reducing overall sugar intake can help promote better oral health, it is not necessarily the most effective step to take. The best way to prevent tooth decay is to brush as quickly as possible after eating any kind of food, not just sugar.”
Liver Decay
“Beating obesity will take action by all of us, based on one simple *common sense* fact: *All calories count*, no matter where they come from, including Coca-Cola and everything else with calories…”

-The Coca Cola Company, “Coming Together”, 2013
The Science

- **Some Calories Cause Disease More than Others**

- **Different Calories are Metabolized Differently**

- **A Calorie is Not A Calorie**
  - Fiber
  - Protein
  - Fat
  - Fructose
High Fructose Corn Syrup is 42-55% Fructose; Sucrose is 50% Fructose

Glucose

Fructose

Sucrose
The toxic truth about sugar

Added sweeteners pose dangers to health that justify controlling them like alcohol, argue Robert H. Lustig, Laura A. Schmidt and Claire D. Brindis.
Hyperbole?

New York Times, April 17, 2011


COMMENT

ECOLOGY Komodo dragons and elephants could reduce fire risk in Australia p.28
NEUROSCIENCE The source of the self is in the brain’s wiring, not individual neurons p.21
LITERATURE How Charles Dickens drew on science, but left room for wonder p.22
OBITUARY Philip Lawley and the discovery that DNA damage can cause cancer p.19

The toxic truth about sugar

Added sweeteners pose dangers to health that justify controlling them like alcohol, argue Robert H. Lustig, Laura A. Schmidt and Claire D. Brindis.
Toxicity:
The degree to which a substance can damage an organism

- Does not distinguish acute vs. chronic toxicity

Requisites:

- Must be an “independent risk factor”
- Must establish causation
- Exclusive of calories
- Exclusive of obesity
Criticisms of Fructose Toxicity

• Animal models, not human studies

• Administration of excessive doses of fructose
Criticisms of Fructose Toxicity

• Animal models, not human studies

• Administration of excessive doses of fructose

WILL LIMIT DISCUSSION TO:
HUMAN DATA,
HUMAN CONSUMPTION,
AND IN DOSES ROUTINELY INGESTED
US Sugar Consumption, 1822-2005

Grams per day

U.S. Commerce Service 1822-1910, combined with Economic Research Service, USDA 1910-2010
US Sugar Consumption, 1822-2005

Grams per day

- Stabilization
- HFCS + Sugar for Fat
- WWII
- Growth of Sugar Industry

U.S. Commerce Service 1822-1910, combined with Economic Research Service, USDA 1910-2010
US Sugar Consumption, 1822-2005

Grams per day

- Theoretical threshold based on EtOH
- Stabilization
- WWII
- Growth of Sugar Industry
- HECS + Sugar for Fat
- AHA threshold for CVD

U.S. Commerce Service 1822-1910, combined with Economic Research Service, USDA 1910-2010
Grams per day

Diabetes rise
In NYC 1924

Theoretical threshold based on EtOH

AHA threshold for CVD

Growth of Sugar Industry

Stabilization

HECS + Sugar for Fat

U.S. Commerce Service 1822-1910, combined with Economic Research Service, USDA 1910-2010
Growth of Sugar Industry

Stabilization

Sugar for Fat

HECS +

Diabetes rise in NYC 1924

Theoretical threshold based on EtOH

AHA threshold for CVD

Emergence of CVD as health issue 1931

WWII

U.S. Commerce Service 1822-1910, combined with Economic Research Service, USDA 1910-2010
U.S. Commerce Service 1822-1910, combined with Economic Research Service, USDA 1910-2010

- Growth of Sugar Industry
- Stabilization
- Emergence of Adolescent T2DM as health issue 1988
- AHA threshold for CVD
- Emergence of CVD as health issue 1931
- Theoretical threshold based on EtOH
- Sugar for Fat
- HFCS + Sugar for Fat
- WWII
- Diabetes rise In NYC 1924
Sugar and Heart Disease
Variation of HDL and triglyceride levels based on consumption of added sugars in NHANES adults

Figure 1. Multivariable-Adjusted Mean HDL-C Levels by Level of Added Sugar Intake Among US Adults, NHANES 1999-2006

Figure 2. Multivariable-Adjusted Geometric Mean Triglyceride Levels by Level of Added Sugar Intake Among US Adults, NHANES 1999-2006
## Meta-Analysis of Effects of Sugar on Triglycerides


### 1.1 Isoaloric energy intake recommendation

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Mean Difference</th>
<th>SE</th>
<th>Weight</th>
<th>Mean Difference IV, Random, 95% CI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birchwood 1970 (27)</td>
<td>0.07</td>
<td>0.1</td>
<td>2.5%</td>
<td>0.07 [-0.13, 0.27]</td>
<td>1970</td>
</tr>
<tr>
<td>Little 1970 (32)</td>
<td>0.82</td>
<td>0.52</td>
<td>5.2%</td>
<td>0.82 [-0.18, 1.4]</td>
<td>1970</td>
</tr>
<tr>
<td>Antar 1970 (33)</td>
<td>1.55</td>
<td>0.51</td>
<td>2.2%</td>
<td>1.55 [-0.53, 2.57]</td>
<td>1970</td>
</tr>
<tr>
<td>Mann 1972 (35)</td>
<td>0.00</td>
<td>0.02</td>
<td>2.2%</td>
<td>0.00 [-0.04, 0.05]</td>
<td>1972</td>
</tr>
<tr>
<td>Grande 1974 (36)</td>
<td>0.15</td>
<td>0.22</td>
<td>0.8%</td>
<td>0.16 [-0.28, 0.59]</td>
<td>1974</td>
</tr>
<tr>
<td>Reiser 1976 women (39)</td>
<td>0.24</td>
<td>0.08</td>
<td>0.8%</td>
<td>0.25 [-0.04, 0.46]</td>
<td>1979</td>
</tr>
<tr>
<td>Reiser 1979 men (40)</td>
<td>0.04</td>
<td>0.19</td>
<td>2.1%</td>
<td>0.04 [-0.66, 0.82]</td>
<td>1979</td>
</tr>
<tr>
<td>Reiser 1981 (40)</td>
<td>0.73</td>
<td>0.16</td>
<td>2.6%</td>
<td>0.73 [0.43, 1.04]</td>
<td>1981</td>
</tr>
<tr>
<td>Hallfrisch 1983 (41)</td>
<td>0.38</td>
<td>0.42</td>
<td>2.1%</td>
<td>0.38 [0.02, 0.74]</td>
<td>1983</td>
</tr>
<tr>
<td>Gripena-Seo 1985 (33)</td>
<td>0.13</td>
<td>0.14</td>
<td>1.2%</td>
<td>0.13 [-0.19, 0.41]</td>
<td>1988</td>
</tr>
<tr>
<td>Cooper 1988 (13)</td>
<td>0.11</td>
<td>0.14</td>
<td>2.7%</td>
<td>0.11 [-0.03, 0.27]</td>
<td>1988</td>
</tr>
</tbody>
</table>

**Heterogeneity Test: Tau² = 0.01; Chi² = 83.8, df = 21 (P < 0.00001); I² = 75%**

**Test for overall effect: Z = 4.12 (P < 0.0001)**

### 1.2 Ad libitum energy intake recommendation

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<td>0.11</td>
<td>0.03</td>
<td>2.8%</td>
<td>0.11 [0.01, 0.22]</td>
<td>1993</td>
</tr>
<tr>
<td>Weiteman 1993 (49)</td>
<td>0.35</td>
<td>0.19</td>
<td>2.5%</td>
<td>0.35 [0.04, 0.66]</td>
<td>1994</td>
</tr>
<tr>
<td>Chantelou 1995 (28)</td>
<td>0.02</td>
<td>0.05</td>
<td>2.0%</td>
<td>0.02 [-0.13, 0.17]</td>
<td>1995</td>
</tr>
<tr>
<td>Peterson 1996 (38)</td>
<td>0.00</td>
<td>0.06</td>
<td>3.1%</td>
<td>0.00 [-0.11, 0.22]</td>
<td>1996</td>
</tr>
<tr>
<td>Verhey 1988 (48)</td>
<td>0.43</td>
<td>0.24</td>
<td>2.8%</td>
<td>0.43 [-0.03, 0.89]</td>
<td>1988</td>
</tr>
<tr>
<td>Colagioi 1989 (29)</td>
<td>0.00</td>
<td>0.01</td>
<td>2.2%</td>
<td>0.00 [-0.03, 0.03]</td>
<td>1989</td>
</tr>
<tr>
<td>Smith 1996 (44)</td>
<td>0.11</td>
<td>0.07</td>
<td>2.2%</td>
<td>0.11 [-0.13, 0.28]</td>
<td>1996</td>
</tr>
<tr>
<td>Marschmann 1990 (36)</td>
<td>0.15</td>
<td>0.14</td>
<td>2.6%</td>
<td>0.15 [0.07, 0.23]</td>
<td>1990</td>
</tr>
<tr>
<td>Saris 2000 (33)</td>
<td>0.17</td>
<td>0.09</td>
<td>2.5%</td>
<td>0.17 [-0.01, 0.33]</td>
<td>2000</td>
</tr>
<tr>
<td>Poppi 2002 (20)</td>
<td>0.58</td>
<td>0.21</td>
<td>2.0%</td>
<td>0.58 [0.18, 1.0]</td>
<td>2002</td>
</tr>
<tr>
<td>Sorensen 2002 (45)</td>
<td>0.13</td>
<td>0.09</td>
<td>2.3%</td>
<td>0.13 [0.07, 0.21]</td>
<td>2003</td>
</tr>
<tr>
<td>Parnell 2008 (13)</td>
<td>0.00</td>
<td>0.01</td>
<td>2.1%</td>
<td>0.00 [-0.01, 0.01]</td>
<td>2008</td>
</tr>
<tr>
<td>Bahram 2009 (24)</td>
<td>0.14</td>
<td>0.04</td>
<td>2.7%</td>
<td>0.14 [-0.1, 0.38]</td>
<td>2009</td>
</tr>
<tr>
<td>Aepet 2011 (11)</td>
<td>0.31</td>
<td>0.14</td>
<td>2.6%</td>
<td>0.31 [-0.01, 0.63]</td>
<td>2011</td>
</tr>
<tr>
<td>Nya 2011 (19)</td>
<td>0.05</td>
<td>0.01</td>
<td>2.5%</td>
<td>0.05 [0.0, 0.1]</td>
<td>2011</td>
</tr>
<tr>
<td>Meek 2012 (12)</td>
<td>0.60</td>
<td>0.13</td>
<td>1.7%</td>
<td>0.60 [0.34, 0.86]</td>
<td>2012</td>
</tr>
</tbody>
</table>

**Heterogeneity Test: Tau² = 0.01; Chi² = 45.9, df = 16 (P < 0.00001); I² = 73%**

**Test for overall effect: Z = 3.41 (P = 0.0007)**

### Total (95% Co)

**100.0% 0.11 (0.07, 0.14)**

**Heterogeneity Test: Tau² = 0.01; Chi² = 142.37, df = 38 (P < 0.00001); I² = 73%**

**Test for overall effect: Z = 5.45 (P < 0.00001)**

**Test for subgroup differences: Chi² = 0.24, df = 1 (P = 0.62), I² = 0%**

---

**Higher sugars protective vs. Higher sugars harmful**
Relations between fructose, uric acid and hypertension in NHANES IV adolescents

\[ P = 0.01 \]
Relations between fructose, uric acid and hypertension in NHANES IV adolescents

$P = 0.0495$

Allopurinol lowers BP in obese adolescents with essential hypertension
Hazard ratio for CV mortality based on percent calories as sugar for US adult population, 1988-2006

Figure 1. Adjusted Hazard Ratio of the Usual Percent of Calories from Added Sugar for CVD Mortality Among US Adults Aged ≥20 Years – NHANES Linked Mortality Files, 1988-2006

Histogram is the distribution of usual percent of calories from added sugar in population. Lines show the adjusted HRs from Cox models. Mid-value of quintile 1 (7.5%) was the reference standard. Model was adjusted for age, sex, race/ethnicity, educational attainment, smoking status, alcohol consumption, physical activity level, family history of CVD, antihypertensive medication use, health eating index score, body mass index, systolic blood pressure, total serum cholesterol and total calories. Solid line indicates point estimates; dashed lines indicate 95% CIs. CVD indicates cardiovascular disease; HR, hazard ratio; NHANES, National Health and Nutrition Examination Survey.

Yang et al. JAMA Int. Med epub Feb 3, 2014
Sugar and Diabetes

— Confound by Obesity
— Plausibility
— Mechanisms
— Human Correlation
— Human Causation
Sugar and Diabetes: Confound by Obesity
Obesity is the problem (?)
Obesity is the problem (?)

Obesity is the problem (?)

Obesity is the problem (?)

Diabetes is NOT a subset of obesity

- Obesity is increasing worldwide by 1% per year
- Diabetes is increasing worldwide by 4% per year
“Exclusive” view of obesity and metabolic dysfunction

240 million adults in U.S.

- 72 million Obese (30%)
- 168 million Normal weight (70%)
“Exclusive” view of obesity and metabolic dysfunction

240 million adults in U.S.

72 million

Obese (30%)

Obese and sick (80% of 30%)

Total: 57 million sick

168 million

Normal weight (70%)

240 million adults in U.S.

Obese (30%)

Obese and sick (80% of 30%)

Total: 57 million sick

168 million

Normal weight (70%)
“Inclusive” view of obesity and metabolic dysfunction

240 million adults in U.S.

72 million Obese (30%)

168 million Normal weight (70%)
“Inclusive” view of obesity and metabolic dysfunction

240 million adults in U.S.

Obese (30%)

Obese and sick (80% of 30%)

72 million

57 million

Obese and sick

Normal weight (70%)

168 million

Normal weight, Metabolic dysfunction (40% of 70%)

67 million

Total: 124 million sick
Sugar and Diabetes: Plausibility
Histology of (N)AFLD

Normal (N)AFLD
MRI Fat Fraction Maps

Obese
Low Liver Fat = 2.6%
Obese
Low Liver Fat = 2.6%
MRI Fat Fraction Maps

Obese
Low Liver Fat = 2.6%

Obese
High Liver Fat = 24%
MRI Fat Fraction Maps

Obese
Low Liver Fat = 2.6%

Obese
High Liver Fat = 24%
MRI Fat Fraction Maps

Obese
Low Liver Fat = 2.6%

Obese
High Liver Fat = 24%

Thin
High Liver Fat = 23%
MRI Fat Fraction Maps

Obese
Low Liver Fat = 2.6%

Obese
High Liver Fat = 24%

Thin
High Liver Fat = 23%
NAFLD and Metabolic Syndrome are congruent (if not the same)

Adults:

Children:
Epidemiology of NAFLD

Non-alcoholic fatty liver disease (NAFLD) has become epidemic

Steatosis:
- 45% Latinos
- 33% Caucasians
- 24% African Americans

NASH
- 5.5% of US Adults

Children:
- Steatosis in 13% of autopsy specimens ages 5-19
- 38% in obese autopsy specimens

NAFLD is a primary predictor of T2DM in Korean adults

**TABLE 2.** OR for T2DM at 5-yr follow-up

|                  | T2DM -no./total no. (%) | OR (95% confidence interval) | Adjusted
d | Adjusted - baseline glucose |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No fatty liver</td>
<td>Fatty liver</td>
<td>Unadjusted</td>
<td>Adjusted</td>
</tr>
<tr>
<td>All</td>
<td>54/8120 (0.7%)</td>
<td>120/2971 (4%)</td>
<td>6.29 (4.55-8.69)</td>
<td>3.24 (2.19-4.78)</td>
</tr>
<tr>
<td>Insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quartile 1</td>
<td>13/2468 (0.5%)</td>
<td>8/307 (2.6%)</td>
<td>5.05 (2.08-12.29)</td>
<td>3.47 (1.23-9.79)</td>
</tr>
<tr>
<td>Quartile 2</td>
<td>16/2262 (0.7%)</td>
<td>6/511 (1.2%)</td>
<td>1.67 (0.65-4.28)</td>
<td>1.34 (0.46-3.87)</td>
</tr>
<tr>
<td>Quartile 3</td>
<td>11/2002 (0.6%)</td>
<td>22/768 (2.9%)</td>
<td>5.34 (2.58-11.06)</td>
<td>3.74 (1.59-8.84)</td>
</tr>
<tr>
<td>Quartile 4</td>
<td>14/1388 (1.0%)</td>
<td>84/1385 (6.1%)</td>
<td>6.34 (3.58-11.21)</td>
<td>3.31 (1.76-6.20)</td>
</tr>
</tbody>
</table>

* Adjusted for age, gender, BMI, alcohol (grams per day), education (< 16 yr, ≥ 16 yr), smoking (never or past, current), and exercise (< 1 time/wk, ≥ 1 time/wk).

Sung and Kim, J Clin Endocrinol Metab 96:1093, 2011
Intrahepatic fat explains metabolic perturbation better than visceral fat

Hepatic Insulin Sensitivity Index

Insulin Stimulated Glucose Disposal Rate

Insulin Stimulated Palmitate Suppression Rate

VLDSL Secretion Rate

Contribution Of Free Fatty Acids To VLDSL

Fabbrini et al. Proc Natl Acad Sci 106:15430, 2009
Sugar and Diabetes: Mechanisms
The first problem: Fructose is not glucose

Common wisdom: A calorie is a calorie, and “Sugar is just “empty calories”

Elliot et al. Am J Clin Nutr, 2002
Bray et al. Am J Clin Nutr, 2004
Teff et al. J Clin Endocrinol Metab, 2004
Gaby, Alt Med Rev, 2005

Le and Tappy, Curr Opin Clin Nutr Metab Care, 2006
Wei et al. J Nutr Biochem, 2006
Rutledge and Adeli, Nutr Rev, 2007
The first problem: Fructose is not glucose

Common wisdom: A calorie is a calorie, and “Sugar is just “empty calories”

But:

- Chronic fructose exposure promotes liver fat accumulation, which promotes Metabolic Syndrome

References:

Elliot et al. Am J Clin Nutr, 2002
Bray et al. Am J Clin Nutr, 2004
Teff et al. J Clin Endocrinol Metab, 2004
Gaby, Alt Med Rev, 2005
Le and Tappy, Curr Opin Clin Nutr Metab Care, 2006
Wei et al. J Nutr Biochem, 2006
Rutledge and Adeli, Nutr Rev, 2007
The first problem: Fructose is not glucose

Common wisdom: A calorie is a calorie, and “Sugar is just “empty calories”

But:

- **Chronic fructose exposure promotes liver fat accumulation, which promotes Metabolic Syndrome**

- **Chronic fructose exposure increases protein glycation, which promotes cellular and structural aging**

Elliot et al. Am J Clin Nutr, 2002
Bray et al. Am J Clin Nutr, 2004
Teff et al. J Clin Endocrinol Metab, 2004
Gaby, Alt Med Rev, 2005
Le and Tappy, Curr Opin Clin Nutr Metab Care, 2006
Wei et al. J Nutr Biochem, 2006
Rutledge and Adeli, Nutr Rev, 2007
Can you name an energy source that is:
Can you name an energy source that is:

Not necessary for life
Can you name an energy source that is:

Not necessary for life

There is no biochemical reaction in the body that requires it
Can you name an energy source that is:

Not necessary for life

There is no biochemical reaction in the body that requires it

Is not nutrition
Can you name an energy source that is:

- Not necessary for life
- There is no biochemical reaction in the body that requires it
- Is not nutrition
- When consumed in excess it is toxic
Can you name an energy source that is:

- Not necessary for life
- There is no biochemical reaction in the body that requires it
- Is not nutrition
- When consumed in excess it is toxic
- We love anyway
Can you name an energy source that is:

- Not necessary for life
- There is no biochemical reaction in the body that requires it
- Is not nutrition
- When consumed in excess it is toxic
- We love anyway

**Answer: Ethanol**
Metabolism of Ethanol

(80%) Ethanol

Ethanol → Alcohol Dehydrogenase 1B → Acetaldehyde → ROS → Inflammation → JNK1

Acetaldehyde → Aldehyde Dehydrogenase 2 → Acetyl-CoA

Acetyl-CoA → Citrate → ACCS2 → TCA cycle

TCA cycle: O2 → ATP + CO2

Acetyl-CoA → Malonyl-CoA → Fatty Acids

FFA → Lipid droplet → SREBP1

Insulin → Muscle IR

Dyslipidemia

TG
Histology of (N)AFLD

Normal

Alcohol?
Sugar?
Isocaloric fructose vs. complex carbohydrate increases intrahepatic lipid in adults

**Figure 7:** Decrease in lipids after one week on the complex-carbohydrate diet (right) after the fructose based diet (left) MRI (white box marks MRS location) & MR spectra for a subject showing: Complex-CHO based diet: lipids:water = 27% of the fructose-based diet (45).

**Figure 8:** Hepatic lipid: water for all subjects after a 7-day fructose based diet [% of values after a 7-day complex-carbohydrate diet]. The box indicates the median, first and third quartiles, with the bars indicating the extreme values (45).
The second problem
The common link

The browning reaction or Maillard reaction or non-enzymatic glycation

Instead of roasting 1 hour at 375 degrees, we slow cook at 98.6 degrees for 75 years.
Aging and costal cartilage

Courtesy Dr Baynes
The Amadori Reaction

Hemoglobin

\[ \text{Glucose} \rightarrow \text{(Schiff base)} \rightarrow \text{Hemoglobin A}_{1c} \]

NH₂

CHO

H - C - OH

H - COH

CH₂OH

N

H - C = O

H - COH

H - C - OH

H - C - OH

H - C - OH

H - C - OH

H - C - OH

H - C - OH

NH

H - C - H

H - C - OH

H - C - OH

H - C - OH

H - C - OH

H - C - OH

H - C - OH

H - C - OH

H - C - OH

H - C - OH

H - C - OH

H - C - OH

H - C - OH
Generation of reactive oxygen species by carbohydrate metabolism.
The furan ring of fructose is more unstable, so at equilibrium, fructose exists in the linear form.

\[ \text{\(\beta\)-Glucose (linear form)} \]

\[ \text{\(\alpha\)-\(\beta\)-Glucopyranose (Haworth projection)} \]

\[ \text{\(\beta\)-Fructose (linear form)} \]

\[ \text{\(\alpha\)-\(\beta\)-Fructofuranose (Haworth projection)} \]

Lim et al. Nat Rev Gastro Hepatol 7:251, 2010
Non-enzymatic glycation: fructose >> glucose

Fructose and glycation *in vitro*

<table>
<thead>
<tr>
<th>Sugar</th>
<th>Rate (/mM/hr)</th>
<th>Carbonyl (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>0.6</td>
<td>0.002</td>
</tr>
<tr>
<td>Galactose</td>
<td>2.8</td>
<td>0.02</td>
</tr>
<tr>
<td>Fructose</td>
<td>4.5</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Bunn and Higgins, Science 213:222, 1981
Association of fructose consumption with severity of steatosis and fibrosis

Sugar and Diabetes: Human Correlation
10 Most Obese States

> 30% obese
10 Most Obese States

10 Laziest States

> 30% obese

< 63% active
10 Most Obese States

10 Laziest States

10 Most Unhappy States

> 30% obese

< 63% active
10 Most Obese States

> 30% obese

10 Laziest States

< 63% active

10 Most Unhappy States

Adult Diabetes Rate

Adult Heart Disease Rate
10 Most Obese States
> 30% obese

10 Laziest States
< 63% active

10 Most Unhappy States

Adult Diabetes Rate

Adult Heart Disease Rate

Soda Per Capita
Global consumption of sugar/sugarcrops
Calories per day, 2007

Data from Food and Agriculture Organization, World Health Organization, 2007
Prevalence of diabetes, 2010
SSB’s and BMI-adjusted risk of diabetes in EPIC-Interact (Europe)

<table>
<thead>
<tr>
<th>Variable and model</th>
<th>&lt;1 glass/day/ month HR</th>
<th>1–4 glasses/day/ month HR&lt;sup&gt;b&lt;/sup&gt; (95% CI)</th>
<th>&gt;1–6 glasses/day/ week HR&lt;sup&gt;b&lt;/sup&gt; (95% CI)</th>
<th>≥1 glass/day/ day HR&lt;sup&gt;b&lt;/sup&gt; (95% CI)</th>
<th>p for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Juices and nectars (median intake, g/day)</td>
<td>(0.0)</td>
<td>(17.1)</td>
<td>(100.0)</td>
<td>(338.3)</td>
<td></td>
</tr>
<tr>
<td>No. cases</td>
<td>5,837</td>
<td>1,702</td>
<td>3,425</td>
<td>720</td>
<td></td>
</tr>
<tr>
<td>Crude model</td>
<td>1.00 (ref)</td>
<td>0.88 (0.80, 0.98)</td>
<td>0.89 (0.83, 0.94)</td>
<td>0.97 (0.85, 1.11)</td>
<td>0.64</td>
</tr>
<tr>
<td>Adjusted model</td>
<td>1.00 (ref)</td>
<td>0.91 (0.80, 1.02)</td>
<td>0.96 (0.88, 1.04)</td>
<td>1.00 (0.87, 1.15)</td>
<td>0.63</td>
</tr>
<tr>
<td>Adjusted model + EI</td>
<td>1.00 (ref)</td>
<td>0.91 (0.81, 1.02)</td>
<td>0.96 (0.88, 1.04)</td>
<td>0.99 (0.86, 1.14)</td>
<td>0.84</td>
</tr>
<tr>
<td>Adjusted model + EI + BMI</td>
<td>1.00 (ref)</td>
<td>0.97 (0.86, 1.10)</td>
<td>1.04 (0.96, 1.13)</td>
<td>1.06 (0.90, 1.25)</td>
<td>0.21</td>
</tr>
<tr>
<td>Total soft drinks (median intake, g/day)</td>
<td>(0.0)</td>
<td>(20.0)</td>
<td>(95.1)</td>
<td>(413.1)</td>
<td></td>
</tr>
<tr>
<td>No. cases</td>
<td>5,794</td>
<td>1,604</td>
<td>2,987</td>
<td>1,299</td>
<td></td>
</tr>
<tr>
<td>Crude model</td>
<td>1.00 (ref)</td>
<td>1.21 (1.07, 1.36)</td>
<td>1.30 (1.18, 1.43)</td>
<td>1.78 (1.55, 2.04)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted model</td>
<td>1.00 (ref)</td>
<td>1.21 (1.07, 1.37)</td>
<td>1.26 (1.13, 1.42)</td>
<td>1.58 (1.35, 1.84)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted model + EI</td>
<td>1.00 (ref)</td>
<td>1.21 (1.07, 1.37)</td>
<td>1.27 (1.12, 1.43)</td>
<td>1.59 (1.35, 1.88)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted model + EI + BMI</td>
<td>1.00 (ref)</td>
<td>1.17 (0.97, 1.42)</td>
<td>1.11 (0.98, 1.26)</td>
<td>1.21 (1.05, 1.41)</td>
<td>0.0005</td>
</tr>
<tr>
<td>Sugar-sweetened soft drinks (median intake, g/day)</td>
<td>(0.0)</td>
<td>(19.3)</td>
<td>(94.3)</td>
<td>(425.7)</td>
<td></td>
</tr>
<tr>
<td>No. cases</td>
<td>3,948</td>
<td>964</td>
<td>1,599</td>
<td>605</td>
<td></td>
</tr>
<tr>
<td>Crude model</td>
<td>1.00 (ref)</td>
<td>1.14 (0.97, 1.35)</td>
<td>1.16 (1.05, 1.28)</td>
<td>1.68 (1.40, 2.02)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted model</td>
<td>1.00 (ref)</td>
<td>1.13 (0.97, 1.31)</td>
<td>1.04 (0.94, 1.15)</td>
<td>1.39 (1.16, 1.67)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted model + EI</td>
<td>1.00 (ref)</td>
<td>1.12 (0.96, 1.31)</td>
<td>1.04 (0.94, 1.15)</td>
<td>1.39 (1.15, 1.69)</td>
<td>0.001</td>
</tr>
<tr>
<td>Adjusted model + EI + BMI</td>
<td>1.00 (ref)</td>
<td>1.19 (0.91, 1.56)</td>
<td>1.07 (0.94, 1.21)</td>
<td>1.29 (1.02, 1.63)</td>
<td>0.013</td>
</tr>
<tr>
<td>Artificially sweetened soft drinks (median intake, g/day)</td>
<td>(0.0)</td>
<td>(18.3)</td>
<td>(89.0)</td>
<td>(500.0)</td>
<td></td>
</tr>
<tr>
<td>No. cases</td>
<td>5,242</td>
<td>689</td>
<td>894</td>
<td>291</td>
<td></td>
</tr>
<tr>
<td>Crude model</td>
<td>1.00 (ref)</td>
<td>1.09 (0.97, 1.23)</td>
<td>1.52 (1.36, 1.69)</td>
<td>1.84 (1.52, 2.23)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted model</td>
<td>1.00 (ref)</td>
<td>1.10 (0.93, 1.29)</td>
<td>1.46 (1.29, 1.65)</td>
<td>1.93 (1.47, 2.54)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted model + EI</td>
<td>1.00 (ref)</td>
<td>1.08 (0.93, 1.26)</td>
<td>1.46 (1.29, 1.65)</td>
<td>1.88 (1.44, 2.45)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Adjusted model + EI + BMI</td>
<td>1.00 (ref)</td>
<td>1.05 (0.81, 1.35)</td>
<td>1.18 (1.03, 1.35)</td>
<td>1.13 (0.85, 1.52)</td>
<td>0.24</td>
</tr>
</tbody>
</table>
## Associations between consumption of sugar sweetened beverages and fruit juice and incident type 2 diabetes: meta-analysis of prospective cohort studies

<table>
<thead>
<tr>
<th>Sugar Sweetened Beverages (n=17)</th>
<th>Not Adjusted for Adiposity: Relative Risk</th>
<th>$I^2$</th>
<th>Adjusted for Adiposity: Relative Risk</th>
<th>$I^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta-analysis, crude:</td>
<td>1.25 (1.14 to 1.37)</td>
<td>89</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>+multivariable adjusted</td>
<td>1.18 (1.09 to 1.28)</td>
<td>89</td>
<td>1.13 (1.06 to 1.21)</td>
<td>79</td>
</tr>
<tr>
<td>+calibration for information bias</td>
<td>1.43 (1.20 to 1.70)</td>
<td>86</td>
<td>1.28 (1.12 to 1.46)</td>
<td>73</td>
</tr>
<tr>
<td>+calibration for publication bias</td>
<td>1.42 (1.19 to 1.69)</td>
<td>85</td>
<td>1.27 (1.10 to 1.46)</td>
<td>73</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Fruit Juices (n=13)</th>
<th>Not Adjusted for Adiposity: Relative Risk</th>
<th>$I^2$</th>
<th>Adjusted for Adiposity: Relative Risk</th>
<th>$I^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta-analysis, crude:</td>
<td>0.97 (0.90 to 1.06)</td>
<td>79</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>+multivariable adjusted</td>
<td>1.05 (0.99 to 1.11)</td>
<td>58</td>
<td>1.07 (1.01 to 1.14)</td>
<td>51</td>
</tr>
<tr>
<td>+calibration for information bias</td>
<td>1.06 (0.98 to 1.14)</td>
<td>49</td>
<td>1.10 (1.01 to 1.20)</td>
<td>29</td>
</tr>
<tr>
<td>+calibration for publication bias</td>
<td>Not detected</td>
<td>—</td>
<td>Not detected</td>
<td>—</td>
</tr>
</tbody>
</table>

Imamura et al. BMJ  dx.doi.org/10.1136/bmj.h3576 (epub 21 July 2015)
Adjusted\(^1\) Prevalence Odds Ratio for Metabolic Syndrome, NHANES 2005-2012

- **1st Quintile**: 30g
- **2nd Quintile**: 58g
- **3rd Quintile**: 82g
- **4th Quintile**: 113g
- **5th Quintile**: 186g

- **Prevalence Odds Ratio**:
  - 2.4
  - 5.3\(^*\)
  - 9.9\(^*\)¥
  - 8.7\(^*\)

\(^1\) Adjusted for age, BMI z-score, energy intake, and physical activity

\(^*\) Statistically significant compared to 1st quintile (p < 0.05)

\(^¥\) Statistically significant compared to 2nd quintile (Wald test, p < 0.05)

Rodriguez et al., Public Health Nutr 2016
Sugar and Diabetes: Human Causation
An international econometric analysis of diet and diabetes

Food and Agriculture Organization (FAO); FAOSTAT
Food Supply data in kcal/capita/day calculation:
Food Supply= ∑Supply Elements - ∑Utilization Elements =
(Production + Import Quantity + Stock Variation – Export Quantity)
- (Feed + Seed + Processing + Waste).
Only industrial waste factored in.

Extracted Food Supply data for 2000 and 2007:
Total Calories
Roots & Tubers, Pulses, Nuts, Vegetables
Fruits-Excluding Wine
Meat
Oils
Cereals
Sugar, Sugarcrops & Sweeteners

International Diabetes Federation (IDF)
2000 (1st ed) and 2010 (3rd ed)

The World Bank World Development Indicators Database
GDP expressed in purchasing power parity in 2005 US dollars for comparability among countries

An international econometric analysis of diet and diabetes

Diabetes prevalence rose from 5.5% to 7.0% for 175 countries 2000-2010

Effect of Sugar on Diabetes Prevalence

<table>
<thead>
<tr>
<th>Model</th>
<th># countries</th>
<th>Effect (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sugar</td>
<td>175</td>
<td>1.02 (0.82, 1.23)</td>
</tr>
<tr>
<td>Sugar+controls</td>
<td>137</td>
<td>0.63 (0.24, 1.02)</td>
</tr>
<tr>
<td>Sugar+controls+period</td>
<td>137</td>
<td>0.72 (0.34, 1.11)</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>0.90 (0.73, 1.06)</td>
</tr>
</tbody>
</table>

% change in diabetes for each 100kcal sugar/person/day

An international econometric analysis of diet and diabetes

Adjusted Association of Sugar with Diabetes Prevalence

coef = .00717465, (robust) se = .00228186, t = 3.14

An international econometric analysis of diet and diabetes

Only changes in sugar availability predicted changes in diabetes prevalence.

Every extra 150 calories increased diabetes prevalence by 0.1%.

But if those 150 calories were a can of soda, diabetes prevalence increased 11-fold, by 1.1% (95% CI 0.03 — 1.71%, p <0.001).

This study meets the Bradford Hill criteria for Causal Medical Inference:

—dose  —duration  —directionality  —precedence

We estimate that 25% of diabetes worldwide is explained by sugar.

Interventional Proof

Isocaloric Fructose Restriction and Metabolic Improvement in Children with Obesity and Metabolic Syndrome

Robert H. Lustig, Kathleen Mulligan, Susan M. Noworolski, Viva W. Tai, Michael J. Wen, Ayca Erkin-Cakmak, Alejandro Gugliucci, and Jean-Marc Schwarz

Strategy

- Isocaloric fructose restriction x 9 days in children who are habitual sugar consumers
- No change in weight
- Substitute complex carbs for sugar
- Maintain baseline macronutrient composition of the diet
- Study in PCRC at Day 0 and Day 10
- Assess changes in organ fat, de novo lipogenesis, and metabolic health
DNL is the Conversion of Dietary Carbohydrates into Lipids

New Tracer Method using MIDA: Hellerstein and Neese, AJP 1999
DNL AUC Pre and Post Fructose Restriction

Endocrine Society, March 5, 2015
Triglyceride-rich Lipoprotein DNL AUC (n=17)
Changes in liver, visceral, and subcutaneous fat 
(n = 37)
Oral glucose tolerance test before and after isocaloric fructose restriction

Lustig et al. Obesity (in press)
For pediatric subjects with hepatic steatosis (n = 25)
Change in Liver Fat and Insulin Sensitivity

Liver Fat
-30% (-50, -20); p <0.001

Composite Insulin Sensitivity Index
+0.65 (0.41, 0.88); p <0.001

Adjusted for change in weight

Lustig et al. Obesity Society, Nov. 4, 2015
## Correlation between Insulin Sensitivity & Liver Fat vs Visceral Fat

<table>
<thead>
<tr>
<th>Spearman R</th>
<th>Day 0</th>
<th>Day 10</th>
<th>Change in fat (Absolute)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Liver Fat Fraction</td>
<td>Visceral Fat</td>
<td>Liver Fat Fraction</td>
</tr>
<tr>
<td>Insulin Sensitivity (CISI) DAY 0</td>
<td>- 0.36 §</td>
<td>- 0.57*</td>
<td></td>
</tr>
<tr>
<td>Insulin Sensitivity (CISI) DAY 10</td>
<td></td>
<td>- 0.28</td>
<td>- 0.34 §</td>
</tr>
<tr>
<td>Change in Insulin sensitivity (ΔCISI)</td>
<td></td>
<td></td>
<td>- 0.54*</td>
</tr>
</tbody>
</table>

* p < 0.05  
§ 0.05 < p < 0.1

Lustig et al. Obesity Society, Nov. 4, 2015
What the data say

• Prospective correlational data demonstrate associations between added sugar and heart disease and diabetes, exclusive of calories or obesity

• Econometric data show causal medical inference for added sugar and diabetes, exclusive of calories or obesity

• Interventional isocaloric glucose for fructose exchange shows improvements in fatty liver disease, insulin resistance and metabolic health in children in 10 days, and insulin resistance is driven by liver fat
Recognition at the American Heart Association

AHA Scientific Statement

Dietary Sugars Intake and Cardiovascular Health
A Scientific Statement From the American Heart Association

Rachel K. Johnson, PhD, MPH, RD, Chair; Lawrence J. Appel, MD, MPH, FAHA; Michael Brands, PhD, FAHA; Barbara V. Howard, PhD, FAHA; Michael Lefevre, PhD, FAHA; Robert H. Lustig, MD; Frank Sacks, MD, FAHA; Lyn M. Steffen, PhD, MPH, RD, FAHA; Judith Wylie-Rosett, EdD, RD; on behalf of the American Heart Association Nutrition Committee of the Council on Nutrition, Physical Activity, and Metabolism and the Council on Epidemiology and Prevention

Recommends reduction in sugar intake from 22 tsp/day to 9 tsp/day (males) and 6 tsp/day (females)

Circulation 120:1011, 2009
How our food dollars have been reallocated

Philpott, Mother Jones 2012 (from Bureau of Labor Statistics)
An inconvenient truth

The “medical” model isn’t the medical model;

It’s the “sugar” model
U.S. Commerce Service 1822-1910, combined with Economic Research Service, USDA 1910-2010
http://ushealthcarespending.gov
Growth of Sugar Industry

Stabilization

HFCS + Sugar for Fat

Theoretical threshold based on EtOH

AHA threshold for CVD

versus US health care spending (% GDP)

U.S. Commerce Service 1822-1910, combined with Economic Research Service, USDA 1910-2010

http://ushealthcarespending.gov
ESPECIALISTAS PROponen un IMPUESTO Más ALTO a REFrescos

octubre 16, 2013

La organización civil el Poder del Consumidor y especialistas recomendaron imponer un gravamen de dos pesos a las bebidas azucaradas, a fin de disminuir su consumo y evitar daños en la salud como el sobrepeso y la diabetes.
YES ON D

Berkeley vs. Big Soda

Paid for by Yes on Measure D, Healthy Child Initiative Ballot Measure Committee.
Diabetes experts tell G20 to tax sugar to save lives and money

BY BEN HIRSCHLER

Diabetes experts called on world leaders on Thursday to use sugar taxes to fight obesity, arguing such a move would save lives and slash healthcare budgets.

Ahead of a meeting of G20 leaders this weekend, the International Diabetes Federation (IDF) wants the dual epidemics of obesity and diabetes to be placed on the global agenda alongside major geopolitical and financial issues.
George Osborne unveils sugar tax in eighth budget as growth forecast falls

- Proceeds of levy on soft drinks to fund school sports
- Cuts to business rates, capital gains and corporation tax
- Income tax personal allowance increased
- Growth forecast down from 2.4% to 2%

Katie Allen, Anushka Asthana and Rowena Mason

Wednesday 16 March 2016 10.58 EDT

George Osborne has unveiled a new tax on sugary drinks, such as Coca-Cola, Red Bull and Irn Bru, pledging to use the takings to provide more sports funding for schools.
Policy Efforts in Northern California: SSB Distributor Tax

Join the Movement:
Endorse
Contribute
Share on Social Media

Oakland:
www.yes4healthyoaklandchildren.com
San Francisco
www.sfunitedtoreducediabetes.com
Proposal #1

UCSF Healthy Beverage Initiative
Proposal #2

Type 2 Diabetes should be renamed:

PROCESSED FOOD DISEASE
Proposal #3

Rollback the subsidies for processed food:

CORN
WHEAT
SOY
SUGAR
Proposal #4

REAL FOOD APPROVED
Proposal #5

Remove Sugar from the FDA
“Generally Recognized as Safe” (GRAS) List
Conclusions

• The dentists knew about fructose/sugar toxicity long before the doctors did, but fluoride allowed for “selective amnesia”

• Although dietary fat can induce NAFLD, fat ingestion does not explain the current epidemic of NAFLD/NASH; but fructose does

• A calorie is NOT a calorie, and fructose is NOT glucose

• Fructose is “alcohol without the buzz”; it is a dose-dependent chronic hepatotoxin; NASH and ASH share the same pathogenesis

• Evolution doesn’t lie: the overlap between tooth and silver decay inform us about the changes in our environment, and what to do about them

• But understanding the science often doesn’t translate into policy
Released November 10, 2014
SUGARSCIENCE.ORG

Outdoor

Hidden sugar is like a ticking time bomb.
Fed Up blows the lid off everything we thought we knew about food and weight loss, revealing a 30-year campaign by the food industry, aided by the U.S. government, to mislead and confuse the American public, resulting in one of the largest health epidemics in history.
Canadian Documentary  On NETFLIX
SWEET REVENGE
TURNING THE TABLES ON PROCESSED FOOD

Featuring New York Times Bestselling Author
Robert H. Lustig, MD, MSL
Professor of Pediatrics
Division of Endocrinology
University of California, San Francisco
President, Institute for Responsible Nutrition

AS SEEN ON PUBLIC TELEVISION

Public Television Special, USA
Now also in Spanish
“Dulce Venganza”
We have started a non-profit to provide medical, nutritional and legal analysis and consultation to promote personal and public health vs. Big Food.

responsiblefoods.org
Collaborators

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