The Sugar “Maize”: Sugar, High Fructose Corn Syrup, Obesity and Metabolic Risk: From Genes to Policy

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Brief History of Sugar (sucrose)

- 8,000 BC - first domestication of sugar cane
- 400 BC - first written mention of sugar in Indian literature referring to use in sweet puddings and drinks
- 500 AD - evidence of sugar making in India
- 400-800 AD - major production of sugar spreads west from India across the Persian Gulf to Arab countries
- 1000 AD - sugar spread to Europe through the Arab conquest
- 1200 - medicinal use of sugar
Brief History of Sugar (sucrose)

• 16th century - production centered in the Mediterranean and Atlantic Islands
• 1650 - Major sugar consumption among English nobility and wealthy
• 1800 - sugar has become a necessity of the diet
• 1900 - sugar supplies 20% of calories in the English diet
• 1957 - development of high fructose corn syrup
• 1970 onwards - proliferation of HFCS and sugar in the diet correlated with increases in obesity
$10 BILLION IS SPENT ANNUALLY ADVERTISING FOOD AND BEVERAGES TO CHILDREN; $500 MILLION ON SUGARY BEVERAGES

IOM, 2005

FTC, 2008
17 teaspoons
Amount of sugar in a 20-oz serving

41 percent
Kids age 2-11 that drink at least 1 soda per day

62 percent
Kids aged 12-17 who drink at least 1 soda per day

39 pounds
Amount of sugar consumed in 1 year from 1 soda per day
venti frappuccino with whipped cream
89g sugars
(17 teaspoons)
US sugar consumption
= 70kg/person/year

if you stacked all the sugar as cubes from 1 day of sugar consumption in the US it would tower half way to the moon
Ounces of Prevention — The Public Policy Case for Taxes on Sugared Beverages

Kelly D. Brownell, Ph.D., and Thomas R. Frieden, M.D., M.P.H.

A couple of local ballot measures in the US have failed. The beverage industry has lobbied hard against them.

One study has projected that even a 20% tax on sodas would only lead to a long-term weight loss of 3 pounds.

Legislation - Soda Tax?
mechanisms
Mechanisms Linking Increased Sugar to Negative Health Outcomes: The Double Edged Sword

- Sugars (esp fructose)
- Obesity
- Metabolic syndrome
- Insulin resistance
- Fatty liver
- Dyslipidemia
- Metabolic disruption
- Inflammation
why has high sugar become such an important issue in terms of obesity and metabolic outcomes?

1. trends in food and beverage consumption; related to economics
2. advent and proliferation of high fructose corn syrup
3. exacerbation of effects of sugars on metabolism in the obese state
4. earlier introduction of fructose in the diet from sugar (glucose + fructose) relative to breastfeeding (lactose = glucose+galactose)
Per Capita US Trends in Calories from Beverages

Duffy & Popkin: Obesity, 2007
advent of High Fructose Corn Syrup: different from sugar
Consumer Price Index - Sodas are a good deal
6.5 oz (1920s)  
12 oz (1960s)  
20 oz (1990s)  
33 oz (1L) Today

10 teaspoons sugar
27 teaspoons sugar
As you become more obese and insulin resistant, the demand on beta-cells to secrete insulin in response to glucose, rises exponentially.
Adjusted HOMA-IR by Intake of Added Sugars in US Adolescents

Copyright © American Heart Association
Sugar and obesity: the evidence
Sugar Sweetened Beverages and Obesity in Children: Key Prospective Studies

  - 19 month study of 548 middle school students
  - Every additional serving of per day increased risk of obesity by 60%

  - 1 year study of 10,904 children ages 2 to 3 years
  - Children were 2-times more likely to become or remain overweight if they drank sugar-sweetened beverages
Sugar Sweetened Beverages and Obesity in Children: Key Intervention Studies


• Randomized controlled trial, 600 children 7 - 11 yr
• Educational program designed to eliminate all “fizzy drinks” (including non-nutritively sweetened)
• Consumption differed between groups by < 2 oz per day
• Incidence of overweight/obesity significantly lower in the intervention group: 0.2 vs 7.7%
• 6-month randomized controlled trial of 103 normal weight and overweight adolescents
• Delivery of non-sugar sweetened beverages to participants homes (to replace regular beverages)
• Sugar-sweetened beverages decreased by 82% vs no change among controls (p < 0.0001)
• Among overweight/obese participants, BMI was 0.75 BMI units less in the intervention group, p = 0.03
Ebbeling et al; NEJM 2012

- 224 overweight & obese adolescents (mean age ~15 years)
- 1-year intervention to reduce caloric-sweetened beverages followed by 1-year follow-up
- Main outcome body weight and BMI
<table>
<thead>
<tr>
<th>Servings/day of CSB</th>
<th>Treatment</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.60</td>
<td>0.86</td>
<td>0.88</td>
</tr>
<tr>
<td>1.20</td>
<td>0.85</td>
<td>0.88</td>
</tr>
<tr>
<td>1.00</td>
<td>0.85</td>
<td>0.88</td>
</tr>
<tr>
<td>0.80</td>
<td>0.85</td>
<td>0.88</td>
</tr>
<tr>
<td>0.60</td>
<td>0.85</td>
<td>0.88</td>
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**Body weight (kg)**

<table>
<thead>
<tr>
<th>Baseline</th>
<th>1 Year</th>
<th>2 Year</th>
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<tbody>
<tr>
<td>85.0</td>
<td>86.6</td>
<td>88.2</td>
</tr>
<tr>
<td>89.8</td>
<td>91.4</td>
<td>93.0</td>
</tr>
</tbody>
</table>

Small treatment effect at 1-year; not sustained after 1-Year follow-up.
~10kg reduced weight gain in Hispanics sustained over 2 years

Ebbeling et al, NEJM 2012
sugar and fatty liver disease
Spectrum of NAFLD

Diet, genes, cellular factors and food policy
NAFLD in Children

- Autopsy study of 742 children aged 2-19 years by Schwimmer et al 2006
- Fatty liver defined by liver fat >5%
- Overall prevalence = 13%
- African American (1.5%); Whites (8.6%); Asian (10.2%); Hispanic (11.8%)
- Prevalence in obese children = 38%
Genetics of Fatty Liver

- A recent GWAS in adults from the Dallas Heart Study at UT Southwestern identified an amino-acid substitution (C to G) in the PNPLA3 gene associated with 2-fold higher liver fat
- Effect strongest in Hispanics in whom the frequency of the variant was much higher (49%) than African Americans (10%)
- Aim was to examine if the effect of this gene was manifested in a pediatric population
Liver Fat Fraction by Ethnicity & Genotype

- African American:
  - -ve for gene: n=61
  - -/+ for gene: n=11
  - +ve for gene: n=0

- Hispanic:
  - -ve for gene: n=45
  - -/+ for gene: n=90
  - +ve for gene: n=53
Liver Fat Fraction in 8-10 year olds

Goran et al; Diabetes 2010
PNPLA3 Gene * Diet Interaction
Davis et al, AJCN 2010

CC Genotype

CG Genotype

GG Genotype

Liver Fat Fraction (%)
Sugar Intake (% Kcal/d)
sugar in early life
1483 Latino children (2 to 4 yrs) from WIC LA County

Completed early life nutrition measures on breastfeeding and SSB intake - 2008

height/weight/BMI data

Multinominal regressions – differences in prevalence of ow/ob in children between BF and SSB categories
Combined Effects of Low Breastfeeding and High Sugar Consumption

Davis et al; AJCN 20012
Other Animal Studies

- Sugars and especially fructose programs for obesity and metabolic risk starting with exposure in utero and during breastfeeding
- Fructose affects fat cell and hypothalamic development in ways that favor obesity
high fructose corn syrup (HFCS)

HFCS magnifies many of the worst aspects of table sugar (sugar on steroids)
Sucrose versus HFCS

Sucrose = $\text{C}_{12}\text{H}_{22}\text{O}_{11}$

Glucose-fructose

Purified from sugar cane or beets

HFCS

Made from corn starch through conversion of sugars

Typically 55% fructose, 40% glucose, 5% other sugars;

Can be 90% fructose

Advantages in food production:

Cheaper, more stable, makes food more appealing
Glucose versus Fructose

- Glucose and fructose are structurally very similar but functionally very different sugars
  - Fructose is much sweeter
  - has a specific absorption in the gut; in high doses can get fructose malabsorption with GI symptoms
  - it is metabolized almost entirely in the liver where it can be a substrate for new fat synthesis in the liver
  - does not stimulate insulin release therefore less well regulated
Differential Effects of Fructose vs Glucose

Fructose

Triose-P

TG

Liver Fat

Insulin resistance

Fructose

DNL

VLDL-TG

NEFA

Insulin

Glucose

Glucose

CO2

IMCL

DNL

Insulin resistance
Fructose as a % of Sugars in Popular Drinks

Suggests HFCS is 65:35

Fructose intake ~18% higher than assumed from label and 30% higher than soda made with sucrose
Other Sugars

- Agave - mostly all fructose
- Fructose itself being used as a sweetener now in many yoghurts
- “Fruit sugar” on a label probably means fructose
- Juices from fruit probably very high in fructose and likely to have a higher fructose load than a soda made with HFCS
Fructose versus Glucose in Foods

- 50g sugar
  - 25g fructose/25g glucose (sucrose)
  - 28g fructose/22g glucose (HFCS 55)
  - 33g fructose/17g glucose (HFCS 65)

- 15g Fructose + other dietary benefits
  - fiber, antioxidants

Keck School of Medicine
USC

Childhood Obesity Research Center
**Implication:**
fructose consumption might be higher than we think and contributing to obesity and obesity complications like NAFLD

**Policy Implication:**
Need better label information on fructose content of foods and beverages
Global Influence of Dietary Sugar & HFCS on Obesity & Diabetes

Goran et al
Global Public Health, 2012
# Global Implications: Data from 170 Countries

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Prevalence (%)</td>
<td>6.8 ± 3.0</td>
<td>1.6 - 18.7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.9 ± 2.3</td>
<td>20.1 - 31.1</td>
</tr>
<tr>
<td>Total Intake (kcal/day per capita)</td>
<td>2711 ± 510</td>
<td>1559 - 3781</td>
</tr>
<tr>
<td>Total Sugar (kg/day per capita)</td>
<td>29.8 ± 16.0</td>
<td>2.2 - 68.6</td>
</tr>
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Goran et al; in preparation
Global Influence of Sugar on Diabetes

Saudi Arabia

USA

r = 0.55; p<0.001
Dietary Sugar is Associated with Obesity and Diabetes

- Obesity
  - Sugar: $r=0.70, p<0.0001$
  - Diabetes: $r=0.58, p<0.0001$

- Sugar
  - Diabetes: $r=0.54, p<0.0001$

- Controlling for obesity: $r=0.23, p=0.003$
Global Pattern in HFCS Use

High Fructose Corn Syrup (kg/capita per year)

Zero or < 0.5kg per capita/year: Australia, China, Cyprus, Czech Republic, Denmark, Estonia, France, India, Indonesia, Ireland, Italy, Latvia, Lithuania, Luxemburg, Malta, Netherlands, Romania, Slovenia, Sweden, United Kingdom, Uruguay
<table>
<thead>
<tr>
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<th>Countries not Using HFCS (n=22)</th>
<th>Countries Using HFCS (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>25.5 ± 1.6</td>
<td>25.9 ± 1.4</td>
</tr>
<tr>
<td>Total Intake (kcal/day per capita)</td>
<td>3230 ± 377</td>
<td>3221 ± 365</td>
</tr>
<tr>
<td>Total Sugar (kg/day per capita)</td>
<td>38.2 ± 12.8</td>
<td>39.9 ± 11.3</td>
</tr>
<tr>
<td>HFCS (kg/day per capita)</td>
<td>0.1 ± 0.2</td>
<td>5.8 ± 6.1</td>
</tr>
<tr>
<td>Diabetes Prevalence (%)</td>
<td>6.7 ± 1.3</td>
<td>7.9 ± 1.8</td>
</tr>
<tr>
<td>Fasting Glucose (mmol/L)</td>
<td>5.23 ± 0.17</td>
<td>5.33 ± 0.17</td>
</tr>
</tbody>
</table>
sugar → obesity → Diabetes 

high fructose corn syrup

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HFCS Exports from the US to Mexico

Year

Metric tons of HFCS-55 and above
0 200000 400000 600000 800000 1000000

- All US Exports
- US Exports to Mexico
- All Imports to Mexico

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Policy Implications:
EU policy on HFCS quotas and their trading between countries may be a factor influencing that countries public health.

Trade policy between countries in sugar and HFCS may be a factor driving public health.
Africa: Coke’s Last Frontier

Cover story in Bloomberg Businessweek, Nov 1, 2010

- Per Capita consumption of coke in Kenya = 39 servings
- Mexico = 665 servings (highest in the world)
- Coke sales stagnant in developed countries (in the US: $2.6b in 1989 vs $2.9b in 1999)
- Coke plans to invest $12b in Africa in next 10 years.
Global Consumption of Coke

Mexico = 665 servings
(highest in the world)
Hispanics: A “perfect storm” for Fatty Liver

- High prevalence of GG Genotype in PNPLA3
- Obesity
- PNPLA3* sugar interaction
- Liver disease
- Liver cancer
- Insulin resistance
- Type 2 diabetes
- Exponential increase in HFCS export to Mexico
- High sugar consumption: Mexico has highest consumption of coca-cola in the world
Simple Tips

• Avoid products with high fructose corn syrup
• Replace sugary drinks with water or dilute juice with water (50:50)
• Avoid foods with >10g sugar per serving
• Avoid flavored milk
• Watch for “hidden” sugar which can be high in surprising products (eg yogurts, breads)
Summary

• Sugar is a contributing factor to obesity and related outcomes

• Double-edged sword: effects of sugar on obesity and separate effects on metabolic outcomes like diabetes

• Not all sugars are equal in their health effects - fructose is more damaging because of the way it is metabolized

• Dietary fructose is increasing because of HFCS - fructose content of foods made with HFCS is higher than we think

• The more we tip the balance towards increasing fructose, the greater the metabolic problems (diabetes, gout, hypertension)
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