From fruit flies to fruit juice. Exploring the complex causes of obesity
“Remember when we used to have to fatten the kids up first?”
The Problem is Not Entirely New.

“In relative terms, then, obesity was spreading at least as fast at the beginning of the twentieth century as at the end of the twentieth century.”

Central Thesis

Everyday experiences with obesity-related phenomena exacerbate social/philosophical biases causing us to be unduly confident in some putative explanations and solutions and to overlook others.
Outline

• Genetic & environmental influences within populations

• Some *populist putative* explanations for the population increase

• Some less discussed putative explanations for the population increase

• What should we do or should we do anything?
Changes in Pig Backfat and Human Mean BMI

Year for Pig Data

Changes in Pig Backfat (mm) since 1980

Year for Human Data

Changes in Human Mean BMI since 1960

Pig (Canadian Yorkshire) data from the Canadian Swine Breeders Association.
Human data from The National Health and Nutrition Examination Surveys.
EFFECT of ENVIRONMENT

Pima in Arizona

Pima in Mexico
Environmental Influences

"As some day it may happen that a victim must be found, I've got a little list..."

The Mikado
Libretto by William S. Gilbert,
Music by Sir Arthur Sullivan,
Sung by Ko-Ko and Chorus
Results: Lower real prices for vegetables and fruits were found to predict a significantly lower gain in BMI between kindergarten and third grade; half of that effect was found between kindergarten and first grade. Lower meat prices had the opposite effect, although this effect was generally smaller in magnitude and was insignificant for BMI gain over 3 years. Differences across subgroups were not statistically significant due to smaller sample sizes in subgroup analyses, but the estimated effects were meaningfully larger for children in poverty, children already at risk for overweight or overweight in kindergarten, and Asian and Hispanic children. There were no significant effects for dairy or fast-food prices, nor for outlet density, once we had controlled for individual characteristics and random intercepts to adjust standard errors for the sampling design.

Sturm R, Datar A. Body mass index in elementary school children, metropolitan area food prices and food outlet density. Public Health. 2005 Sep 2; [Epub ahead of print]

Key Points
1. Numerator of one is denominator of other.
2. Scaled to energy content, not serving size.
The Pecuniary Economy of Food

“There is no true economy in saving twenty-five cents’ worth of nutriment when the time it requires is worth in other directions a greater sum. Many waste food because they will not or can not take the time for the proper preparation of the cheaper sorts. To make the most economical use of food requires time and trouble. It is easier to broil the toothsome sirloin or porter-house than to boil or stew some cheaper cut. We find that the wife of the coal-laborer who furnished his family the best of every thing on seven dollars a week, “had to cook before six in the morning, or after half-past six at night, because she worked all day in the factory.” Her time was worth more in the factory than in the home. This probably accounts in some measure for the waste on the part of wage-earners, the balance being attributed to ignorance, or, as Professor Atwater puts it, ‘innocently committing an immense economical and hygienic blunder.’

Necessity is the mother of invention,” and therefore we believe that when time is of less value in the United States than at present, and there is greater necessity for economy in the use of food, the average American will lead in getting the maximum amount of proteine at the minimum of cost.”
Environmental Effects may be Paradoxical

Consider Fat Storage in *Parus major*

- *Parus major* (and many other birds) *increase* their fat reserves when food is scarce and variable.
- This effect is primarily among birds low in the social hierarchy.


Consider Fat Storage in Humans (*homo sapiens*)

- Humans of lower SES report more frequent food insecurity.
- Humans of lower SES tend to have *increased* fat reserves.


What might this say about proposals to restrict access to foods as a public health strategy?
Genetic Factors Influencing Obesity
The sons of Israel said to them, “Would that we had died by the LORD’S hand in the land of Egypt, when we sat by the pots of meat, when we ate bread to the full; for you have brought us out into this wilderness to kill this whole assembly with hunger.”

- Exodus 16 Verse 3
Among 296 couples prior to marriage, the intermate correlation for BMI was .13.
How Heritable is BMI?

♦ What the behavioral psychologists like to report: Family & Adoption Studies ~ 25 to 50% (c.f., Maes et al., 1997, Behavior genetics)

♦ What the molecular geneticists like to report: Ordinary Twin Studies ~ 50 to 85% (c.f., Maes et al., 1997, Behavior genetics)

Best Estimates

♦ MZAs ~ 70% (Allison et al., 1997, Int J Obesity).
Specific genes
Bayesian QTL Mapping and Deficiency Complementation

Fine Mapping led to:

- *Tout velu* a significant influence of TAG and PRO levels

Work led by Maria De Luca at UAB.
Tg737 Conditional Mutant (Tamoxifen inducible actin)

Red – Tg737<sup>loxP/null</sup>:CAGG-creER
Males (top) or Females (bottom)
Black – Tg737<sup>loxP/wt</sup>:CAGG-creER
Males (top) or Females (bottom)

Body Weight (g)

Weeks Post Initial Tamoxifen Injection

Slide Courtesy Brad Yoder UAB
POMC - factors that contribute to obesity

A fat "knockout" mouse that lacks the gene that encodes pro-opiomelanocortin (POMC)—shown with its normal littermate—is providing new insights into the factors that contribute to obesity.

(Photo credit: Nature Medicine)

Stephenson J. Knockout science: chubby mice provide new insights into obesity. JAMA. 1999 Oct 27;282(16):1507-8
POMC mutations in humans

Mutation in the gene encoding Myostatin

http://www.bbc.co.uk/science/genes/gene_safari/wild_west/bigger_and_better02.shtml

Transience of Typical Within-Population Environmental Effects


Ob: An example of an obesity gene affecting weight through behavior

Adapted from Bray (1996)
Clear Evidence for a Genetic Influence on Spontaneous Physical Activity

“We used selective breeding to increase levels of voluntary wheel running... After 13 generations, mice from selected lines ran 2.2 times as many revolutions per day as controls... This increase was caused primarily by mice from selected lines running faster, not more minutes per day...”

### Clear Evidence for a Genetic Influence on Food Intake by Selective Breeding

<table>
<thead>
<tr>
<th>Animal</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouse</td>
<td>Meyer &amp; Hill; (1991); Parker &amp; Bhatti (1982)</td>
</tr>
<tr>
<td>Chicken</td>
<td>Pym &amp; Nicholls (1979); O'Sullivan et al (1992)</td>
</tr>
<tr>
<td>Ducks</td>
<td>Farhat &amp; Chavaz (1999)</td>
</tr>
<tr>
<td>Quail</td>
<td>Marks (1996)</td>
</tr>
<tr>
<td>Pigs</td>
<td>Cameron et al (2000); Vangen (1980)</td>
</tr>
<tr>
<td>Cattle</td>
<td>Aass, &amp; Vangen (1997)</td>
</tr>
</tbody>
</table>
An example of a Gene x Environment interaction effecting food intake.

Amount of cued (black bars) and non-cued (open bars) food eaten (mean±SEM) in the social transmission of food preference.

Mayeux-Portas et al. (2000). Mice lacking the cell adhesion molecule Thy-1 fail to use socially transmitted cues to direct their choice of food. *Current Biology, 10* (2), 68-75.
Genetic Influences on Ad Lib Human Eating: A Twin Study

$h^2 = 33\%$

$c^2 = 48\%$

$e^2 = 19\%$

Outline

• Genetic & environmental influences within populations

• Some *populist putative* explanations for the population increase

• Review of some less discussed putative explanations for the population increase

• What should we do or should we do anything?
The ‘Big Two’ Usual Suspects

1. Food Marketing Practices

2. Institutionally and technologically driven reductions in physical activity

- Evidence mainly comes from ecological correlations and hypothesized mechanisms of action.
- Evidence from epidemiological and experimental studies is weak and inconsistent and in some cases refuting.
- Probably important to some extent, but almost certainly not omnipotent.
Too strong or too feeble, as regards the digestive power of the individual considered, the proportion of the carbohydrates exerts an influence either upon its own digestibility or upon that of the albuminoids which accompany it; and in either case it has a depressing effect upon digestion. But, as regards a regimen preventive or remedial of obesity, the case is different. It is evident, that, if the formation of fat is dependent upon carbohydrates, a diet composed largely of them, so often practised, can only be an error so far as obesity is concerned.

Weight change not predicted via snack food intake

**Method:** Prospective study of 8203 girls and 6774 boys, 9 – 14 y of age in 1996, in an ongoing cohort study who completed at least two questionnaires between 1996 and 1999. Intake of snack foods was assessed in 1996 – 1998 with validated food frequency questionnaire designed specifically for children and adolescents. The outcome measure was change in age- and gender-specific z-score of body mass index (BMI).

**Results:** After controlling for Tanner stage of development, age, height change, activity, and inactivity, there was no relation between intake of snack foods and subsequent changes in BMI z-score among the boys ($\beta = -0.004$), but snack foods had a weak inverse association ($\beta = -0.007$, $P < 0.05$) with weight change among the girls. After controlling for dieting status and whether the mother was overweight, the association between servings per day of snack foods and subsequent changes in BMI z-score were not significant in either gender.

**Discussion:** Our results suggest that although snack foods may have low nutritional value, they were not an important independent determinant of weight gain among children and adolescents.

Food Intake Surveys: The Basic Problem

“Southwest Airlines doesn’t offer food, but in surveys it is consistently rated as serving good meals.”

Glenn Engel, N. Y. Times, 2/10/02

Slide courtesy Denny Bier
Beverages

HFCS; Artificial Sweeteners, Sugar-Sweetened Beverages; Liquid Calories
Foods and beverages that are restricted from sale to students are classified in the following four categories:

1. **Soda Water-** Any carbonated beverage. No product shall be excluded from this definition because it contains discrete nutrients added to the food such as vitamins, minerals, or proteins. **NO CARBONATED DRINKS ARE PERMITTED.**

[emphasis in original]

“In God We Trust... All Others Bring Data.”

- T-shirt sold by the American Statistical Association
The effect of aspartame as part of a multidisciplinary weight-control program on short- and long-term control of body weight.


163 obese women randomly assigned to consume or to abstain from aspartame-sweetened foods and beverages during 16 wk of a 19-wk weight-reduction program (active weight loss), a 1-y maintenance program, and a 2-y follow-up period.

- Women in both treatment groups lost approximately 10% of initial body weight (10 kg) during active weight loss.
- In the aspartame-treatment group, aspartame intake was positively correlated with percentage weight loss during active weight loss (r = 0.32, P < 0.01).

- Participants in the aspartame group experienced a 2.6% (2.6 kg) and 4.6% (4.6 kg) regain of initial body weight after 71 and 175 wk, respectively, whereas those in the no-aspartame group gained an average of 5.4% (5.4 kg) and 9.4% (9.4 kg), respectively.
- The aspartame group lost significantly more weight overall (P = 0.028) and regained significantly less weight during maintenance and follow-up (P = 0.046) than did the no-aspartame group.
Energy Intake
(N=40)

<table>
<thead>
<tr>
<th>Carbohydrate</th>
<th>Fat</th>
<th>Protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Watermelon)</td>
<td>(Coconut)</td>
<td>(Dairy)</td>
</tr>
</tbody>
</table>

- Carbohydrate: *
- Fat: *
- Protein: *

*Kcals*
Sugar-Sweetened Beverages: Growth & Life on a Diet of Chocolate Milk

No effect of feeding chocolate vs regular milk as the sole diet in Sprague-Dawley rats for 4 weeks (and 16 weeks, data not shown).

“Results…show that animals can be raised on a diet consisting solely of mineralized chocolate milk without any ill effect.”

Obesity & Sugar Sweetened Beverages?

“The role of sugar-sweetened beverages (SSBs) in promoting obesity is controversial…randomized, controlled trials are lacking and necessary to resolve the debate.”

“The only pediatric trial to date, James et al …change in BMI did not differ between groups…”

“[For BMI in our study] …net difference…was not significant overall.” [post-hoc subgroup analyses did show significant result].

Physical Education and Physical Activity
Objective: To review the empirical evidence of associations between television (TV) viewing, video/computer game use and (1) body fatness, and (b) physical activity.

Design: Meta-analysis

Method: ...Included studies presented at least one empirical association between TV viewing, video/computer game use and body fatness or physical activity among samples of children and youth aged 3 – 18 y.

Main outcome measure: The mean sample-weighted corrected effect size (Pearson r).

Results: Based on data from 52 independent samples, the mean sample-weighted effect size between TV viewing and body fatness was 0.066 (95% CL = 0.056 – 0.078; total N = 44707). The sample-weighted fully corrected effect size was 0.084.

Conclusion: A statistically significant relationship exists between TV viewing and body fatness among children and youth although it is likely to be too small to be of substantial clinical relevance.
“…numerous public health and education institutions including the Centers of Disease Control and Prevention (CDC), American Academy of Pediatrics (AAP), Institute of Medicine (IOM), and the National Association for Sport and Physical Education (NASPE) [14, 19-22] have called for increased daily PE for obesity prevention.” Baskin & Allison (submitted).

However, among 273 respondents in a national survey, child BMI was unrelated to frequency of participation in PE (Baskin & Allison, submitted).
Childhood Obesity — What We Can Learn From Existing Data on Societal Trends, Part 2

Roland Sturm, PhD

Figure 2. Changes in time (in minutes per week) spent on activities between 1981 to 1997 by U.S. children aged three to 12 years. Calculations based on data from Hofferth and Sandberg (5).
Race/ethnicity-specific average BMI growth among children

**Results.** Growth in BMI was typically faster and more variable during summer vacation than during the kindergarten and first-grade school years.

**Conclusions.** Although a school's diet and exercise policies may be less than ideal, it appears that early school environments contribute less to obesity than do nonschool environments.

FIGURE 2—Race/ethnicity-specific average body mass index (BMI) growth among children who were comparable on other variables: Early Childhood Longitudinal Study, Kindergarten Cohort, 1998-2000.
A shortage of credible information exists on practical dietary and physical activity patterns that have potential to reverse the national obesity epidemic and reduce the risk of major cancers and other chronic diseases.

Environmental Effects are Difficult to Predict

**Caballero et al.**

Pathways: a school-based, randomized controlled trial for the prevention of obesity in American Indian schoolchildren.

**Am. J. Clinical Nutrition, Nov 2003; 78: 1030 - 1038.**

**FIGURES.** Frequency distribution of BMI at follow-up for girls in the intervention (-----) and control (----) groups from the Pathways Study. The distribution from the Centers for Disease Control and Prevention's 2000 growth charts reference population is also depicted (--.--).
Outline

• Genetic & environmental influences within populations

• Some *populist putative* explanations for the population increase

• Some less discussed putative explanations for the population increase

• What should we do or should we do anything?
In the recent past the human gene pool hasn’t changed much … But, our genotype frequencies may have.

Hypothetical Data: Increasing Prevalence of Obesity as a Result of Assortative Mating

Redden & Allison (2006; Behavior Genetics)
Potential Endurance and Lagged Effects of Population-Level Environmental Changes

3 Groups of Female Rats across 3 Generations

Naturally Nursed  Gastric Control  Gastric Overfed

F1  A ≈ B < C
F2  A ≈ B > C
F3  A ≈ B < C


Woman/Grandmother
Fetus/mother
Oocyte/Child
### Table 5 Characteristics of twin sample ($n = 28$ pairs), Study 2

<table>
<thead>
<tr>
<th></th>
<th>Antibody positive</th>
<th>Antibody negative</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>33.0 ± 15.7</td>
<td>33.0 ± 15.7</td>
</tr>
<tr>
<td>Sex (% female/male)</td>
<td>79/21</td>
<td>79/21</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.1 ± 9.8</td>
<td>24.5 ± 9.5*</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>29.6 ± 9.5</td>
<td>27.5 ± 9.9*</td>
</tr>
<tr>
<td>Cholesterol (mmol/l)</td>
<td>4.73 ± 1.37</td>
<td>4.75 ± 1.26</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)^a</td>
<td>1.48 ± 0.59</td>
<td>1.48 ± 0.42</td>
</tr>
</tbody>
</table>

± Standard deviation. *$P<0.04$ vs antibody positive. ^aTriglycerides measured on only 16 of the twin pairs because the others were not fasting.
**Hours of Sleep & Children’s predicted standardized BMI**

*Figure 3. Hours of sleep a night at Time 1 and children’s predicted standardized body mass index (BMI) at Time 2.*

Snell EK, Adam EK, Duncan GJ. Sleep and the body mass index and overweight status of children and adolescents. Child Dev. 2007 Jan-Feb;78(1):309-23
Antipsychotic use among US young people has risen sixfold.

Source: Archives of General Psychiatry

Red Hot & Cool.

Average Internal Home Temperature (Fahrenheit) in the UK.

- 13° C in 1970
- 18° C in 2000
- 55.4°F in 1970
- 64.4°F in 2000

Percent of US Households with Central vs No A/C


From:
http://www.eia.doe.gov/emeu/reps/appli/us_table.html
Enter the Zone. (the thermoneutral zone)

Feeding Growing-Finishing Pigs to Maximize Lean Growth Rate. RD. Coffey et al.

From: http://www.genome.iastate.edu/edu/PIH/prod_grow_finish.pdf

Figure 1. Effect of environmental temperature on growing-finishling pig performance
Making Pseudo-Sense of Nonsense

Sources
http://www.ojp.usdoj.gov/bjs/glance/tables/fedipctab.htm
http://www.eeoc.gov/stats/harass.html
http://auctions.bloodhorse.com/history/

\[ R = .96 \]
\[ p = .001 \]
Outline

• Prevalence

• Genetic & environmental influences within populations

• Review of some *populist putative* explanations for the population increase

• review of some less discussed putative explanations for the population increase

• What should we do or should we do anything?
## Summary Evidence Regarding Macrolevel Environmental Approaches to the Problems of Food, Eating, and Obesity

<table>
<thead>
<tr>
<th>Research Question</th>
<th>Outcome</th>
<th>Evidence Category</th>
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<tbody>
<tr>
<td>Effects of taxing or subsidizing food</td>
<td>Food purchase</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>Food intake</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>Body weight</td>
<td>D</td>
</tr>
<tr>
<td>Effects of manipulating rapidity and ease with which food are obtained</td>
<td>Food purchase</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>Food intake</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>Body weight</td>
<td>B for randomized trials, but D for general population studies</td>
</tr>
<tr>
<td>Effects of restricting access to foods</td>
<td>Food purchase</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>Food intake</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>Body weight</td>
<td>D</td>
</tr>
</tbody>
</table>

Who Could Disagree with Trying to Prevent Sexual Abuse, Suicide, Eating Disorders & PTSD?

Carter, JC et al. Primary prevention of eating disorders: Might it do more harm than good? Int J Eat Disorders, 22, 1997, 167-72. “These findings suggest that the intervention had been counterproductive since it led to an increase in dietary restraint, and that school-based prevention programs may do more harm than good.”

Callahan, J. Negative effects of a school suicide postvention program--a case example. Crisis, 17, 1996, 108-15. -- “…a substantial increase in suicidal talk, threats, and attempts took place. Inadvertently, some of the postvention activities appeared to contribute to the romanticization and glorification of the deaths.”

Taal, M & Edelaar, M. Positive and negative effects of a child sexual abuse prevention program. Child Abuse & Neglect, 21, 1997, 399-410. “Immediately after participation in the program the youngest and the oldest children felt less in control of an abusive interaction, the youngest pupils thought that refusal was less feasible … As an unwanted side effect of the program the oldest children developed feelings of discomfort about being touched.”

McNally, RJ. Does early psychological intervention promote recovery from posttraumatic stress? Psychological Science in the Public Interest, 4, 2003. “In the wake of the terrorist attacks at the World Trade Center, more than 9,000 counselors went to New York City to offer aid to rescue workers, families, and direct victims of the violence … there is no convincing evidence that debriefing reduces the incidence of PTSD, and some controlled studies suggest that it may impede natural recovery from trauma.”

Moral: The road to hell is paved with good intentions.
Utility Analysis: Scientific Knowledge is a Necessary but Insufficient Basis for Logical Decision Making

<table>
<thead>
<tr>
<th>Two Roulette Tables</th>
<th>Table A</th>
<th>Table B</th>
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</thead>
<tbody>
<tr>
<td>Probability of Black</td>
<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Probability of Red</td>
<td>0.4</td>
<td>0.6</td>
</tr>
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</table>

Black: You Win
Red: I win
Utility Analysis: Scientific Knowledge is a Necessary but Insufficient Basis for Logical Decision Making

### Two Roulette Tables

<table>
<thead>
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<th></th>
<th>Table A</th>
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</tr>
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<tbody>
<tr>
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<td>0.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Probability of Red</td>
<td>0.4</td>
<td>0.6</td>
</tr>
<tr>
<td>Value of Black</td>
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<td>$1,000</td>
</tr>
<tr>
<td>Value of Red</td>
<td>-$1,000</td>
<td>-$100</td>
</tr>
<tr>
<td>Utility</td>
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<td>$340</td>
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</table>

Black: You Win
Red: I win

### Two Public Health Policies (clinical treatments, etc.)

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<tr>
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<th>Action B</th>
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<tr>
<td>Probability of Desired Outcome</td>
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<td>0.7</td>
</tr>
<tr>
<td>Probability of Undesired Outcome</td>
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<td>0.3</td>
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<tr>
<td>Value of Desired Outcome</td>
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<td>Value of Undesired Outcome</td>
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<tr>
<td>Utility</td>
<td>???</td>
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</tr>
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Science

Values
Conclusions

- There are *many* factors that influence relative adiposity.
- No one factor seems to account for much variance.
- Recognize that recommending courses of action depends on subjective values and not just empirical evidence.
- The effects of environmental manipulations are difficult to predict and may be counter to intuitive predictions.
- Environmental manipulations probably need to be in place throughout the lifespan.
- Rigorous evaluations of putatively contributing factors and proposed Creative ‘out-of-the-box’ solutions are warranted.
- ‘Same-old same-old’ school-based approaches seem unwarranted.
- Don’t just do something, stand there! (and think).