Energetics and Obesity: Epistemological, Evidentiary, and Social Challenges in Advancing Knowledge.

David B. Allison, Ph.D.
### Disclosure & Acknowledgments

Dallison@UAB.edu

<table>
<thead>
<tr>
<th>AFFILIATION/FINANCIAL INTERESTS</th>
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</table>
Wilbur Olin Atwater (1844-1907)
LIQUOR MEANS ALCOHOL
ALCOHOL MEANS POISON

Why drink POISON?

“WET” OR “DRY”

“VOTE WET FOR MY SAKE!”

“VOTE DRY FOR MINE!”

Shall the Mothers and Children be Sacrificed to the Financial Greed of the Liquor Traffic?

IT IS UP TO YOU, VOTER, TO DECIDE

VOTE DRY

Sources: [http://prohibition.osu.edu/asl/default.cfm](http://prohibition.osu.edu/asl/default.cfm), [http://wctu.org/](http://wctu.org/)
Atwater, Alcohol, and the Temperance Movement

- Mary Hunt (1830–1906) was one of the most powerful women in the US temperance movement (i.e. promoting prohibition of alcohol).

- In the early 1880s, in alliance with the Woman’s Christian Temperance Union (WTCU), Hunt was able to gain control of physiology textbooks publishing by lobbying politicians, religious leaders, and college presidents on the dangers of alcohol.

- Her work led to the passage of laws requiring that physiology textbooks promote complete abstinence and alcohol prohibition.

- By 1888, the ‘endorsement’ by Hunt and the WCTU was tantamount to a necessity for the production of a new physiology text.

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Atwater’s Position

• Atwater: Alcohol was not a poison and children should be taught “the simple facts which science attests and which they can believe hereafter, rather than exaggerated theories, whose errors, when they learn them, will tend to undo the good we strive to do.”

Attack on Atwater by Hunt

• In 1900, in reference to Atwater, Hunt told the National Education Association meeting “we are not so idiotic…to want untruth about alcohol taught.”

• In 1901, she petitioned the Secretary of Agriculture James Wilson to ensure that Atwater receive no further funding from the USDA, nor should he be able to publish his results in department bulletins.

• She was successful and received federal backing to have her reply to Atwater’s and other physiologists’ claims about alcohol published as a U.S. Senate document. Over one hundred thousand copies were produced.

• Atwater persevered but had to shift his publications to the National Academy of Sciences.

Sources:
Initial Premises

I will take this as axiomatic:

Obesity is a prevalent, serious, and complex problem that has been increasing for several hundred years and increased to an especially great extent in the last 3rd of the 20th century.
When we take a long view, positive progress has been made in the overall field of nutrition at a practical level.

Unlike the ancient Romans, we have effectively eliminated lead from our wine and many other toxins from our foods. [http://penelope.uchicago.edu/~grout/encyclopaedia_romana/wine/leadpoisoning.html](http://penelope.uchicago.edu/~grout/encyclopaedia_romana/wine/leadpoisoning.html)

Since the time of Columbus and the subsequent world-wide introduction of guano and potatoes followed by many other advances in agriculture, we have radically reduced previous challenges in feeding the world’s populations (though hunger remains a future threat and an ongoing tragedy in some parts of the world). [1493: Uncovering the New World Columbus Created. By Charles C. Mann.](http://penelope.uchicago.edu/~grout/encyclopaedia_romana/wine/leadpoisoning.html)

We have come to understand nutrient deficiencies and radically reduced them in most of the developed world.
If we switch our focus from general nutrition to obesity, much positive progress has been made in our ability to study and our basic understanding of obesity and energetics. And we can trace these through some historical intellectual lineages.

[Please forgive my very abbreviated and idiosyncratic lineages.]

Lavoisier ➔ Atwater ➔ Schoeller ➔ Thomas/Chow/Hall

Mendel/Darwin ➔ Fisher ➔ Stunkard/Bouchard ➔ Coleman/Leibel/Friedman ➔ Loos
James Lind ➔ Benjamin Franklin ➔ Student ➔ Sir Harold Himsworth ➔ Consortia
But questions are being raised about the progress, value, scientific quality, and integrity of our field.

“The New Obesity Campaigns Have It All Wrong” or “Science, Pseudoscience, Nutritional Epidemiology, and Meat”

“…research is important to determine which of these well-intentioned policies and programs are working and for whom. …What seems reasonable to try is not always effective and may even have unanticipated effects.”

“Implausible results in human nutrition research”

“AHRQ: Policy-based non-evidence evidence?”

“Three Holes in the Obesity Evidence Base”

“Myths, Presumptions, and Facts about Obesity”
We might dismiss the aforementioned as gadflies, except that we must acknowledge that, at the population level, our progress in reducing obesity levels has been nil to negative.
So…why do we so struggle to make progress in obesity and nutrition?

I will try to identify a (sub)set of factors and practices that I believe impede our progress in both understanding and in reducing obesity levels.

For each factor, I will try to illustrate with an example and offer a proposed solution.
"The 12 clinical trials tested 52 observational claims. They all confirmed no claims in the direction of the observational claims...To put it another way, 100% of the observational claims failed to replicate. In fact, five claims (9.6%) are statistically significant in the clinical trials in the opposite direction to the observational claim." – Young & Karr. 2011, Significance; 8: 116-120.

<table>
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<th>Neg.</th>
<th>No. of claims</th>
<th>Treatment(s)</th>
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<td>JAMA. 2006; 295: 655–666</td>
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<td>HRT + Vitamins</td>
<td>JAMA 2002; 288: 2431–2440</td>
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"The 12 clinical trials tested 52 observational claims. They all confirmed no claims in the direction of the observational claims...To put it another way, 100% of the observational claims failed to replicate. In fact, five claims (9.6%) are statistically significant in the clinical trials in the opposite direction to the observational claim." – Young & Karr. 2011, Significance; 8: 116-120.
Is the Problem with Observational Studies Just in the Execution, or Is It Inherent?

Suppose we could effectively eliminate measurement error, genetic variation, smoking, socioeconomic status, and other ‘usual’ suspects as confounders?

Would An Observational Study Then Recapitulate a Randomized Effect Estimate?

But, within ad lib group, the correlation between self-selected average lifetime daily intake and lifespan is positive (r=0.45, p=0.0056.).

Allison, Yang, Smith, & Nagy (ongoing study)
Short-Term Studies Are Insufficient: Example - *Learned* Compensation in Humans

*Appetite, 1989, 12, 95–103*

**Learned Caloric Adjustment of Human Intake**

JEANINE LOUIS-SYLVESTRE, ALAIN TOURNIER, PHILIPPE VERGER, MICHÈLE CHABERT and BRIGITTE DELORME

*Laboratoire de Neurobiologie de la Nutrition E.P.H.E., Université Paris 6*

JOSEPH HOSSENLOPP

*Ecole Nationale des Sciences de l’Industrie Alimentaire*

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**Diagram:**

- **Time 1:**
  - LoCal: 900 kcal
  - HiCal: 1200 kcal

- **Time 2:**
  - LoCal: 1200 kcal
  - HiCal: 1500 kcal

- **Categories:**
  - Snack
  - Other Food

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*Note: For a detailed understanding, please refer to the original study.*
Biological Organisms Are Adaptive Systems

Free-living Compensation Model Project (submitted)

- RCTs of interventions that change one aspect of energy balance, but leave others free to vary
- Free-living adults with at least one objective measure of compliance >=80%
- Studies N=28
- Diet (n=3), Exercise (n=15), Overfeeding (n=9), Diet plus exercise (n=2)
- Weight change significantly less than expected if no behavioral compensation were to occur (Slope 0.399).
Conducting Studies Beyond the Point Where They Are Probative & The Mere Exposure Effect

‘A reliable way to make people believe in falsehoods is frequent repetition, because familiarity is not easily distinguished from truth. Authoritarian institutions and marketers have always known this fact. …you do not have to repeat the entire statement of a fact or idea to make it appear true. People who were repeatedly exposed to the phrase “the body temperature of a chicken” were more likely to accept as true the statement that “the body temperature of a chicken is 144˚” (or any other arbitrary number).’

So, we often devote our journal pages, time, and resources to research that increases belief, instead of to research that increases knowledge.


Fifty-two moderately obese adult women were stratified according to their baseline breakfast-eating habits and randomly assigned a weight-loss program.

The no-breakfast group ate two meals per day and the breakfast group ate three meals per day.

After 12-wk, this treatment-by-strata-by-time interaction effect (P less than 0.06) suggests that those who had to make the most substantial changes in eating habits to comply with the program achieved better results.

Insufficient Open-Mindedness and Ambitious in Pursuit of the Roads Less Traveled


<table>
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<th>Year</th>
<th>Adult obesity prevalence (%)</th>
<th>Nonsmoker prevalence (%)</th>
<th>Antidepressant prescriptions (millions)</th>
<th>Average home temperature (°F)</th>
<th>Mean age of mothers at first birth (years)</th>
<th>Proportion of Hispanic and/or aged between 35 and 55 years</th>
<th>PBDE concentration (pg/g)</th>
<th>Prevalence of AC (%)</th>
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<td>64</td>
<td>10</td>
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<td>36.4%</td>
<td>5.5</td>
<td>35.5</td>
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<td>1965</td>
<td>13</td>
<td>65</td>
<td>12</td>
<td>56.5</td>
<td>21.75</td>
<td>36.9%</td>
<td>6.0</td>
<td>36.5</td>
<td>15.7</td>
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<td>1970</td>
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<td>14</td>
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<td>37.4%</td>
<td>6.5</td>
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<td>17</td>
<td>68</td>
<td>16</td>
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<td>22.75</td>
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<td>7.0</td>
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<td>16.4</td>
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<td>18</td>
<td>70</td>
<td>18</td>
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<td>8.0</td>
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<td>1990</td>
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<td>39.5%</td>
<td>8.5</td>
<td>41.5</td>
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<td>1995</td>
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<td>2000</td>
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<td>74</td>
<td>25</td>
<td>60</td>
<td>25.25</td>
<td>40.5%</td>
<td>9.5</td>
<td>43.5</td>
<td>18.0</td>
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</table>
They left out global warming. I'm saying that in jest,' said a skeptical Dr. Thomas Robinson, director of the Center for Healthy Weight at Lucile Packard Children's Hospital at Stanford University.


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Marmots fatten up on climate change

Rodent population boom linked to bigger bellies and longer summers.

Lucas Laursen

In the Upper East River Valley of Colorado's Rocky Mountains, yellow-bellied marmots (*Marmota flaviventris*) are thriving thanks to climate change. The rodents' startling population boom — their numbers have tripled in ten years — has now been linked to the increasing size of their bellies, which is probably caused by climate-driven changes in hibernation patterns.


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The Dynamics of Phenotypic Change and the Shrinking Sheep of St. Kilda

Arpat Ozgul,¹ Shripad Tuljapurkar,² Tim G. Benton,³ Josephine M. Pemberton,⁴ Tim H. Clutton-Brock,⁵ Tim Coulson⁶

Environmental change, including climate change, can cause rapid phenotypic change via both ecological and evolutionary processes. Because ecological and evolutionary dynamics are intimately linked, a major challenge is to identify their relative roles. We exactly decomposed the change in mean body weight in a free-living population of Soay sheep into all the processes that contribute to change. Ecological processes contribute most, with selection—the underlying cause of observed phenotypic traits—playing a role only when the environment has so little effect even then, adaptive change has caused a decline.

Science 24 July 2009 325: 464-467
Failure to take measurement as seriously as we do in other domains.


http://www.cdc.gov/obesity/data/adult.html
Difficulty and Neglect in Controlling for Non-specific Effects: Consider 2 Different Studies

A Randomized Trial of Sugar-Sweetened Beverages and Adolescent Body Weight
Cara B. Ebbeling, Ph.D., Henry A. Feldman, Ph.D., Virginia R. Chomitz, Ph.D.,
Tracy A. Antonelli, M.P.H., Steven L. Gortmaker, Ph.D.,
Stavroula K. Osganian, M.D., Sc.D., and David S. Ludwig, M.D., Ph.D.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Control</th>
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<tr>
<td>• Water and Diet Drinks</td>
<td>$50 supermarket gift cards</td>
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<tr>
<td>• Monthly motivational messages</td>
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A Trial of Sugar-free or Sugar-Sweetened Beverages and Body Weight in Children
Janne C. de Ruyter, M.Sc., Margreet R. Olthof, Ph.D., Jacob C. Seidell, Ph.D.,
and Martijn B. Katan, Ph.D.

<table>
<thead>
<tr>
<th>Treatment</th>
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<tbody>
<tr>
<td>Custom can of non-caloric sweetened drink</td>
<td>Identical can of calorically sweetened drink</td>
</tr>
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</table>

N Engl J Med. 2012 October; 367(15)
Two Equally Misleading Opposing Press Releases

Tighter economic regulation needed to reverse obesity epidemic -- study

Fast food, body mass index and market deregulation

This news release is available in Spanish, French, and Arabic.

Geneva, 3 February 2014. Governments could slow — and even reverse — the resulting increase in fast food transactions on obesity over time, health consequences including diabetes, heart disease, stroke and cancer. Rather than looking at the density of fast food outlets or self-reporte number of fast food transactions per capita from 1999 to 2008 in 25 time period as an indication of fast food consumption.

A person with BMI of 25 or more is considered overweight, while one with a BMI of 30 or more is considered obese.

The authors of the study found that while the average number of annual fast food transactions per capita from 1999 to 2008 in 25 countries increased from 200 to 43, the number of fast food transactions per capita per year decreased from 1.5 to 1.2.

PUBLIC RELEASE DATE: 15-Jan-2014

Contact: Thania Benios
thania_benios@unc.edu
919-962-8596
University of North Carolina at Chapel Hill

Fast food not the major cause of rising childhood obesity rates

For several years, many have been quick to attribute rising fast-food consumption as the major factor causing childhood obesity. But the researchers at Chapel Hill report that fast-food consumption is simply a byproduct of a much bigger problem: poor nutrition.

The study, led by Barry Popkin, W.R. Kenan Jr. Distinguished Professor of nutrition at UNC’s Gillings School of Public Health, is one of the first to consider the role of fast food in the overall diet of children.

"Fast food is not the major cause of rising childhood obesity rates, but it is a significant contributor," said Popkin.

The study looked at data from the National Health and Nutrition Examination Survey between 2009 and 2010 which collected information from children between 2 and 18 years old about whether they ate at fast-food establishments or elsewhere. The children were classified as fast-food consumers (less than or equal to 30 percent of calories from fast foods; 40 percent of the children), low consumers (less than or equal to 10 percent of calories from fast foods; 60 percent of the children), and not at all fast-food consumers (less than or equal to 5 percent of calories from fast foods; 20 percent of the children).

The researchers determined which factors were most related to dietary adequacy and were then able to create a model that predicted how much fast food a child is likely to eat, based on those factors.

"This is really what is driving children's obesity," said Popkin, whose work appears in The American Journal of Human Nutrition. "Just because children who eat more fast food are the most likely to become obese does not prove that fast food is the problem."

The study was funded by the National Institutes of Health and the National Cancer Institute.
Distortions via Statistical Fiddling?
Example in Obesity Trials

Simulated Distribution of p-values all nulls true.

Simulated Distribution of p-values some nulls false.

Simulated p-values all nulls true + ‘Fiddling’.

Real data (N=347 obesity RCTs; p for dip = .052)
Distortions Via Publication Bias

Simulated Data

WHO Report on Breast-Feeding and Obesity

Norma Terrin, Christopher H. Schmid, Joseph Lau
Journal of Clinical Epidemiology, Volume 58, Issue 9, September 2005, Pages 894–901
http://dx.doi.org/10.1016/j.jclinepi.2005.01.006

WHO report: “Evidence of the Long-Term Effects of Breastfeeding: Systematic Reviews and Meta-Analysis”
Use of Causal Language in Observational Studies of Obesity and Nutrition

Stacey S. Cofield, Rachel V. Corona, David B. Allison

Percent of articles using unjustified causal language.
The impact of area-based initiatives on physical activity trends in deprived areas; a quasi-experimental evaluation of the Dutch District Approach

Daniëlle Kramer¹*, Mariël Droomers¹, Birthe Jongeneel-Grimen¹, Marleen Wingen², Karlien Stronks² and Anton E Kunst³

* Corresponding author: Daniëlle Kramer d.kramer@amc.uva.nl

For all author emails, please log on.

Published: 11 March 2014

Wow, that’s a lot of null.

Results
Deprived target districts showed a significantly positive change in walking trend between the pre-intervention and intervention period. The trend change in the deprived target districts was significantly larger compared to the rest of the Netherlands, but not compared to other deprived districts. For cycling and sports, neither deprived districts nor control districts showed a significant trend change. For all leisure-time PA outcomes, trend changes were not related to the intensity of environmental interventions in the deprived target districts.

Conclusion
Some evidence was found to suggest that ABIs like the District Approach have a positive impact on leisure-time PA in deprived districts, regardless of the intensity of environmental interventions.

But, wait...
Intersection/Union (expressed as percent) of articles with phrases “Implicated In” and (“Obesity” or “Weight Gain”).

From Scopus Search 3/30/14.
Confusion Resulting From Testing Against Baseline Differences

- “Randomised groups should be compared directly by two-sample methods and separate tests against baseline are highly misleading.”
- Pre-Post
  - Treatment $p < .05$
  - Control $p > .05$
- Between Groups
  - $p > .05$
- Misleading

Examples of Obesity Papers Utilizing the Approach Bland & Altman recommend against:

- http://www.kip.or.kr/upload/JustAccepted_KJP-13-254.pdf
- http://www.ncbi.nlm.nih.gov/pubmed/?term=stanhope%5Bau%5D+fong%5Bau%5D

**Hypothetical Data.**
Conflating the Moral with the Empirical

“Science can only ascertain what is, but not what should be, and outside of its domain value judgments of all kinds remain necessary.” ~Albert Einstein

### Two Roulette Tables

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<td>Probability of Red</td>
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<td>$1,000</td>
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<td>Value of Red</td>
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<td>-$100</td>
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<tr>
<td>Utility</td>
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<td>$340</td>
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Black: You win
Red: I win

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

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<td>Probability of Undesired Outcome</td>
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<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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Going Forward

• Recognize that humans are adaptive systems.
• Treat obesity as a science as meriting the same rigor as any other science.
• Recognize that short-term studies, studies of intermediary endpoints, and observational studies all have their place, but should not be our stopping points or bases for overreaching conclusions.
• Develop a set of ‘meta-methods’ (e.g. clinical trials registries, CONSORT statements, public data sharing) which will collectively buttress/ensure the implementation of the fundamental scientific methods that already exist.
• Put resources in place to implement those meta-methods.
• Unfailingly pursue truth through science is not a job, but a discipline, a vocation, and a privilege.
Wherever I Have Gone, It has Been with Guides and Companions.
And I Am Truly Grateful...
To USDA & ASN for this great honor
To UAB for always supporting my pursuit of ideas and adventure
To My Nominator, who knows what he stands for and stands
To My Mentors, who inspired me
  • Bernard S. Gorman
  • Harold E. Yuker
  • Steven B. Heymsfield

To My Mentorees, who sustain me

To My Friends and Colleagues, who have stuck by me through the thick and thin
And, To My Family, who are my reason when all reason is gone.
Come visit us in Alabama and we can talk some more on the trail.

Cheaha Mountain
Photo courtesy Rohan Dhurandhar.
Contact or slide requests: Dallison@uab.edu

Want regular information:
http://www.obesityandenergetics.org/

A few key references:


