DEBATE:
Weight as a Measure of Health

VS.
Health at Every Size Concepts

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Professor of Medicine
Nutrition Scientist
Stanford Prevention Research Center
Stanford University, Department of Medicine
No Conflicts of Interest to Disclose
The Global Food System
Summer Camp for Underserved Kids
Full Circle Farm
at Peterson Middle School

STANFORD
SCHOOL OF MEDICINE
Stanford University Medical Center

STANFORD
School of Humanities and Sciences
Outline

- My research & lessons learned
  - Evidence for Obesity links to Morbidity/Mortality
  - Health at Every Weight
  - Take Home / Actionable Conclusions
Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults

≥55% energy from carbohydrate
≤30% energy from fat
and approximately 15% energy from protein
Low carb ←  High carb
From Low-Carb to Low-Fat

Gardner, JAMA 2007;297:969-77
Atkins  

8 weeks: 28% Carb, 17% Fat, 55% Protein  
6 months: 23% Carb, 30% Fat, 47% Protein  
1 year: 22% Carb, 32% Fat, 46% Protein

Zone

8 weeks: Data not presented
6 months: Data not presented
1 year: Data not presented

LEARN

8 weeks: 16% Carb, 21% Fat, 63% Protein  
6 months: 18% Carb, 29% Fat, 53% Protein  
1 year: 19% Carb, 29% Fat, 52% Protein

Ornish

8 weeks: Data not presented
6 months: Data not presented
1 year: Data not presented

A TO Z Study Diet Data NDS 3-day unannounced 24-hr recalls (3,137 recalls)

Gardner, JAMA 2007;297:969-77
Percent weight change across time, by group

Weight change as % of baseline

Participants with available data

<table>
<thead>
<tr>
<th></th>
<th>Atkins</th>
<th>Zone</th>
<th>LEARN</th>
<th>Ornish</th>
</tr>
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<tr>
<td>Baseline</td>
<td>77</td>
<td>79</td>
<td>79</td>
<td>76</td>
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<tr>
<td>8 weeks</td>
<td>72</td>
<td>72</td>
<td>72</td>
<td>71</td>
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<tr>
<td>6 months</td>
<td>71</td>
<td>66</td>
<td>64</td>
<td>65</td>
</tr>
<tr>
<td>1 year</td>
<td>68</td>
<td>61</td>
<td>60</td>
<td>58</td>
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</tbody>
</table>

% Retention 1-year

- Atkins: 88%
- Zone: 77%
- LEARN: 76%
- Ornish: 78%

Gardner, JAMA 2007;297:969-77

A vs. Z p<0.03 (Tukey’s studentized range test)
Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults
Obes Res 1998;6(Suppl)2:51S-209S.

<table>
<thead>
<tr>
<th>Low-Carbohydrate</th>
<th>National Guidelines</th>
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<tbody>
<tr>
<td>Carb</td>
<td>Fat</td>
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<tr>
<td>~15%</td>
<td>≤30%</td>
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</table>

Favored Group assigned to Atkins
WEIGHT p=0.03
HDL-C p=0.0004
SBP p=0.001
DBP p=0.004
(not adjusted for multiple testing)

Gardner, JAMA
2007;297:969-77
12-month net weight change (kg): Individual results

Gardner, JAMA 2007;297:969-77
12-month net weight change (kg): Individual results

~30 kg RANGE of weight change WITHIN each diet group.

From losing 20-25 kg to gaining 5-10 kg

Gardner, JAMA 2007;297:969-77
A Randomized Trial of a Low-Carbohydrate Diet vs Orlistat Plus a Low-Fat Diet for Weight Loss

William S. Yancy Jr, MD, MHS; Eric C. Westman, MD, MHS; Jennifer R. McDuffie, PhD, RD, MPH; Steven C. Grambow, PhD; Amy S. Jeffreys, MStat; Jamiyla Bolton, MS; Allison Chalecki, RD; Eugene Z. Oddone, MD, MHS

Figure 3. Individual percentage body weight change trajectories by diet group. The bold line represents a smoothed spline of the observed trajectory for the mean percentage body weight change in the low-carbohydrate, ketogenic diet group (A) or the orlistat plus low-fat, reduced-calorie diet group (B).

Yancy et al., Arch Int Med, 2010;170:143

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Dansinger et al.,
Comparison of the Atkins, Ornish, Weight Watchers, and Zone Diets for Weight Loss and Heart Disease Risk Reduction: A Randomized Trial.
JAMA, 2005; 293:43-53
Explanations for Heterogeneity
Insulin Resistance
Percent weight change across time, by group

Weight change as % of baseline

Participants with available data

<table>
<thead>
<tr>
<th></th>
<th>Atkins</th>
<th>Ornish</th>
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<tr>
<td>Base-line</td>
<td>77</td>
<td>76</td>
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<tr>
<td>8 weeks</td>
<td>72</td>
<td>71</td>
</tr>
<tr>
<td>6 months</td>
<td>71</td>
<td>65</td>
</tr>
<tr>
<td>1 year</td>
<td>68</td>
<td>58</td>
</tr>
</tbody>
</table>

% Retention 1-year

- Atkins: 88%
- Ornish: 78%
Fasting Insulin Tertiles

Most Insulin Sensitive (<7 µIU/mL)

Most Insulin Resistant (>10 µIU/mL)

Mean, SEM

A TO Z Study: Exploratory analyses

Ornish Diet (very low fat, high carb)

Atkins (very low carb, unrestricted fat and protein)

Weight loss (kg)

Months

Ornish Diet

Atkins

Mean, SEM

n=19

n=24

n=23

n=21
Fasting Insulin Tertiles

A TO Z Study: Exploratory analyses

- Most Insulin Sensitive (<7 µIU/mL)
- Most Insulin Resistant (>10 µIU/mL)

Success with either diet for those who are relatively insulin sensitive.

For those who are insulin resistant, low-fat diet ineffective compared to low-carb diet.
Adherence
Weight Loss by Adherence Tertile (A TO Z Study)

12-Month Weight Change (kg)

Atkins: n=23, p=0.0006
Zone: n=19, p=0.01
Ornish: n=19, p=0.06

Adherence tertiles
Highest
Lowest

Insulin resistance, Low carb vs. Low Fat, & Adherence
Change in % Carbs

Fasting Insulin Tertiles

- Lowest (most Ins Sens)
- Highest (most Ins Res)

Assigned to Atkins (Lowest Carb)
- Red

Assigned to Ornish (Lowest Fat)
- Blue

McClain et al., *Diabetes Obes Metab* 2013;15:87-90
Differential Adherence by Insulin Resistance Status

Insulin resistant individuals may find it inherently more difficult to adhere to a lower-fat/higher-carb diet
Ongoing Study: NIH R01 DK091831 + NuSI

- **Study Population:** Women & men, BMI 28-40, age 18-50, non-diabetic, general good health
- **Sample size:** n=609 (enrollment complete)
- **Intervention:** Healthy Low-Fat vs. Healthy Low-Carb Weight loss diets
  Delivered in 22 instructional sessions (~17/class)
- **Primary outcome:** 12-month weight loss
- **Possible mediators/moderators:**
  Genome, metabolome, microbiome
  Insomnia, food addiction, psychosocial, many others
HOW LOW?
How Low can you go?

~20 grams/day (carbs or fat)?

Titrate up to a level you can maintain..... FOREVER
Healthy Low-Fat vs. Healthy Low-Carb
Variability
**ID 14: Low Fat**

**BREAKFAST**
2 slices whole wheat bread w/mustard  
Multigrain cereal w/skim milk  
Water

**LUNCH**
4 c salad mix w/ fat-free dressing  
Spinach spaghetti w/ marinara sauce  

*Mid-afternoon snack*
Coffee

**DINNER**
Stir fried veggies w/ kung pao sauce, soy sauce and garlic on brown rice  
Water  
*Evening Snack*
Pita bread w/ low-fat red pepper hummus
ID 36: Low Fat

BREAKFAST
- Low Fat Latte
- Scone

LUNCH
- Vegetable lasagna
- Soda

Mid-afternoon snack
- Water
- Martini w/ olives

DINNER
- Minestrone soup
- Linguini w/ shrimp, alfredo & marinara sauce
- Caesar Salad

Evening Snack
- Red wine
- Chocolate cake
Low Fat
<table>
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<th>ID 14</th>
<th>ID 36</th>
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<tr>
<td>Kcal</td>
<td>1,700</td>
<td>1,950</td>
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<tr>
<td>Fat</td>
<td>13%</td>
<td>36%</td>
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<tr>
<td>Carbohydrate</td>
<td>73%</td>
<td>37%</td>
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</tr>
<tr>
<td>Protein</td>
<td>14%</td>
<td>17%</td>
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<tr>
<td>Alcohol</td>
<td>0%</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>Fiber</td>
<td>45 g</td>
<td></td>
<td>15 g</td>
</tr>
<tr>
<td>Omega-3</td>
<td>1 g</td>
<td>1 g</td>
<td></td>
</tr>
<tr>
<td>Saturated fat</td>
<td>4 g</td>
<td>36 g</td>
<td></td>
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<tr>
<td>Added Sugars</td>
<td>20 g</td>
<td>39 g</td>
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</tbody>
</table>
ID 10: Low Carb

BREAKFAST
- Tuna salad w/ tomatoes, olives & lettuce
- Fat free dressing
- Water

LUNCH
- Deli ham
- Laughing cow cheese

Afternoon Snack
- Coffee w/ half and half

DINNER
- Chicken w/o skin
- Zucchini & Broccoli sautéed in butter

Evening Snack
- Strawberries & sparkling water
ID 51: Low Carb

BREAKFAST
- Omelette w/ cheese, ham, spinach
- Coffee with half & half
- Water

LUNCH
- Steak w/ cheese
- Pork ribs
- Bratwurst
- Broccoli salad
- Water

DINNER
- Cheeseburger
- Sausage
- Avocado, tomato, spinach
- Red wine
Low Carb

ID 10

ID 51
<table>
<thead>
<tr>
<th></th>
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<tr>
<td>Kcal</td>
<td>1,200</td>
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<tr>
<td>Fat</td>
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<tr>
<td>Carbohydrate</td>
<td>13%</td>
<td>5%</td>
</tr>
<tr>
<td>Protein</td>
<td>39%</td>
<td>23%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>0%</td>
<td>6%</td>
</tr>
<tr>
<td>Fiber</td>
<td>13 g</td>
<td>8 g</td>
</tr>
<tr>
<td>Omega-3</td>
<td>2 g</td>
<td>2 g</td>
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<tr>
<td>Saturated fat</td>
<td>21 g</td>
<td>61 g</td>
</tr>
<tr>
<td>Added Sugars</td>
<td>5 g</td>
<td>4 g</td>
</tr>
</tbody>
</table>
Do Genotype Patterns Predict Weight Loss Success for Low Carb vs. Low Fat Diets? R01 DK091831 (2013-17) + NuSI

n=609
BMI 28-40 kg/m²
non-diabetic
generally healthy
adults 18-50 yrs
~55% women

Low Carbohydrate (n=305)

Low Fat (n=304)

INTERVENTION:
22 group classes, 15-22 participants/group

MONTHS
0 3 6 12

WEIGHT (1° outcome) X X X X

Blood (DNA, lipids, glucose, insulin, OGTT, cytokines) X (no OGTT) X

Diet Assessment (NDS-R) X X X

Psychosocial (Questionnaires) X X X

DEXA,REE (Metabolic cart) X X

Other: Microbiome (fecal samples) Adipocytes (fat biopsies), Other – Various times points, specific cohorts
Blood Glucose (mg/dL)

>125 mg/dL cut off for diabetes

75 grams glucose

Non-Diabetic, Insulin Resistant

Minutes

Serum Insulin uU/mL
Obesity is a heterogeneous and complex disease influenced by exogenous and endogenous exposures.

Stratifying obesity into meaningful subtypes could provide a better understanding of its causes and enable the design and delivery of more effective prevention and treatment interventions.
Outline

- My research & lessons learned
- Evidence for Obesity links to Morbidity/Mortality
  - Health at Every Weight
  - Take Home / Actionable Conclusions
Age-Adjusted Prevalence of Obesity and Diagnosed Diabetes Among U.S. Adults Aged 18 Years or older

**Obesity (BMI $\geq 30$ kg/m$^2$)**

- **1994**
- **2000**
- **2010**

**Diabetes**

- **1994**
- **2000**
- **2010**

2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society

Endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation, American Pharmacists Association, American Society for Nutrition, American Society for Parenteral and Enteral Nutrition, American Society for Preventive Cardiology, American Society of Hypertension, Association of Black Cardiologists, National Lipid Association, Preventive Cardiovascular Nurses Association, The Endocrine Society, and WomenHeart: The National Coalition for Women With Heart Disease
Obesity raises the risk of **MORBIDITY** from hypertension, dyslipidemia, type 2 diabetes, heart disease, stroke, gallbladder disease, osteoarthritis, sleep apnea, respiratory problems, and some cancers. Obesity is also associated with increased risk of all-cause and **CVD MORTALITY**.

...biomedical, psychosocial, and economic consequences...
All of the following are associated with weight loss

AHA-style Step 1
Higher protein
Higher protein Zone-type
Lacto–ovo–vegetarian–style
Low calorie
Low carbohydrate
Low fat
Low fat vegan-style
Lower fat, high-dairy
Low–glycemic–load
Macronutrient targeted diets
Mediterranean style
Moderate protein

With prescribed energy restriction, or

Without formal prescribed energy restriction, but with a realized energy deficit.

…if reduction in dietary energy intake is achieved:
Second Expert Report
Food, Nutrition,
Physical Activity, and the
Prevention of Cancer:
a Global Perspective

2007

American Institute for Cancer Research
World Cancer Research Fund
### Body Fatness

<table>
<thead>
<tr>
<th>Foods containing dietary fibre</th>
<th>Abdominal fatness</th>
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<tr>
<td>Allium vegetables</td>
<td>Adult weight gain</td>
</tr>
<tr>
<td>Garlic</td>
<td>Adult attained height</td>
</tr>
<tr>
<td>Fruits</td>
<td>Greater birth weight</td>
</tr>
<tr>
<td>Fats</td>
<td>Lactation</td>
</tr>
<tr>
<td>Folic acid</td>
<td>Being breastfed</td>
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</table>

#### Key

- **Convincing decreased risk**
- **Probable decreased risk**
- **Probable increased risk**
- **Convincing increased risk**

1. Includes evidence from foods containing carotenoids for mouth, pharynx, larynx, foods containing beta-caroten for oesophagus, foods containing vitamin C for oesophagus.
2. Includes evidence from foods containing carotenoids for mouth, pharynx, larynx and lung, foods containing beta-caroten for oesophagus, foods containing vitamin C for oesophagus.
3. Includes evidence from supplements for prostate.
4. Evidence is from studies using supplements for colorectal.
5. Includes "best foods".
6. Convincing harm for men and probable harm for women for Lactation.
7. The evidence is derived from studies using supplements for lung.
8. Includes evidence on television viewing.
9. Judgement for physical activity applies to raise and not restore.
Association of All-Cause Mortality With Overweight and Obesity Using Standard Body Mass Index Categories
A Systematic Review and Meta-analysis

Katherine M. Flegal, PhD
Brian K. Kit, MD
Heather Orpana, PhD
Barry I. Graubard, PhD

**Importance** Estimates of the relative mortality risks associated with normal weight, overweight, and obesity may help to inform decision making in the clinical setting.

**Objective** To perform a systematic review of reported hazard ratios (HRs) of all-cause mortality for overweight and obesity relative to normal weight in the general population.
Random-Effects Hazard Ratios of All-Cause Mortality for Overweight and Obesity Relative to Normal Weight

97 Prospective Studies

Hazard Ratio

Body Mass Index

Reference

“Normal”

Overweight

Obese

< 25

25 to <30

≥30

0.93

95% CI:

0.89 – 0.95

1.13

95% CI:

1.06 – 1.19

1.00

0.80
Relative to those who are “normal” weight (BMI <25), those who are **overweight** (BMI 25 to <30) have a 7% **LOWER** risk of all-cause mortality, while those who have **obesity** (BMI >30) have a 13% **higher risk**.
Random-Effects Hazard Ratios of All-Cause Mortality for Overweight and Obesity Relative to Normal Weight

97 Prospective Studies

<table>
<thead>
<tr>
<th>Body Mass Index</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
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<td>&lt; 25</td>
<td>0.93</td>
<td>0.89 – 0.95</td>
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<td>25 to &lt;30</td>
<td>0.94</td>
<td>0.86 – 1.03</td>
</tr>
<tr>
<td>30 to &lt;35</td>
<td>1.25</td>
<td>1.13 – 1.39</td>
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<tr>
<td>&gt;35</td>
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</table>
The **higher** risk of all-cause mortality, is observed in those who have obesity at the higher levels of stage 2 and 3 and morbid obesity (BMI ≥35).

Even those with **stage 1 obesity** (BMI 30 to <35) have a **lower** risk of mortality (not significant) than those with BMI <25.
Body-Mass Index and Mortality among Adults with Incident Type 2 Diabetes

Deirdre K. Tobias, Sc.D., An Pan, Ph.D., Chandra L. Jackson, Ph.D., Eilis J. O’Reilly, Sc.D., Eric L. Ding, Sc.D., Walter C. Willett, M.D., Dr.P.H., JoAnn E. Manson, M.D., Dr.P.H., and Frank B. Hu, M.D., Ph.D.
Body-Mass Index and Mortality among Adults with Incident Type 2 Diabetes

Hazard Ratio

Reference

NHS & HPFS, >12,000, ~16 years, >3,000 deaths

Body Mass Index

Hazard Ratio

95% CI: 1.05 to 1.59
n=426

95% CI: 0.98 to 1.29
n=1,074

95% CI: 1.08 to 1.42
n=2,010

95% CI: 1.14 to 1.55
n=2,462

95% CI: 0.94 to 1.26
n=2,095

95% CI: 1.08 to 1.42
n=3,360
We found no evidence of lower mortality among patients with diabetes who were overweight or obese at diagnosis, as compared with their normal-weight counterparts, or of an obesity paradox.
Conclusions and Relevance  In MZ twin pairs, higher BMI was not associated with an increased risk of MI or death but was associated with the onset of diabetes. These results may suggest that lifestyle interventions to reduce obesity are more effective in decreasing the risk of diabetes than the risk of cardiovascular disease or death.
Outline

- My research & lessons learned
- Evidence for Obesity links to Morbidity/Mortality

- Health at Every Weight
- Take Home / Actionable Conclusions
All-cause deaths per 10,000 men per year

Relative Risk
all-cause mortality

Conclusion: Fit and obese healthier than lean and unfit

Same Gender, Age, BMI
Different % Body Fat

<table>
<thead>
<tr>
<th>Gender</th>
<th>Woman</th>
<th>Woman</th>
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<tr>
<td>Age</td>
<td>42y</td>
<td>42y</td>
</tr>
<tr>
<td>BMI</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>% Body Fat</td>
<td>41%</td>
<td>30%</td>
</tr>
</tbody>
</table>

![Bar Chart](chart.png)

- **LDL-C**: mg/dL
- **HDL-C**: mg/dL
- **TG**: mg/dL
- **Glucose**: mg/dL
- **INS-AUC**: mg/dL
- **DBP**: mmHg
- **SBP**: mmHg

*mg/dL* and *mmHg*
Same Gender, Age, BMI, and % Body Fat

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age</th>
<th>BMI</th>
<th>% Body Fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Woman</td>
<td>39y</td>
<td>31</td>
<td>42%</td>
</tr>
<tr>
<td>Woman</td>
<td>39y</td>
<td>30</td>
<td>41%</td>
</tr>
</tbody>
</table>

- LDL-C: 155 mg/dL
- HDL-C: 50 mg/dL
- TG: 250 mg/dL
- Glucose: 100 mg/dL
- INS-AUC: 150 mg/dL
- DBP: 90 mmHg
- SBP: 120 mmHg
# Healthier at a Higher % Body Fat

<table>
<thead>
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<th>Gender</th>
<th>Man</th>
<th>Man</th>
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<td>25y</td>
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<td>BMI</td>
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<td>34</td>
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<tr>
<td>% Body Fat</td>
<td>25%</td>
<td>34%</td>
</tr>
<tr>
<td>LDL-C</td>
<td>88</td>
<td>114</td>
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<tr>
<td>HDL-C</td>
<td>27</td>
<td>44</td>
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<tr>
<td>Triglycerides</td>
<td>429</td>
<td>101</td>
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<tr>
<td>Glucose</td>
<td>103</td>
<td>103</td>
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<tr>
<td>INS-AUC</td>
<td>224</td>
<td>119</td>
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<td>SBP</td>
<td>125</td>
<td>118</td>
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<tr>
<td>DBP</td>
<td>82</td>
<td>78</td>
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</tbody>
</table>
Outline

- My research & lessons learned
- Evidence for Obesity links to Morbidity/Mortality
- Health at Every Weight

- Take Home / Actionable Conclusions
Reframe the Question

What is the “best diet”?
Reframe the Question

What is the “best diet”?

Which diet is best for whom?
Stop using the term "diet"

For many people a "diet" is something you go on and off. Which meal plan(?) is best for whom?
Evidence for long-term weight loss maintenance?

Inadequate / lacking
Take Home Point: #4

**Individually**
Embrace the Variability

**Societally**
Food System
Food Environment
Social Justice
Thank You