The Calculus of Calories: What Mathematical Modeling Can Teach Us about Obesity

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The 3500 kcal per pound rule
Weight Loss Rule of Thumb

Reductions of 500 to 1,000 kcal/day will produce a recommended weight loss of 1 to 2 pounds per week.

3500 kcal per pound

Taxing Caloric Sweetened Beverages: Potential Effects on Beverage Consumption, Calorie Intake, and Obesity

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Soda Tax Predictions

The figure below represents a hypothetical individual’s intake and the calculations used to derive changes in calorie intake and body weight. This method is carried out for all individuals in 2003-06 NHANES who drank caloric-sweetened beverages. Those who did not drink caloric sweetened beverages were unaffected by the tax.

### Calculating Changes in Calorie Consumption and Weight Status

<table>
<thead>
<tr>
<th>Beverages</th>
<th>Elasticity</th>
<th>Percent</th>
<th>Calories/day</th>
<th>Calories/day</th>
<th>Calories/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caloric sweetened</td>
<td>-1.264</td>
<td>-25.28</td>
<td>216</td>
<td>-54.6</td>
<td>-39.5 calories/day</td>
</tr>
<tr>
<td>Diet</td>
<td>-0.457</td>
<td>-9.14</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Skim milk</td>
<td>0.198</td>
<td>3.96</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Low-fat milk</td>
<td>0.115</td>
<td>2.30</td>
<td>122</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Whole milk</td>
<td>0.222</td>
<td>4.44</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Juices</td>
<td>0.557</td>
<td>11.14</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Coffee/tea</td>
<td>-0.383</td>
<td>-7.66</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bottled water</td>
<td>0.749</td>
<td>14.98</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

3500 kcal per lb

Soda Taxes & Obesity Reversal?

3500 kcal per lb rule

Human Macronutrient Metabolism

**Food Intake**
- Carbohydrate Intake
- Fat Intake
- Protein Intake

**Physical Activity**

**Fuel Selection**
- Carbohydrate Oxidation
- Fat Oxidation
- Nitrogen Excretion

**Body Composition**
- Body Weight
- Lean Mass
- Fat Mass
- Body Water

**Mathematical Model of Human Metabolism**

**Energy Expenditure**
- Resting Metabolic Rate
- Total Energy Expenditure

**Metabolic Fluxes**
- Glucose Turnover
- Gluconeogenesis
- Lipolysis
- Lipogenesis
- Protein Turnover
Model Equations

\[
\frac{dG}{dt}_C = CI - DNL + GNG_p + GNG_p - G3P - CarbOx
\]

\[
\frac{dF}{dt}_P = 3M_{FFA}FI + M_{TG} + \epsilon_d_{DNL} - KU_{excr} - (1 - \epsilon_k)KTG - FatOx
\]

\[
\frac{dP}{dt}_P = PI - GNG_p - ProtOx
\]

FFM = BM + ECF + ECP + LCM

\[
= BM + ECF + ECP + ICW + P + G + ICS
\]

\[
= BM + ECF + ECP + ICW + P(1 + h_{p}) + G(1 + h_{g}) + ICS
\]

\[
\frac{dECF}{dt} = \frac{1}{[Na]}(\Delta N_{diet} - \xi_{Na}(ECF - ECF_{init}) - \xi_{CI}(1 - CI/CI_b)) + \Delta ECF
\]

\[
\tau_{BW} \frac{d\Delta ECF}{dt} = \xi_{BW}(BW - BW_{init}) - \Delta ECF
\]

\[
TEE = TEF + PAE + RMR
\]

\[
RMR = E_c + \gamma_B M_B + \gamma_{FFM} \left[ \frac{FFM - M_B - \Delta G(1 + h_g)}{(1 + h_g)(ECF - ECF_{init})} \right] + \gamma_F F
\]

\[
+ (1 - \epsilon_d)DNL + (1 - \epsilon_g)(GNG_F + GNG_p) + (1 - \epsilon_K)KTG
\]

\[
+ \eta_N_{excr} + (\eta_p + \epsilon_p)D_P + \eta_P D_F + \eta_F + \eta_D D_G + \eta_{DG} + \frac{dG}{dt}
\]

\[
\tau_T \frac{dT}{dt} = \begin{cases} 
\lambda_1(\Delta E/I_{E_b}) - T, & \text{if } E/I < E/I_b \\
\lambda_2(\Delta E/I_{E_b}) - T, & \text{else} 
\end{cases}
\]

\[
\gamma_{FFM} = \sum_i \gamma_i \frac{dM_i}{dFFM}
\]

\[
\gamma_{FFM} = \gamma_{FFM} \left[ 1 + (1 - \sigma)T \right]
\]

\[
CarbOx = GNG_F + GNG_p - G3P + f_c \times TEE
\]

\[
FatOx = KetOx + f_F \times TEE
\]

\[
PAE = \delta(1 + \sigma T)BW + uBW
\]

\[
ProtOx = f_P \times TEE
\]

\[
TEF = \alpha_F FI + \alpha_P PI + \alpha_C CI
\]

\[
\rho_c \frac{dG}{dt} = CI - DNL + GNG_p + GNG_p - G3P - CarbOx
\]

\[
\rho_F \frac{dF}{dt} = 3M_{FFA}FI + M_{TG} + \epsilon_d_{DNL} - KU_{excr} - (1 - \epsilon_k)KTG - FatOx
\]

\[
\rho_P \frac{dP}{dt} = PI - GNG_p - ProtOx
\]

\[
FFM = BM + ECF + ECP + LCM
\]

\[
DNL = \frac{CI \times (G/G_{init})^d}{(G/G_{init})^d + K_{DNL}^d}
\]

\[
D_p = \frac{P}{P_{Keys}} + \chi \left( \frac{\Delta P}{P_{b}} \right)
\]

\[
D_F = \frac{F}{F_{Keys}} \left[ L_{diet} + L_{PA} \right]
\]

\[
\tau_L \frac{dL_{diet}}{dt} = K_L^{S_i} \left[ 1 + (A_L - B_L) \exp(-k_L CI/CI_b) + B_L \right] - L_{diet}
\]

\[
K_L^{S_i} + MAX \left\{ 0, \left( \frac{F}{F_{Keys}} - 1 \right)^{S_i} \right\}
\]

\[
GNG_F = F I \left( \frac{P_c M_G}{P_{F} M_{TG}} \right) + D_F P_c \left( \frac{M_G}{M_{TG}} \right)
\]

\[
L_{PA} = \psi \left( \frac{\delta + \nu}{\delta_{init} + \nu_{init}} - 1 \right)
\]

\[
GNG_p = \hat{G} - F P \left( P_{b} \right) \left( \frac{P C}{P_{b}} \right) \left( \frac{M_G}{M_{TG}} \right)
\]

\[
KMG = \exp \left( \frac{\Delta C/F}{CI_b} \right)
\]

\[
\gamma_{FFM} = \gamma_{FFM} \left[ 1 + (1 - \sigma)T \right]
\]

\[
\gamma_{FFM} = \gamma_{FFM} \left[ 1 + (1 - \sigma)T \right]
\]

\[
CarbOx = GNG_p + GNG_p - G3P + f_c \times TEE
\]

\[
FatOx = KetOx + f_F \times TEE
\]

\[
PAE = \delta(1 + \sigma T)BW + uBW
\]

\[
ProtOx = f_P \times TEE
\]

\[
TEF = \alpha_F FI + \alpha_P PI + \alpha_C CI
\]
Fat Ox  →  DNL  →  GNGGf →  Fat Ox
Carb Ox  →  DNL  →  GNGGf →  Carb Ox
Prot Ox  →  GNGGp →  Prot Ox

Model Validation

Compare model predictions with data from independent experiments *only changing the initial conditions of the model to match the study* & no parameter fitting!

Integrative Physiology of Fasting

Data from F. Benedict *A study of prolonged fasting* (1915)
Data from F. Benedict *A study of prolonged fasting* (1915)
Fasting & Fuel Mobilization

Data from F. Benedict. *A study of prolonged fasting* (1915)
Fasting & Fuel Utilization

Data from F. Benedict A study of prolonged fasting (1915)
Principle of Indirect Calorimetry

1 g Carbohydrate + 0.831 L O₂ → 0.831 L CO₂

1 g Fat + 2.03 L O₂ → 1.43 L CO₂

\[ RQ = \frac{CO_2}{O_2} = \]

1 for Carbohydrate Oxidation

0.7 for Fat Oxidation
Fasting & Respiratory Exchange

Data from F. Benedict *A study of prolonged fasting* (1915)
Data from F. Benedict A study of prolonged fasting (1915)
Fasting & Energy Expenditure

Data from F. Benedict *A study of prolonged fasting* (1915)
Fasting & Ketone Excretion

Data from F. Benedict *A study of prolonged fasting* (1915)
Fasting & Nitrogen Excretion

Data from F. Benedict *A study of prolonged fasting* (1915)
Eucaloric High Fat Diet

Macronutrient Intake (kcal/d)

Fat Intake

Carbohydrate Intake

Protein Intake

Time (days)

Eucaloric High Fat Diet

Burning Carbs

Burning Fat

Weight Loss in Obese Women

Data from J.O. de Boer et al. Am J Clin Nut 44:585-95 (1986)
Weight Loss in Obese Women

![Graph showing body weight change and fat mass change over time.](image)

Data from J.O. de Boer et al. *Am J Clin Nut* 44:585-95 (1986)
CALERIE Study: LCD group

CALERIE Study: LCD group

CALERIE Study: CR group

CALERIE Study: CR group

Individual Weight Loss Variability?

CALERIE Study: CR group

Total Energy Expenditure
~ 3-5% measurement error

25% Energy Restriction

Time (months)
Impact of Initial Uncertainty

Initial Energy Imbalance = 0 ± 150 kcal/d
Impact of Initial Uncertainty

Expected Weight Change Variability!
Simulation of Long-term Dieting

Major Limitation of Human Obesity Research

Can we estimate free-living energy intake using a mathematical model of metabolism given measured changes of body weight?
Weight Plateau and Regain

Predicting Free-living Energy Intake

Energy Intake

Total Energy Expenditure

Progressive Loss of Diet Adherence!

Weight Loss Maintenance

Energy Intake for Maintenance

Energy Intake for Maintenance

Replace the 3500 kcal/lb rule?
Simplified Model Equations

Lean Mass:
\[ \frac{dL}{dt} = \left( \frac{\alpha \rho_L}{\alpha \rho_L + \rho_F} \right)(I - E) \]

Fat Mass:
\[ \frac{dF}{dt} = \left( \frac{\rho_F}{\alpha \rho_L + \rho_F} \right)(I - E) \]

Sum:
\[ \frac{dL}{dt} + \frac{dF}{dt} = (I - E) \]

Assuming \( \alpha \) is a particular constant:
\[ \frac{dBW}{dt} \approx \frac{(I - E)}{3500 \text{ kcal/lb}} \]
Simplified Model Equations

Lean Mass:
\[
\rho_L \frac{dL}{dt} = \left( \frac{\alpha \rho_L}{\alpha \rho_L + \rho_F} \right) (I - E)
\]

Fat Mass:
\[
\rho_F \frac{dF}{dt} = \left( \frac{\rho_F}{\alpha \rho_L + \rho_F} \right) (I - E)
\]

Energy Expenditure:
\[
E = K + \gamma_L L + \gamma_F F + \delta BW + \beta \Delta I + \eta_F \frac{dF}{dt} + \eta_L \frac{dL}{dt}
\]

Resting Metabolism
Adaptive Thermogenesis
Physical Activity
Tissue Deposition

\[
\frac{1}{1 - \beta} \left( \frac{\eta_F + \rho_F + \alpha \eta_L + \alpha \rho_L}{1 + \alpha} \right) \frac{dBW}{dt} = \Delta I - \frac{1}{1 - \beta} \left[ \left( \frac{\gamma_F + \alpha \gamma_L}{1 + \alpha} \right) (BW - BW_0) + \delta BW - \delta_0 BW_0 \right]
\]

New Rules…

\[
\frac{dBW}{dt} \approx \frac{\Delta I - 10 \text{ kcal/lb/d} \times (BW - BW_0)}{4100 \text{ kcal/lb}}
\]

\[
BW(t) - BW_0 = \left[ 1 - \exp\left(\frac{-t}{410 \text{ d}}\right) \right] \left( \frac{\Delta I}{10 \text{ kcal/d}} \right) \text{ lb}
\]

Long Time Scale!

Steady State Weight Change

\[
\Delta BW = \left( \frac{\Delta I}{10 \text{ kcal/d}} \right) \text{ lb}
\]

Differences in Weight Loss?

Initial BW = 80 kg

Initial BW = 100 kg

http://bwsimulator.niddk.nih.gov
Estimating Individual Intake Changes

\[
\rho \frac{dBW}{dt} = \Delta I - \varepsilon \left( BW - BW_0 \right)
\]

Slope by Linear Regression of BW Measurements

\[
\Delta I = \rho \frac{dBW}{dt} + \varepsilon \left( BW - BW_0 \right)
\]

\[
\text{var}(\Delta I) = \left( 2\varepsilon^2 + \frac{12\rho^2}{n(n^2-1)T^2} + \frac{12\varepsilon\rho}{(n+1)T^2} \right) \text{var}(BW)
\]

Number of BW data points

Period between BW measurements

KD Hall, CC Chow. AJCN 94:66-74 (2011)
Typical Weight Loss Curve

Body Weight (kg)

-1000 kcal/d  -500 kcal/d  -0 kcal/d

Time (weeks)
Estimated Free-Living Intake Change

KD Hall, CC Chow. *AJCN* (2011)
Modeling Policy Changes

Taxing Caloric Sweetened Beverages: Potential Effects on Beverage Consumption, Calorie Intake, and Obesity

Travis A. Smith, tsmith@ers.usda.gov
Biing-Hwan Lin, blin@ers.usda.gov
Jonq-Ying Lee, jonqying@ufl.edu
Predicted Weight Change from Taxing Sweetened Drinks

Dynamic Model

3500 kcal per lb rule

Predicted Obesity Prevalence after Taxing Sweetened Drinks

N = 4293

Dynamic Model

3500 kcal per lb rule

BH Lin, TA Smith, HY Lee, KD Hall. *Econ Hum Biol* (2011)
Modeling the Rise of Obesity

Average Body Weight

Data from National Health and Nutrition Examination Survey (NHANES)
U.S. Food Supply

Per Capita Food Energy (kcal/d)

Year

FAO Food Supply

Food Intake (model)


If we had eaten all of the USDA Food Available...

Average Body Weight (kg)

Year


Simulated Body Weight

NHANES Body Weight
Food Supply, Intake, and Waste

Progressive Increase of Food Waste

Progressive Increase of Food Waste

Per Capita Food Waste (kcal/d)

Per Capita Solid Food Waste (kg/yr)


Year

The Push Hypothesis

Agriculture subsidies & policy

Increased production

Increased food waste

More Cheap food

Obesity

Increased food waste

Thanks!

**NIDDK**

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Bernard Miller (LBM)
Juen Guo (LBM)
Peter Jordan (LBM)
Dhruva Chandramohan (LBM)
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Vipul Periwal (LBM)
Heather Bain (LBM)
Monica Skarulis (DEOB)
Gail Hall (DEOB)
Kong Chen (DEOB)
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Graham Finlayson (Leeds)
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