A FAST way to longer life...

Harvey S. Hahn, MD, FACC
Program Director, Cardiovascular Fellowship Training Program
Fasting? Crashing?
The Big 3....

- Diet
- Exercise
- Sleep / stress
- What is the ONE thing that can tie all 3 together?
- Intermittent fasting!
Effects of intermittent fasting on body composition and clinical health markers in humans

Grant M. Tinsley and Paul M. La Bounty

<table>
<thead>
<tr>
<th></th>
<th>Wt</th>
<th>Fat (kg)</th>
<th>Chole</th>
<th>Trig</th>
<th>Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADF</td>
<td>↓3-7%</td>
<td>↓3-5.5</td>
<td>↓10-21%</td>
<td>↓14-42%</td>
<td>3-12 wks</td>
</tr>
<tr>
<td>Whole day</td>
<td>↓3-9%</td>
<td>↓3-9</td>
<td>↓5-20%</td>
<td>↓17-50%</td>
<td>12-24 wks</td>
</tr>
</tbody>
</table>
Things always happen in 3s...

- The NEJM publishes a review article on intermittent fasting Dec 2019.
- Wilkinson et al publishes the easiest and best outcomes data on IF in Jan 2020.
Lifespan...

- Information theory of aging.
- Low level stress activates your survival pathways and tunes up your epigenetic makeup.
- Hunger, exercise, cold exposure all help you live longer!
Calorie restriction (CR)

Calorie restriction is the most robust way to prevent cancer, heart disease or pretty much all diseases.

David Sinclair

Fasting is a subgroup of CR.
“I’ll just work it off...”
CALERIE Study

- Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy
- Reduced caloric intake by 25%.
- Average caloric reduction was ~12%.
- Resulted in 10% wt loss.
- BP dropped by 4%, total cholesterol 6%, CRP 47%.
Effects of Intermittent Fasting on Health, Aging, and Disease

Rafael de Cabo, Ph.D., and Mark P. Mattson, Ph.D.
Figure 2. Metabolic Adaptations to Intermittent Fasting.

Energy restriction for 10 to 14 hours or more results in depletion of liver glycogen stores and hydrolysis of triglycerides (TGs) into fatty acids (FFAs) in adipocytes. FFAs released into the circulation are transported into hepatocytes, where they produce ketone bodies, specifically acetacetate and β-hydroxybutyrate (β-HB). FFAs also activate the transcription factors peroxisome proliferator-activated receptor-α (PPAR-α) and activating transcription factor 4 (ATF4), resulting in the production and release of fibroblast growth factor-21 (FGF21) protein with widespread effects on cells throughout the body and brain. β-HB and acetacetate are actively transported into the liver and then they can be metabolized to acetyl CoA, which enters the tricarboxylic acid (TCA) cycle and generates ATP. β-HB also has neurotrophic functions, including the activation of transcription factors such as cyclic AMP response element-binding protein (CREB) and nuclear factor-κB (NF-κB) and the expression of brain-derived neurotrophic factor (BDNF) in neurons. Reduced levels of glucose and amino acids during fasting result in reduced activity of the mTOR pathway and up-regulation of autophagy. In addition, energy restriction stimulates mitochondrial biogenesis and mitochondrial uncoupling.
**Figure 3. Cellular and Molecular Mechanisms Underlying Improved Organ Function and Resistance to Stress and Disease with Intermittent Metabolic Switching.**

Periods of dietary energy restriction sufficient to cause depletion of liver glycogen stores trigger a metabolic switch toward use of fatty acids and ketones. Cells and organ systems adapt to this bioenergetic challenge by activating signaling pathways that bolster mitochondrial function, stress resistance, and antioxidant defenses while up-regulating autophagy to remove damaged molecules and recycle their components. During the period of energy restriction, cells adopt a stress-resistance mode through reduction in insulin signaling and overall protein synthesis. Exercise enhances these effects of fasting. On recovery from fasting (eating and sleeping), glucose levels increase, ketone levels plummet, and cells increase protein synthesis, undergoing growth and repair. Maintenance of an intermittent-fasting regimen, particularly when combined with regular exercise, results in many long-term adaptations that improve mental and physical performance and increase disease resistance. HRV denotes heart-rate variability.
Figure 4. Incorporation of Intermittent-Fasting Patterns into Health Care Practice and Lifestyles.

As a component of medical school training in disease prevention, students could learn the basics of how intermittent fasting affects metabolism and how cells and organs respond adaptively to intermittent fasting, the major indications for intermittent fasting (obesity, diabetes, cardiovascular disease, and cancers), and how to implement intermittent-fasting prescriptions to maximize long-term benefits. Physicians can incorporate intermittent-fasting prescriptions for early intervention in patients with a range of chronic conditions or at risk for such conditions, particularly those conditions associated with overeating and a sedentary lifestyle. One can envision inpatient and outpatient facilities staffed by experts in diet, nutrition, exercise, and psychology that will help patients make the transition to sustainable intermittent-fasting and exercise regimens (covered by basic health insurance policies). As an example of a specific prescription, the patient could choose either a daily time-restricted feeding regimen (an 18-hour fasting period and a 6-hour eating period) or the 5:2 intermittent-fasting regimen (fasting [i.e., an intake of 500 calories] 2 days per week), with a 4-month transition period to accomplish the goal. To facilitate adherence to the prescription, the physician’s staff should be in frequent contact with the patient during the 4-month period and should closely monitor the patient’s body weight and glucose and ketone levels.
Cell Metabolism

Ten-Hour Time-Restricted Eating Reduces Weight, Blood Pressure, and Atherogenic Lipids in Patients with Metabolic Syndrome

Graphical Abstract

In Brief

Wilkinson and Manoogian et al. studied the impact of time-restricted eating in metabolic syndrome by reducing participant’s daily eating window from ≥14 h to a self-selected 10 h window for 12 weeks. Time-restricted eating led to weight loss, healthier body composition, lower blood pressure, and decreased levels of cardiovascular disease-promoting lipids.

Authors

Michael J. Wilkinson, Emily N.C. Manoogian, Adena Zadourian, ..., Saket Navlakha, Satchidananda Panda, Pam R. Taub

Correspondence

satchin@salk.edu (S.P.), ptaub@ucsd.edu (P.R.T.)

Highlights

- 10 h time-restricted eating (TRE) in metabolic syndrome (MetS) promotes weight loss
- TRE in MetS reduces waist circumference, percent body fat, and visceral fat
- TRE in MetS lowers blood pressure, atherogenic lipids, and glycated hemoglobin
- Benefits of TRE are “add-ons” to statin and anti-hypertensive medications

Wilkinson et al., 2020, Cell Metabolism 31, 92–104
January 7, 2020 © 2019 Elsevier Inc.
https://doi.org/10.1016/j.cmet.2019.11.004
• Small study.
• 10 hr feeding, not 8.
• No change in diet quality.
• No exercise component.
• Pt already on BP meds and statins!
• CR of 8.6%.
• Lost 3.3 kg (7.3 lbs).
• 12 wks long.
So what’s the easiest way to fast?

RMR persists even when you sleep
More Than A Third Of U.S. Adults Don’t Get Enough Sleep

Percent of adults by self-reported sleep duration

- Less than 5 hours: 11.8%
- 6 hours: 23%
- 7 hours: 29.5% *Adults should get 7 or more hours of sleep.*
- 8 hours: 27.7%
- 9 hours: 4.4%
- More than 10 hours: 3.6%

Source: CDC
Interplay of Objective Sleep Duration and Cardiovascular and Cerebrovascular Diseases on Cause-Specific Mortality

Julio Fernandez-Mendoza, PhD, CBSM, DBSM; Fan He, MS; Alexandros N. Vgontzas, MD, ScD; Duanping Liao, MD, PhD; Edward O. Bixler, PhD

(J Am Heart Assoc. 2019;8:e013043. DOI: 10.1161/JAHA.119.013043.)
Figure 1. Multivariable-adjusted survival curves for all-cause mortality associated with cardiometabolic risk factors (CMRs) and cardiovascular and cerebrovascular disease (CBVD) at baseline. A, Survival curves for all-cause mortality associated with CMRs or CBVD. B, Survival curves for all-cause mortality associated with CMRs and CBVD. All data adjusted for age, race, sex, education, body mass index, smoking, alcohol use, apnea-hypopnea index, other physical health conditions, and mental health conditions.
Sleep Duration and Myocardial Infarction

Iyas Daghlas, BS, Hassan S. Dashti, PhD, RD, Jacqueline Lane, PhD, Krishna G. Aragam, MD, MS, Martin K. Rutter, MD, Richa Saxena, PhD, Céline Vetter, PhD

**CENTRAL ILLUSTRATION** Associations of Sleep Duration With Coronary Disease: Observational and 2-Sample Mendelian Randomization

<table>
<thead>
<tr>
<th>Multivariable Hazard Ratio</th>
<th>Mendelian Randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short (&lt;6 h)</strong></td>
<td><strong>Long (&gt;9 h)</strong></td>
</tr>
<tr>
<td>▲20% risk of incident MI</td>
<td>▲34% risk of incident MI</td>
</tr>
</tbody>
</table>


Magnitude of effects observed for effects of phenotypic and genetically varying sleep duration. Note, that although the clocks show variable sleep timing for short and long sleep, the observed effects are independent of self-reported sleep timing preference. MI = myocardial infarction; MR = Mendelian randomization.
Poor sleep lowers will power.

It also increases caloric consumption and fat intake the next day.

How / why?
“I deserve this...”
An extra ~1000 calories...
Gwen Jorgenson

Sleeps 40-50% of her LIFE!
Myth: Cardio is the best way to drop weight...

What do you call doing cardio 5 days a wk?

The road to nowhere!

Why?
The Law of Diminishing Returns...

Constrained Total Energy Expenditure and Metabolic Adaptation to Physical Activity in Adult Humans

Herman Pontzer,1,2,* Ramon Durazo-Arvizu,3 Lara R. Dugas,3 Jacob Plange-Rhule,4 Pascal Bovet,5,6 Terrence E. Forrester,7 Estelle V. Lambert,8 Richard S. Cooper,3 Dale A. Schoeller,9 and Amy Luke3
1Department of Anthropology, Hunter College, City University of New York, 695 Park Avenue, New York, NY 10065, USA
2New York Consortium for Evolutionary Primatology, New York, NY 10065, USA
3Public Health Sciences, Stritch School of Medicine, Loyola University Chicago, 2160 South First Avenue, Maywood, IL 60153, USA
4Kwame Nkrumah University of Science and Technology, Kumasi, Ghana
5Institute of Social & Preventive Medicine, Lausanne University Hospital, Rue de la Corniche 10, 1010 Lausanne, Switzerland
6Ministry of Health, PO Box 52, Victoria, Mahé, Seychelles
7UWI Solutions for Developing Countries, The University of the West Indies, 25 West Road, UWI Mona Campus, Kingston 7, Jamaica
8Research Unit for Exercise Science and Sports Medicine, University of Cape Town, PO Box 115, Newlands 7725, Cape Town, South Africa
9Nutritional Sciences, Biotechnology Center, University of Wisconsin–Madison, 425 Henry Mall, Madison, WI 53705, USA
*Correspondence: herman.pontzer@hunter.cuny.edu
http://dx.doi.org/10.1016/j.jcb.2015.12.046
Two theories...

Figure 1. Schematic of Additive Total Energy Expenditure and Constrained Total Energy Expenditure Models

In Additive total energy expenditure models, total energy expenditure is a simple linear function of physical activity, and variation in physical activity energy expenditure (PA) determines variation in total energy expenditure. In Constrained total energy expenditure models, the body adapts to increased physical activity by reducing energy spent on other physiological activity, maintaining total energy expenditure within a narrow range.
Figure 1. Schematic of Additive Total Energy Expenditure and Constrained Total Energy Expenditure Models

In Additive total energy expenditure models, total energy expenditure is a simple linear function of physical activity, and variation in physical activity energy expenditure (PA) determines variation in total energy expenditure. In Constrained total energy expenditure models, the body adapts to increased physical activity by reducing energy spent on other physiological activity, maintaining total energy expenditure within a narrow range.

Figure 3. The Effect of Physical Activity on Total Energy Expenditure and Its Components

The winner is...
IF vs keto in Exercise

• What are the 2 main questions about fasted and ketogenic exercise?
• #1-will it increase performance?
• #2-will it lead to more fat burn?
This is a picture tracking bullet holes on Allied planes that encountered Nazi anti-aircraft fire in WW2.

What was the logic error?
IF vs keto

**Keto**
- Early wt loss is due to water loss.
- Biggest change is eliminating garbage processed carbs (50-60% of the SAD).
- If increased bad fats then lipids levels can rise.
- *Most never really achieve ketosis.*
- *Most don’t even try to measure ketosis.*

**IF**
- Shrinks stomach.
- Increases leptin which reduces hunger in the long run.
- Associated with a survival benefit.
- **8-12 hours of fasting typically induces a state of ketosis.**
The data

• Carbs are best for performance.
• Fat is not.
• Protein is best for muscle gains.
• Keto is trendy and cool. Exclusive diets sell better. Hard to make the case that your program is better if it’s like other programs.
• The internet and social media are terrible.
• Pubmed hits as of 1.23.2020

<table>
<thead>
<tr>
<th></th>
<th>Performance</th>
<th>Fat loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keto (2880)</td>
<td>13</td>
<td>17</td>
</tr>
<tr>
<td>IF (118,980)</td>
<td>526</td>
<td>1908</td>
</tr>
</tbody>
</table>
Why do people lose weight on a #keto diet? Um, because they end up eating less calories (than their former diet): Laws of Thermodynamics. But remember weight loss does" not always equal "better health". That should not always be the goal. One can have a low BMI and be unhealthy.

6:57 AM - 9 Mar 2019

21 Retweets 260 Likes

Sage uses carbs during races!

Sage also does his long runs fasted.

Give me a list of low carb high animal fat "keto cultures" doing well health and longevity-wise long term...there simply aren't any. That's not my opinion. You obviously haven't looked into this much.

7:12 AM - 8 Feb 2019
Currently we don’t know!

Mixed data for both keto and IF on exercise performance.

Everyone is different.

Recommend experimenting on yourself.
Exercise and timing of food intake

Acute response + Chronic adaptation

Energy balance behaviours

↓ daily energy intake\(^{27,31}\)

↓ daily energy expenditure?

Glycaemic control – variable \(^{23,25,26}\)

↓ TAG\(^{21,22}\)

↔ Liver fat\(^{15}\)

↓ glycogen use\(^{12}\)

↑ IMTAG use\(^{14}\)

↑ GLUT\(^{45}\)

↑ FAT/CD36\(^{44}\)

↑ CPT\(^{144}\)

↑ PDK\(^{44}\)

↑ AMPK\(^{44}\)

↑ glycogen (basal)\(^{35}\)

↑ GLUT\(^{40}\)

↑ FAT/CD36\(^{40}\)

↑ FABP\(^{47}\)

↑ NEFA use\(^{13}\)

↑ GLUT\(^{43}\)

↑ FAT/CD36\(^{43}\)

↑ PDK\(^{43}\)

↑ IRS\(^{243}\)
• Decreased insulin production.
• Decreased glucose levels.
• And...
More fat oxidation!

<table>
<thead>
<tr>
<th>Study name</th>
<th>Difference in means</th>
<th>SE</th>
<th>Variance</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>Z-value</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bergman &amp; Brooks, 1999a</td>
<td>-7.87</td>
<td>7.65</td>
<td>58.57</td>
<td>-22.87</td>
<td>7.13</td>
<td>-1.03</td>
<td>0.304</td>
</tr>
<tr>
<td>Bergman &amp; Brooks, 1999b</td>
<td>-4.49</td>
<td>5.24</td>
<td>27.46</td>
<td>-14.76</td>
<td>5.78</td>
<td>-0.86</td>
<td>0.391</td>
</tr>
<tr>
<td>Farah &amp; Gill, 2013</td>
<td>-5.70</td>
<td>1.84</td>
<td>3.38</td>
<td>-9.30</td>
<td>-2.10</td>
<td>-3.10</td>
<td>0.002</td>
</tr>
<tr>
<td>Gonzalez et al., 2013</td>
<td>-6.00</td>
<td>4.46</td>
<td>19.86</td>
<td>-14.74</td>
<td>2.74</td>
<td>-1.35</td>
<td>0.178</td>
</tr>
<tr>
<td>Isacco et al., 2012a</td>
<td>-4.59</td>
<td>1.86</td>
<td>3.48</td>
<td>-8.24</td>
<td>-0.94</td>
<td>-2.46</td>
<td>0.014</td>
</tr>
<tr>
<td>Isacco et al., 2012b</td>
<td>-1.74</td>
<td>1.20</td>
<td>1.45</td>
<td>-4.10</td>
<td>0.62</td>
<td>-1.45</td>
<td>0.148</td>
</tr>
<tr>
<td>Little et al., 2010</td>
<td>-5.15</td>
<td>3.43</td>
<td>11.74</td>
<td>-11.87</td>
<td>1.57</td>
<td>-1.50</td>
<td>0.133</td>
</tr>
<tr>
<td>Massicotte et al., 1990</td>
<td>-5.00</td>
<td>4.99</td>
<td>24.99</td>
<td>-14.80</td>
<td>4.80</td>
<td>-1.00</td>
<td>0.317</td>
</tr>
<tr>
<td>Maughan &amp; Gleeson, 1988</td>
<td>-0.90</td>
<td>7.63</td>
<td>58.27</td>
<td>-15.86</td>
<td>14.06</td>
<td>-0.12</td>
<td>0.906</td>
</tr>
<tr>
<td>Paul et al., 1996</td>
<td>-41.40</td>
<td>17.54</td>
<td>307.60</td>
<td>-75.78</td>
<td>-7.03</td>
<td>-2.36</td>
<td>0.018</td>
</tr>
<tr>
<td>Whitley et al., 1998</td>
<td>-14.38</td>
<td>9.67</td>
<td>93.52</td>
<td>-33.33</td>
<td>4.57</td>
<td>-1.49</td>
<td>0.137</td>
</tr>
<tr>
<td>Wilcutts et al., 1988</td>
<td>-2.62</td>
<td>1.02</td>
<td>1.04</td>
<td>-4.62</td>
<td>-0.62</td>
<td>-2.57</td>
<td>0.010</td>
</tr>
<tr>
<td>Wu et al., 2003</td>
<td>-18.10</td>
<td>5.16</td>
<td>26.65</td>
<td>-28.22</td>
<td>-7.98</td>
<td>-3.51</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>-3.53</td>
<td>0.63</td>
<td>0.40</td>
<td>-4.76</td>
<td>-2.30</td>
<td>-5.62</td>
<td>0.000</td>
</tr>
</tbody>
</table>

**Fig. 4.** Fat oxidation (g) during exercise performed in the fasted state v. fed state. ■, Study-specific estimates; ←, pooled estimates of fixed-effects meta-analyses.
Alternate Day Fasting and Endurance Exercise Combine to Reduce Body Weight and Favorably Alter Plasma Lipids in Obese Humans

Surabhi Bhutani, Monica C. Klempel, Cynthia M. Kroeger, John F. Trepanowski and Krista A. Varady

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Week 1</th>
<th>Week 12</th>
<th>P-value&lt;sup&gt;a&lt;/sup&gt;</th>
<th>P-value&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Change&lt;sup&gt;c&lt;/sup&gt;</th>
<th>P-value&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body weight (kg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination</td>
<td>91 ± 6</td>
<td>85 ± 6</td>
<td>&lt;0.001</td>
<td>0.393</td>
<td>−6 ± 4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ADF</td>
<td>94 ± 3</td>
<td>91 ± 3</td>
<td>&lt;0.001</td>
<td></td>
<td>−3 ± 1&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>93 ± 2</td>
<td>92 ± 2</td>
<td>0.027</td>
<td></td>
<td>−1 ± 0&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>93 ± 5</td>
<td>93 ± 5</td>
<td>0.577</td>
<td></td>
<td>0 ± 0&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td><strong>Body mass index (kg/m²)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination</td>
<td>35 ± 1</td>
<td>33 ± 1</td>
<td>&lt;0.001</td>
<td>0.334</td>
<td>−2 ± 0&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ADF</td>
<td>35 ± 1</td>
<td>34 ± 1</td>
<td>&lt;0.001</td>
<td></td>
<td>−1 ± 0&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>35 ± 1</td>
<td>34 ± 1</td>
<td>0.030</td>
<td></td>
<td>−1 ± 0&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>35 ± 1</td>
<td>35 ± 1</td>
<td>0.707</td>
<td></td>
<td>0 ± 0&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td><strong>Fat mass (kg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination</td>
<td>45 ± 2</td>
<td>40 ± 2</td>
<td>&lt;0.001</td>
<td>0.054</td>
<td>−5 ± 1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ADF</td>
<td>43 ± 2</td>
<td>41 ± 2</td>
<td>0.008</td>
<td></td>
<td>−2 ± 1&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>46 ± 2</td>
<td>45 ± 2</td>
<td>0.182</td>
<td></td>
<td>−1 ± 0&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>43 ± 4</td>
<td>43 ± 4</td>
<td>0.570</td>
<td></td>
<td>0 ± 1&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td><strong>Fat free mass (kg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination</td>
<td>46 ± 2</td>
<td>46 ± 2</td>
<td>0.221</td>
<td>0.299</td>
<td>0 ± 1</td>
<td>0.527</td>
</tr>
<tr>
<td>ADF</td>
<td>51 ± 2</td>
<td>50 ± 2</td>
<td>0.031</td>
<td></td>
<td>−1 ± 1</td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>48 ± 1</td>
<td>47 ± 1</td>
<td>0.321</td>
<td></td>
<td>−1 ± 0</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>50 ± 2</td>
<td>49 ± 2</td>
<td>0.693</td>
<td></td>
<td>−1 ± 1</td>
<td></td>
</tr>
<tr>
<td><strong>Waist circumference (cm)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Combination</td>
<td>96 ± 2</td>
<td>88 ± 1</td>
<td>&lt;0.001</td>
<td>0.310</td>
<td>−8 ± 1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ADF</td>
<td>100 ± 2</td>
<td>95 ± 2</td>
<td>&lt;0.001</td>
<td></td>
<td>−5 ± 1&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Exercise</td>
<td>98 ± 2</td>
<td>95 ± 2</td>
<td>&lt;0.001</td>
<td></td>
<td>−3 ± 1&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>98 ± 3</td>
<td>97 ± 2</td>
<td>0.640</td>
<td></td>
<td>−1 ± 1&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>
### TABLE 5 LDL particle size during the 12-week trial

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Week 1</th>
<th>Week 12</th>
<th>P-value&lt;sup&gt;a&lt;/sup&gt;</th>
<th>P-value&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Change&lt;sup&gt;c&lt;/sup&gt;</th>
<th>P-value&lt;sup&gt;d&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL particle size (Å)</td>
<td>Combination</td>
<td>260 ± 1</td>
<td>264 ± 2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;0.001</td>
<td>0.031</td>
<td>4 ± 1&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>ADF</td>
<td>261 ± 1</td>
<td>266 ± 1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;0.001</td>
<td>5 ± 1&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>261 ± 2</td>
<td>262 ± 2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.426</td>
<td>1 ± 1&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>259 ± 1</td>
<td>260 ± 2&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.884</td>
<td>0 ± 1&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Large LDL particles (%)</td>
<td>Combination</td>
<td>38 ± 4</td>
<td>45 ± 5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.142</td>
<td>0.014</td>
<td>7 ± 5</td>
</tr>
<tr>
<td></td>
<td>ADF</td>
<td>36 ± 3</td>
<td>51 ± 4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;0.001</td>
<td>15 ± 3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>39 ± 3</td>
<td>40 ± 4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.792</td>
<td>1 ± 5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>30 ± 3</td>
<td>31 ± 4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.883</td>
<td>1 ± 4</td>
<td></td>
</tr>
<tr>
<td>Medium LDL particles (%)</td>
<td>Combination</td>
<td>37 ± 2</td>
<td>38 ± 2</td>
<td>0.845</td>
<td>0.301</td>
<td>1 ± 3</td>
</tr>
<tr>
<td></td>
<td>ADF</td>
<td>37 ± 1</td>
<td>35 ± 1</td>
<td>0.288</td>
<td>-2 ± 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>41 ± 3</td>
<td>40 ± 3</td>
<td>0.453</td>
<td>-1 ± 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>41 ± 2</td>
<td>40 ± 2</td>
<td>0.717</td>
<td>-1 ± 2</td>
<td></td>
</tr>
<tr>
<td>Small LDL particles (%)</td>
<td>Combination</td>
<td>25 ± 3</td>
<td>18 ± 3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.010</td>
<td>-7 ± 2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>ADF</td>
<td>27 ± 3</td>
<td>15 ± 3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>&lt;0.001</td>
<td>0.023</td>
<td>-12 ± 3&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
<td>21 ± 3</td>
<td>20 ± 4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.972</td>
<td>-1 ± 4&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>29 ± 3</td>
<td>30 ± 3&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.776</td>
<td>1 ± 3&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>
Effects of Prior Fasting on Fat Oxidation during Resistance Exercise

KENDALL FRAWLEY*, GABRIELLE GREENWALD*, REBECCA R. ROGERS‡, JOHN K. PETRELLA‡, and MALLORY R. MARSHALL‡

Department of Kinesiology, Samford University, Birmingham, AL, USA

• NCAA women
• 10 hours fasted vs fed
• Respiratory exchange ratio was lower in the fasted group implying more fat metabolism than carb metabolism.
EPOC, not

- Excess post-exercise oxygen consumption-after burn!
- This is the Holy Grail of weight loss.
- Can it be done?
- HIIT
- Resistance training
Relation of Muscle Mass and Fat Mass to Cardiovascular Disease Mortality

Preethi Srikanthan, MD, MS\textsuperscript{a,g}, Tamara B. Horwich, MD, MS\textsuperscript{b}, and Chi Hong Tseng, PhD\textsuperscript{c}

Figure 2. Kaplan-Meier plot of all-cause mortality for the 4 body composition types based on AMMI and TRFI.

(Am J Cardiol 2016;117:1355–1360)
Brown fat vs white fat...

It’s not just burning fat, but changing it. You can brown your white fat!
The Hunger Games...

Long-Term Persistence of Hormonal Adaptations to Weight Loss

Leptin and brain–adipose crosstalks

Alexandre Caron, Syann Lee, Joel K. Elmquist* and Laurent Gautron*

Abstract | Interactions between the brain and distinct adipose depots have a key role in maintaining energy balance, thereby promoting survival in response to metabolic challenges such as cold exposure and starvation. Recently, there has been renewed interest in the specific central neuronal circuits that regulate adipose depots. Here, we review anatomical, genetic and pharmacological studies on the neural regulation of adipose function, including lipolysis, non-shivering thermogenesis, browning and leptin secretion. In particular, we emphasize the role of leptin-sensitive neurons and the sympathetic nervous system in modulating the activity of brown, white and beige adipose tissues. We provide an overview of advances in the understanding of the heterogeneity of the brain regulation of adipose tissues and offer a perspective on the challenges and paradoxes that the community is facing regarding the actions of leptin on this system.
Leptin

- Anti-hunger hormone.
- NOT an acute reactant.
- Works on a **chronic** basis.
- You get less hungry over time!
Leptin

- Why do β-blockers impede weight loss?
- Decreased HR
- Blocks a signaling pathway for leptin production.
Brown adipose tissue in humans: regulation and metabolic significance

Moe Thuzar\textsuperscript{1,2} and Ken K Y Ho\textsuperscript{1,2}

\textsuperscript{1}Department of Endocrinology and Diabetes, Princess Alexandra Hospital, Brisbane, Queensland, Australia and \textsuperscript{2}School of Medicine, University of Queensland, Brisbane, Queensland 4102, Australia

Correspondence should be addressed to K K Y Ho
Email
k.ho@uq.edu.au
Table 1  Summary of studies reporting detected amount of BAT and associated CIT after acute cold stimulation in adult humans.

<table>
<thead>
<tr>
<th>References</th>
<th>Number of subjects</th>
<th>Cooling temperature (°C)</th>
<th>BAT amount</th>
<th>CIT (kcal/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(33)</td>
<td>6</td>
<td>18</td>
<td>Mean 168 ml</td>
<td>Mean 2000</td>
</tr>
<tr>
<td>(34)</td>
<td>9 with high BAT</td>
<td>15</td>
<td>Mean 59.1 g</td>
<td>Mean 237</td>
</tr>
<tr>
<td></td>
<td>15 with low BAT</td>
<td></td>
<td>Mean 2.2 g</td>
<td>Mean 39</td>
</tr>
<tr>
<td>(35)</td>
<td>19 BAT positive</td>
<td>17 ± 1</td>
<td>Mean 34 g</td>
<td>Mean 287&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>8 BAT negative</td>
<td></td>
<td>Mean 167&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Mean 167&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>(38)</td>
<td>24</td>
<td>19</td>
<td>Mean 63 ml</td>
<td>Mean 88</td>
</tr>
<tr>
<td>(39)</td>
<td>10</td>
<td>14</td>
<td>Median 15 ml</td>
<td>Mean 79</td>
</tr>
<tr>
<td>(153)</td>
<td>6 BAT positive</td>
<td>19</td>
<td>No data</td>
<td>Mean 410</td>
</tr>
<tr>
<td></td>
<td>7 BAT negative</td>
<td></td>
<td></td>
<td>Mean 42</td>
</tr>
</tbody>
</table>

<sup>a</sup>Converted from Megajoule using 1 MJ = 239 kcal, normalised for fat free mass.

Table 2  Summary of cold acclimatisation studies addressing the role of BAT in adiposity and substrate metabolism in humans.

<table>
<thead>
<tr>
<th>References</th>
<th>Number of subjects</th>
<th>Acclimatisation protocol</th>
<th>ΔBAT activity from baseline</th>
<th>ΔMetabolism from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>(24)</td>
<td>22 randomised to cold intervention or usual living (control)</td>
<td>17 °C, 2 h/day for 6 weeks</td>
<td>58% increase (no significant change in the control group)</td>
<td>5.2% or 0.7 kg decrease in body fat mass (no significant change in the control group)</td>
</tr>
<tr>
<td>(21)</td>
<td>6</td>
<td>10 °C, 2 h/day for 4 weeks</td>
<td>45% increase</td>
<td>6.2% decrease in plasma glucose</td>
</tr>
<tr>
<td>(22)</td>
<td>5</td>
<td>19 °C overnight for 1 month</td>
<td>54% increase</td>
<td>&gt;50% increase in insulin sensitivity</td>
</tr>
<tr>
<td>(37)</td>
<td>10</td>
<td>14–15 °C for 10 days</td>
<td>~50% increase</td>
<td>43% increase in insulin sensitivity</td>
</tr>
</tbody>
</table>
Figure 1

Effect of chronic cold exposure on BAT activity, CIT and body fat mass in humans. (A) BAT activity plotted in standardised uptake value (SUV), measured on FDG–PET–CT scans before and after 6 weeks of daily cold exposure. (B) CIT expressed in kcal/day in subjects who underwent the cold intervention (cold group) and those who continued their usual daily living (control group). (C) Change in body fat mass from baseline after 6 weeks in the cold group and control group. Expressed in mean±s.e.m.; *P<0.05 (Adapted with permission from (24)).
Stress leads to growth...
## Stimulus response chart

<table>
<thead>
<tr>
<th>Stimulus</th>
<th>Sign / symptom</th>
<th>Minimal dose</th>
<th>Overdose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calorie restriction</td>
<td>?</td>
<td>10%</td>
<td>Starvation</td>
</tr>
<tr>
<td>Intermittent fasting</td>
<td>Hunger</td>
<td>8 hour fast, 5 days/month</td>
<td>Starvation</td>
</tr>
<tr>
<td>Exercise</td>
<td>Tachy, DOE, sweat, uncomfortable</td>
<td>10-15 mins continuous</td>
<td>Overtraining syndrome, cortisol, injury</td>
</tr>
<tr>
<td>Cold exposure</td>
<td>Shiver, goosebumps</td>
<td>10 min</td>
<td>Frostbite</td>
</tr>
<tr>
<td>Sleep</td>
<td>None, should be asleep.</td>
<td>6 hrs continuous</td>
<td>Coma or death...</td>
</tr>
</tbody>
</table>
Live long and prosper!

EAT  SLEEP  RUN

REPEAT

TRAIN LIKE AN ATHLETE, EAT LIKE A NUTRITIONIST, SLEEP LIKE A BABY, WIN... LIKE A CHAMPION

and FAST!
Back up slides
When Choosing A Health Plan, What We Can Learn From Frankenstein

by HARVEY HARR, MD, FACC

• LifeandHealth.org
• https://lifeandhealth.org/slider/when-choosing-a-health-plan-what-we-can-learn-from-frankenstein/2317658.html
### Summary

<table>
<thead>
<tr>
<th>Health benefits relate to:</th>
<th>Low-carbohydrate</th>
<th>Low-fat/vegetarian/vegan</th>
<th>Low-glycemic</th>
<th>Mediterranean</th>
<th>Mixed/balanced</th>
<th>Paleolithic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Emphasis on restriction of refined starches and added sugars in particular.</td>
<td>Emphasis on plant foods direct from nature; avoidance of harmful fats.</td>
<td>Restriction of starches, added sugars; high fiber intake.</td>
<td>Foods direct from nature; mostly plants; emphasis on healthful oils, notably monounsaturates.</td>
<td>Minimization of highly processed, energy-dense foods; emphasis on wholesome foods in moderate quantities.</td>
<td>Minimization of processed foods. Emphasis on natural plant foods and lean meats.</td>
</tr>
<tr>
<td>Compatible elements:</td>
<td>Limited refined starches, added sugars, processed foods; limited intake of certain fats; emphasis on whole plant foods, with or without lean meats, fish, poultry, seafood.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**And all potentially consistent with:**

Food, not too much, mostly plants\(^a,b,c.\)

---

\(^a\) From Reference 135.
\(^b\) Portion control may be facilitated by choosing better-quality foods which have the tendency to promote satiety with fewer calories.
\(^c\) While neither the low-carbohydrate nor Paleolithic diet need be “mostly plants,” both can be.


- Everyone is different.
- Sustainability is key, not a diet...
- Enjoy life, don’t torture yourself,
- or others for that matter...
Higher compared with lower dietary protein during an energy deficit combined with intense exercise promotes greater lean mass gain and fat mass loss: a randomized trial

Thomas M Longland, Sara Y Oikawa, Cameron J Mitchell, Michaela C Devries, and Stuart M Phillips*

Department of Kinesiology, Exercise Metabolism Research Group, McMaster University, Hamilton, Canada

**FIGURE 2** Four-compartment model-derived changes in BM, LBM, and FM during the intervention in both PRO and CON groups; data were analyzed with the use of an unpaired t test. Values are means ± SDs; n = 40 (20/group). *Significantly different from CON (P < 0.05). BM, body mass; CON, lower-protein (1.2 g · kg⁻¹ · d⁻¹) control diet; FM, fat mass; LBM, lean body mass; PRO, higher-protein (2.4 g · kg⁻¹ · d⁻¹) diet.
The Importance of Breakfast in Atherosclerosis Disease
Insights From the PESA Study

Irina Uzhova, MSc,a Valentín Fuster, MD, PhD,a,b Antonio Fernández-Ortiz, MD, PhD,a,c,d,e José M. Ordovás, PhD,a,f,g Javier Sanz, MD,a,b Leticia Fernández-Friera, MD, PhD,a,c,h Beatriz López-Melgar, MD, PhD,a,h José M. Mendiguren, MD, i Borja Ibáñez, MD, PhD,a,c,j Héctor Bueno, MD, PhD,a,d,k José L. Peñalvo, PhD l
The prevalence of an atherosclerosis is presented for total population, as well as by breakfast habits categories. The SBF group presents the highest proportion of individuals with subclinical, noncoronary, generalized atherosclerosis and increased coronary artery calcium score.

CACs = coronary artery calcium score; HBF = high-energy breakfast; LBF = low-energy breakfast; PESA = Progression of Early Subclinical Atherosclerosis; SBF = skipping breakfast.
<table>
<thead>
<tr>
<th>Nutrient</th>
<th>HBF (n = 1,122)</th>
<th>LBF (n = 2,812)</th>
<th>SBF (n = 118)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Macronutrients, g/day or mg/day</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy intake, kcal</td>
<td>2,234 ± 450†</td>
<td>2,345 ± 467†</td>
<td>2,358 ± 562†</td>
</tr>
<tr>
<td>Total protein</td>
<td>94.3 ± 18.0†</td>
<td>102.4 ± 20.0‡</td>
<td>105.7 ± 24.0‡</td>
</tr>
<tr>
<td>Animal protein</td>
<td>64.8 ± 15.0†‡</td>
<td>72.1 ± 17.1†‡</td>
<td>76.6 ± 20.7‡†</td>
</tr>
<tr>
<td>Vegetable protein</td>
<td>29.08 ± 8.23*</td>
<td>29.84 ± 8.93*</td>
<td>28.69 ± 9.83*</td>
</tr>
<tr>
<td>Total fat</td>
<td>103.1 ± 22.9†‡</td>
<td>108.3 ± 24.2‡</td>
<td>113.6 ± 30.6‡</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>334.4 ± 98.2†‡</td>
<td>361.6 ± 94.8†‡</td>
<td>385.7 ± 110.0†‡</td>
</tr>
<tr>
<td>MUFA</td>
<td>47.0 ± 11.6†‡</td>
<td>49.3 ± 11.5†‡</td>
<td>52.4 ± 13.8‡†</td>
</tr>
<tr>
<td>PUFA</td>
<td>16.62 ± 5.09‡†</td>
<td>17.81 ± 5.48‡†</td>
<td>19.05 ± 7.06†‡</td>
</tr>
<tr>
<td>SFA</td>
<td>29.98 ± 8.62†‡</td>
<td>32.05 ± 9.00‡†</td>
<td>32.84 ± 10.90‡†</td>
</tr>
<tr>
<td>Carbohydrates</td>
<td>218.5 ± 58.1†‡</td>
<td>220.0 ± 58.8†‡</td>
<td>197.0 ± 63.8‡†</td>
</tr>
<tr>
<td>Sugar</td>
<td>94.0 ± 31.8†‡</td>
<td>90.9 ± 30.6†‡</td>
<td>75.5 ± 34.4‡†</td>
</tr>
<tr>
<td>Polysaccharides</td>
<td>119.7 ± 40.6†‡</td>
<td>125.7 ± 43.2†‡</td>
<td>119.2 ± 46.0†‡</td>
</tr>
<tr>
<td><strong>Food group, g/day</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fruits and vegetables</td>
<td>474 ± 210†‡</td>
<td>435 ± 202†‡</td>
<td>369 ± 182‡†</td>
</tr>
<tr>
<td>Dried fruits</td>
<td>7.30 ± 10.76‡</td>
<td>7.94 ± 12.26‡</td>
<td>9.65 ± 16.64‡</td>
</tr>
<tr>
<td>Legumes</td>
<td>25.2 ± 21.2‡</td>
<td>26.0 ± 22.9‡</td>
<td>27.4 ± 23.3‡</td>
</tr>
<tr>
<td>Potatoes</td>
<td>20.0 ± 17.1‡†</td>
<td>21.1 ± 17.7‡</td>
<td>19.3 ± 16.7‡</td>
</tr>
<tr>
<td>Refined grains</td>
<td>216.0 ± 92.8*‡</td>
<td>234.0 ± 98.7*‡</td>
<td>231.0 ± 101.5‡</td>
</tr>
<tr>
<td>Whole grains</td>
<td>14.3 ± 31.9†‡</td>
<td>9.1 ± 21.6†‡</td>
<td>2.5 ± 10.6†‡</td>
</tr>
<tr>
<td>Nuts</td>
<td>5.03 ± 5.92‡</td>
<td>5.41 ± 5.68‡</td>
<td>5.16 ± 4.91‡</td>
</tr>
<tr>
<td>Olives</td>
<td>4.05 ± 6.30†‡</td>
<td>4.65 ± 6.52†‡</td>
<td>7.26 ± 15.13†‡</td>
</tr>
<tr>
<td>Red meat</td>
<td>93.0 ± 42.2†‡</td>
<td>112.9 ± 50.1‡</td>
<td>145.1 ± 68.0†‡</td>
</tr>
<tr>
<td>Lean meat</td>
<td>63.3 ± 30.7‡</td>
<td>66.9 ± 33.5‡</td>
<td>67.7 ± 32.6‡</td>
</tr>
<tr>
<td>Seafood (fish, shellfish)</td>
<td>75.8 ± 36.2*‡</td>
<td>79.1 ± 38.9*‡</td>
<td>78.1 ± 39.9‡</td>
</tr>
<tr>
<td>Dairy</td>
<td>207 ± 151†‡</td>
<td>196 ± 137†‡</td>
<td>141 ± 116†‡</td>
</tr>
<tr>
<td>Low-fat dairy</td>
<td>88.3 ± 125.8‡</td>
<td>90.0 ± 121.8‡</td>
<td>61.4 ± 112.7*‡</td>
</tr>
<tr>
<td>Vegetable oil and fat</td>
<td>5.02 ± 5.92‡</td>
<td>5.40 ± 5.68‡</td>
<td>5.15 ± 4.91‡</td>
</tr>
<tr>
<td>Butter</td>
<td>5.89 ± 6.72‡†</td>
<td>4.26 ± 4.39‡†</td>
<td>2.30 ± 2.03‡†</td>
</tr>
<tr>
<td>Olive oil</td>
<td>31.7 ± 14.1†‡</td>
<td>29.9 ± 12.2†‡</td>
<td>31.0 ± 11.8‡</td>
</tr>
<tr>
<td>Precooked meals, fast food</td>
<td>55.6 ± 34.0†‡</td>
<td>66.9 ± 42.1†‡</td>
<td>68.6 ± 35.6†‡</td>
</tr>
<tr>
<td>Chips and snacks</td>
<td>5.02 ± 7.06†‡</td>
<td>6.49 ± 9.12‡†</td>
<td>8.69 ± 11.73‡†</td>
</tr>
<tr>
<td>Commercial bakery</td>
<td>71.4 ± 50.0†‡</td>
<td>69.6 ± 47.8†‡</td>
<td>54.3 ± 47.5†‡</td>
</tr>
<tr>
<td>Alcohol (distilled spirits, wine, beer)</td>
<td>122 ± 144†‡</td>
<td>190 ± 227†‡</td>
<td>299 ± 328†‡</td>
</tr>
<tr>
<td>SSB</td>
<td>132 ± 184†‡</td>
<td>157 ± 204†‡</td>
<td>256 ± 439†‡</td>
</tr>
<tr>
<td>Tea, coffee</td>
<td>167 ± 131†‡</td>
<td>174 ± 128†‡</td>
<td>202 ± 193†‡</td>
</tr>
</tbody>
</table>

**Dietary quality**

<table>
<thead>
<tr>
<th>Cluster</th>
<th>HBF (n = 1,122)</th>
<th>LBF (n = 2,812)</th>
<th>SBF (n = 118)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mediterranean cluster</td>
<td>533 (47.5)†‡</td>
<td>1,052 (37.4)‡‡</td>
<td>30 (25.4)‡†</td>
</tr>
<tr>
<td>Western cluster</td>
<td>485 (43.2)†‡</td>
<td>1,148 (40.8)‡</td>
<td>35 (29.7)‡†</td>
</tr>
<tr>
<td>Social business cluster</td>
<td>104 (9.3)†‡</td>
<td>612 (21.8)‡‡</td>
<td>53 (44.9)†‡</td>
</tr>
</tbody>
</table>

Values are mean ± SD or n (%). Bonferroni correction was applied for categorical variables (p < 0.017). *p < 0.05 vs. LBF, †p < 0.05 vs. SBF. ‡p < 0.05 vs. HBF.
MUFA = monounsaturated fatty acids; PESA = Progression of Early Subclinical Atherosclerosis; PUFA = polyunsaturated fatty acids; SFA = saturated fatty acids; SSB = sugar-sweetened beverages; other abbreviations as in Table 1.
Dose–Response Relation Between Work Hours and Cardiovascular Disease Risk

Findings From the Panel Study of Income Dynamics

Sadie H. Conway, PhD, Lisa A. Pompeii, PhD, Robert E. Roberts, PhD, Jack L. Follis, PhD, and David Gimeno, PhD

A.D.F. or 5:2 plan

- Fasting may help prevent dementia by causing a low level stress that stimulates brain stem cell activation!
Case study:

- L-knee pain. MRI-torn meniscus. Scope.
- Gained 40 lb since HS.
- Wife, 2 kids, busy job...
- “95%” vegan, portion control, exercise...
- Lost 45 lbs. 5 inches off of waist. % body fat went from 28% to 16%. LDL 143 to 71 (off of lipitor). Got off BP med. Feeling great!
- This is me. Lifestyle works!
Running Helped This Cardiologist Get off His Blood Pressure and Cholesterol Medications

“I now talk to my patients about lifestyle—especially walking and running—as a way to control and even reverse their chronic illnesses and get off of some of their medications.”

By Harvey S. Hahn TUESDAY, APRIL 4, 2017, 2:46 PM
My personal choice!
Summary for long life...

- Restrict calorie intake.
- Consider IF.
- Exercise.
- Sleep 6+ hours a night.
- Get some cold exposure.
- Live long and prosper!
Ketogenics

Low carb, < 50 gm/day.

https://www.medscape.com/viewarticle/874707_1
Keto-off target?

Abraham Wald

This is a picture tracking bullet holes on Allied planes that encountered Nazi anti-aircraft fire in WW2.

At first, the military wanted to reinforce those areas, because obviously that’s where the ground crews observed the most damage on returning planes. Until Hungarian-born Jewish mathematician Abraham Wald pointed out that this was the damage on the planes that made it home, and the Allies should armor the areas where there are no dots at all, because those are the places where the planes won’t survive when hit. This phenomenon is called survivorship bias, a logic error where you focus on things that survived when you should really be looking at things that didn’t.

We have higher rates of mental illness now? Maybe that’s because we’ve stopped killing people for being “possessed” or “witches.” Higher rate of allergies? Anaphylaxis kills, and does so really fast if you don’t know what’s happening. Higher claims of rape? Maybe victims are less afraid of coming forward. These problems were all happening before, but now we’ve reinforced the medical and social structures needed to help these people survive. And we still have a long way to go.

Source: marzipanandminutiae
Effect of a Ketogenic Diet on Submaximal Exercise Capacity and Efficiency in Runners.

Shaw DM¹, Merien F², Braakhuys A³, Maunder ED¹, Dulson DK¹.

Abstract

PURPOSE: We investigated the effect of a 31-d ketogenic diet (KD) on submaximal exercise capacity and efficiency.

METHODS: A randomized, repeated-measures, crossover study was conducted in eight trained male endurance athletes (V'O2max, 59.4 ± 5.2 mL·kg·min). Participants ingested their habitual diet (HD) (13.1 MJ, 43% [4.6 g·kg·d] carbohydrate and 38% [1.8 g·kg·d] fat) or an isonenergetic KD (13.7 MJ, 4% [0.5 g·kg·d] carbohydrate and 78% [4 g·kg·d] fat) from days 0 to 31 (P < 0.001). Participants performed a fasted metabolic test on days -2 and 29 (~25 min) and a run-to-exhaustion trial at 70% V'O2max on days 0 and 31 following the ingestion of a high-carbohydrate meal (2 g·kg) or an isonenergetic low-carbohydrate, high-fat meal (<10 g CHO), with carbohydrate (~55 g·h) or isonenergetic fat (0 g CHO·h) supplementation during exercise.

RESULTS: Training loads were similar between trials and V'O2max was unchanged (all, P > 0.05). The KD impaired exercise efficiency, particularly at >70% V'O2max, as evidenced by increased energy expenditure and oxygen uptake that could not be explained by shifts in respiratory exchange ratio (RER) (all, P < 0.05). However, exercise efficiency was maintained on a KD when exercising at <60% V'O2max (all, P > 0.05). Time-to-exhaustion (TTE) was similar for each dietary adaptation (pre-HD, 237 ± 44 vs post-HD, 231 ± 35 min; P = 0.44 and pre-KD, 239 ± 27 vs post-KD, 219 ± 53 min; P = 0.36). Following keto-adaptation, RER >1.0 vs <1.0 at V'O2max coincided with the preservation and reduction in TTE, respectively.

CONCLUSION: A 31-d KD preserved mean submaximal exercise capacity in trained endurance athletes without necessitating acute carbohydrate fuelling strategies. However, there was a greater risk of an endurance decrement at an individual level.

PMID: 31033901 DOI: 10.1249/MSS.0000000000002008
Insanity...

- Doing the same thing, BUT expecting different results...
I run long distances for the **worst** possible reason: I run to eat.

I punish my body outdoors to atone for my atrocities indoors.

Seriously! Gladiator AGAIN!
Also, I really don't think it's good for you to keep eating like that.

**NONSENSE!** I ran twenty miles today!

---

I know I should stop.

but I'm not going to.
Pick your morphology.
No one is happy...

The Large
I wish I looked normal like that guy.
I bet he’s happy.

The Normal
I wish I could lose these love handles like that guy.
I bet he feels secure.
NO ONE!

The Lean

I wish I had groomless meaty muscles like that guy.
I bet girls line up around the block.

The Meaty

I wish I could say smart, clever things like that guy.
I bet people respect him at work.

If I had a nickel for every time a girl told me she wanted to make love to my beard, well... I'd have a quarter.

hee-hee! It's funny because that's five times.
Ada Wong - not a Loser!
Runner up on Season 10 of Biggest Loser.
And the loser is...

DID SHE GO TOO FAR?
Rachel Frederickson defends her extreme diet and reveals the drastic steps she took to win
Persistent Metabolic Adaptation 6 Years After “The Biggest Loser” Competition

Erin Fothergill\textsuperscript{1}, Juen Guo\textsuperscript{1}, Lilian Howard\textsuperscript{1}, Jennifer C. Kerns\textsuperscript{2}, Nicolas D. Knuth\textsuperscript{3}, Robert Brychta\textsuperscript{1}, Kong Y. Chen\textsuperscript{1}, Monica C. Skarulis\textsuperscript{1}, Mary Walter\textsuperscript{1}, Peter J. Walter\textsuperscript{1}, and Kevin D. Hall\textsuperscript{1}
Biggest Losers Fight a Slower Metabolism

A study of contestants from “The Biggest Loser” found their metabolisms slowed during and after the competition, making it difficult to maintain weight loss.

**REGAINING LOST WEIGHT**

13 of the 14 contestants studied regained weight in the six years after the competition. Four contestants are heavier now than before the competition.

- **Erinn Egbert** is the only contestant who weighs less today than six years ago.
- **Rudy Pauls** regained 80 percent of his lost weight, then had surgery to reduce the size of his stomach.
- **Danny Cahill** lost 239 pounds and won the competition, but has regained over 100 pounds.

**A SLOWING METABOLISM**

Nearly all the contestants have slower metabolisms today than they did six years ago, and burn fewer calories than expected when at rest.

- Body burns 200 more cal. a day
- **Danny Cahill** now burns 800 fewer calories a day than expected.
- Body burns 800 fewer cal. a day

Sources: Obesity; individual contestants

By The New York Times
Figure 2 Individual (●) and mean (gray rectangles) changes in (A) body weight, (B) fat-free mass, and (C) fat mass at the end of “The Biggest Loser” 30-week weight loss competition and after 6 years. Horizontal bars and corresponding $p$ values indicate comparisons between 30 weeks and 6 years. $^*p < 0.05$ compared with baseline.
Why did they fail to keep it off?

- “Reality TV” is NOT real.
- No real gain in muscle mass.
- Serious drop off in exercise program.
- And their metabolic rate dropped significantly.
- Without exercise you can’t cut calories enough!
Relaxation Response Induces Temporal Transcriptome Changes in Energy Metabolism, Insulin Secretion and Inflammatory Pathways

Manoj K. Bhasin1,4,5, Jeffery A. Dusek6, Bei-Hung Chang7,8, Marie G. Joseph5, John W. Denninger1,2, Gregory L. Fricchione1,2, Herbert Benson1,3, Towia A. Libermann1,4,5

1 Benson-Henry Institute for Mind Body Medicine at Massachusetts General Hospital, Boston, Massachusetts, United States of America, 2 Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, United States of America, 3 Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, United States of America, 4 Department of Medicine, Division of Interdisciplinary Medicine and Biotechnology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts, United States of America, 5 BIDMC Genomics and Proteomics Center, Beth Israel Deaconess Medical Center, Boston, Massachusetts, United States of America, 6 Institute for Health and Healing, Abbott Northwestern Hospital, Minneapolis, Minnesota, United States of America, 7 VA Boston Healthcare System, Boston, Massachusetts, United States of America, 8 Department of Health Policy and Management, Boston University School of Public Health, Boston, Massachusetts, United States of America

Epigenetics, again!
The Role of Gratitude in Spiritual Well-Being in Asymptomatic Heart Failure Patients

Paul J. Mills, Laura Redwine, Kathleen Wilson, Meredith A. Pung, Kelly Chinh, Barry H. Greenberg, Ottar Lunde, Alan Maisel, and Ajit Raisinghani
University of California, San Diego

Alex Wood
University of Stirling

Deepak Chopra
University of California, San Diego, and Chopra Center for Wellbeing, Carlsbad, California

Gratitude improved, sleep, mood, self-sufficiency, and inflammatory biomarkers.
Think positive!

<table>
<thead>
<tr>
<th>First Author (Ref. #)</th>
<th>Year</th>
<th>n</th>
<th>Follow-Up (yrs)</th>
<th>Endpoints</th>
<th>Adjusted RR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pessimism as a risk factor</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brummet et al. (13)</td>
<td>2006</td>
<td>6,958</td>
<td>40.0</td>
<td>ACM</td>
<td>1.42 (1.13-1.77)</td>
</tr>
<tr>
<td>Grossbart et al. (14)</td>
<td>2009</td>
<td>7,216</td>
<td>32.0</td>
<td>ACM</td>
<td>1.32 (1.13-1.77)</td>
</tr>
<tr>
<td><strong>Optimism as a buffer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kuzbansky et al. (15)</td>
<td>2004</td>
<td>1,306</td>
<td>10.0</td>
<td>MI/CV death</td>
<td>0.44 (0.26-0.74)</td>
</tr>
<tr>
<td>Giltay et al. (16)</td>
<td>2004</td>
<td>941</td>
<td>9.1</td>
<td>CV death</td>
<td>0.27 (0.12-0.57)</td>
</tr>
<tr>
<td>Giltay et al. (17)</td>
<td>2006</td>
<td>554</td>
<td>15.0</td>
<td>CV death</td>
<td>0.45 (0.29-0.68)</td>
</tr>
<tr>
<td>Tindle et al. (18)</td>
<td>2009</td>
<td>97,253</td>
<td>8.0</td>
<td>CV death</td>
<td>0.76 (0.64-0.90)</td>
</tr>
<tr>
<td>Nabi et al. (19)</td>
<td>2010</td>
<td>23,216</td>
<td>7.0</td>
<td>Stroke</td>
<td>0.52 (0.29-0.93)</td>
</tr>
<tr>
<td>Kim et al. (20)</td>
<td>2011</td>
<td>6,044</td>
<td>2.0</td>
<td>Stroke</td>
<td>0.90 (0.84-0.97)†</td>
</tr>
</tbody>
</table>

*Risk ratios are primarily for first versus third tercile or fourth quartile. †For each unit increase in optimism.

ACM = all-cause mortality; CI = confidence interval; CV = cardiovascular; RR = risk ratio; MI = myocardial infarction.
Change your habits-change your life!

- **Winning is a habit.**
  Watch your thoughts, they become your beliefs.
  Watch your beliefs, they become your words.
  Watch your words, they become your actions.
  Watch your actions, they become your habits.
  Watch your habits, they become your character.
Adam 1 (or Eve)
- Richest...
- Busiest...
- Best...
- Most stuff...

Adam 2 (or Eve)
- Happiest!
- Deepest relationship!
- Most caring!
- Most giving!
The Power of Choice

• I am not a product of my circumstances. I am a product of my decisions.
S. Covey
Life is hOllOw withOut GOD.

100 years vs eternity?
"Your mission if you should choose to accept it..."

Think positive.
Don’t stress - waste of time and energy.
Laugh, be happy.
Helping others helps YOU.
Be social.
Have purpose.
Nothing gives purpose like God!
The Dickens Process

• Tony Robbins.
• What are your beliefs COSTING you?
• In the past?
• In the present?
• What will they cost you in YOUR future?
Work stress and risk of death in men and women with and without cardiometabolic disease: a multicohort study

Prof Mika Kivimäki, FMedSci, Jaana Pentti, MSc, Jane E Ferrie, PhD, Prof G David Batty, DSc, Solja T Nyberg, PhD, Markus Jokela, PhD, Prof Marianna Virtanen, PhD, Prof Lars Alfredsson, PhD, Prof Nico Dragano, PhD, Eleonor I Fransson, PhD, Prof Marcel Goldberg, MD, Prof Anders Knutsson, PhD, Prof Markku Koskenvuo, MD, Aki Koskinen, MSc, Prof Anne Kouvonen, PhD, Ritva Luukkonen, PhD, Tuula Oksanen, MD, Prof Reiner Rugulies, PhD, Prof Johannes Siegrist, PhD, Archana Singh-Manoux, PhD, Sakari Suominen, MD, Prof Töres Theorell, MD, Ari Väänänen, PhD, Prof Jussi Vahtera, MD, Prof Peter J M Westerholm, MD, Prof Hugo Westerlund, PhD, Marie Zins, PhD, Prof Timo Strandberg, MD, Prof Andrew Steptoe, DSc, Prof John Deanfield, FRCP

The Lancet Diabetes & Endocrinology

DOI: 10.1016/S2213-8587(18)30140-2
YOU DISGUST ME RONALD!
YOU'RE NOT EVEN SCARY!

I'VE KILLED MORE PEOPLE THAN YOU
I run because punching people is frowned upon.
Figure 1. Associations of grip strength, physical activity, and cardiorespiratory fitness with coronary heart disease by genetic risk.
Central Illustration: Habitual Physical Activity and Mortality in Patients With Stable Coronary Artery Disease

All-cause mortality risk associated with each doubling of habitual physical activity volume, and by linear increase in physical activity

Characteristics associated with greatest potential to benefit from increase in physical activity

- Sedentary
- Limited by dyspnea
- ↑ ABC-CHD risk score
  - ↑ Age
  - Smoker
  - Diabetes
  - Peripheral artery disease
  - ↑ Troponin T
  - ↑ NT-proBNP
  - ↑ LDL cholesterol

Table 3. Cox Proportional Hazards Regression for Associations Between Physical Activity Pattern and All-Cause Mortality by Sex<sup>a</sup>

<table>
<thead>
<tr>
<th>Physical Activity Pattern&lt;sup&gt;b&lt;/sup&gt;</th>
<th>HR (95% CI) Men (n = 29,181)</th>
<th>HR (95% CI) Women (n = 34,410)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactive</td>
<td>1 [Reference]</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Insufficiently active</td>
<td>0.71 (0.64-0.78)</td>
<td>0.68 (0.71-0.74)</td>
</tr>
<tr>
<td>Weekend warrior</td>
<td>0.78 (0.64-0.95)</td>
<td>0.72 (0.55-0.94)</td>
</tr>
<tr>
<td>Regularly active</td>
<td>0.63 (0.54-0.73)</td>
<td>0.57 (0.47-0.68)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Adjusted for age, smoking, alcohol use, and other potential confounders.

<sup>b</sup> "Weekend Warrior" refers to individuals who engage in vigorous physical activity exclusively on weekends.
Figure 1  Muscular Strength, Cardiorespiratory Fitness, and Mortality in Hypertension

Combined association of muscular strength (thirds) and cardiorespiratory fitness (low fitness, high fitness) with hazard ratio of all-cause mortality after adjustment for age, physical activity, current smoking, alcohol intake, body mass index, systolic and diastolic blood pressure, total cholesterol, diabetes, abnormal electrocardiogram, and family history of cardiovascular disease. Error bars represent 95% confidence interval.
Weight Training, Aerobic Physical Activities, and Long-Term Waist Circumference Change in Men

Rania A. Mekary¹,², Anders Grøntved³, Jean-Pierre Despres⁴, Leandro Pereira De Moura⁵,⁶, Morteza Asgarzadeh⁷, Walter C. Willett⁴,⁷,⁸, Eric B. Rimm⁴,⁷,⁸, Edward Giovannucci⁴,⁷,⁸, and Frank B. Hu¹,⁷,⁸

![Graph showing relative waist circumference change over time for different levels of adherence to aerobic exercise recommendations.](image-url)
HIIT it!

- **High Intensity Interval Training.**
- Short bouts of near max effort (really max effort) with longer recovery periods.
- Many different programs, but most studies show that you only need 4-5 cycles to get the benefit!
Two weeks of high-intensity aerobic interval training increases the capacity for fat oxidation during exercise in women

Jason L. Talanian,¹ Stuart D. R. Galloway,² George J. F. Heigenhauser,³ Arend Bonen,¹ and Lawrence L. Spriet¹

¹Department of Human Health and Nutritional Sciences, University of Guelph, Guelph, Ontario, Canada, ²Department of Sport Studies, University of Stirling, Stirling, Scotland; and ³Department of Medicine, McMaster University, Hamilton, Ontario, Canada
Total daily energy expenditure is increased following a single bout of sprint interval training

Kyle J. Sevits^1, Edward L. Melanson^2,^3, Tracy Swibas^3, Scott E. Binns^4, Anna L. Klochak^4, Mark C. Lonac^4, Garrett L. Peltonen^4, Rebecca L. Scalzo^4, Melani M. Schweder^4, Amy M. Smith^1, Lacey M. Wood^4, Christopher L. Melby^1 & Christopher Bell^4

1 Department of Food Science and Human Nutrition, Colorado State University, Fort Collins, Colorado
2 Division of Endocrinology Metabolism and Diabetes, University of Colorado Anschutz Medical Campus, Denver, Colorado
3 Division of Geriatrics, University of Colorado Anschutz Medical Campus, Denver, Colorado
4 Department of Health and Exercise Science, Colorado State University, Fort Collins, Colorado

A 45-Minute Vigorous Exercise Bout Increases Metabolic Rate for 14 Hours

FIGURE 1—Average 24-h energy expenditure on rest and exercise days. Forty-five minutes of cycling resulted in 519 ± 60.9 kcal of energy expended above rest day (P < 0.001), whereas 190 ± 71.4 kcal was expended above levels on the rest day for 14.2 h after exercise (P < 0.001). Net energy expenditure difference from the start of sleep to 18 h after exercise was 32.0 ± 39.3 kcal (P = 0.030).
Mark D. Schuenke · Richard P. Mikat
Jeffrey M. McBride

Effect of an acute period of resistance exercise on excess post-exercise oxygen consumption: implications for body mass management
Muscle burns more calories than fat!