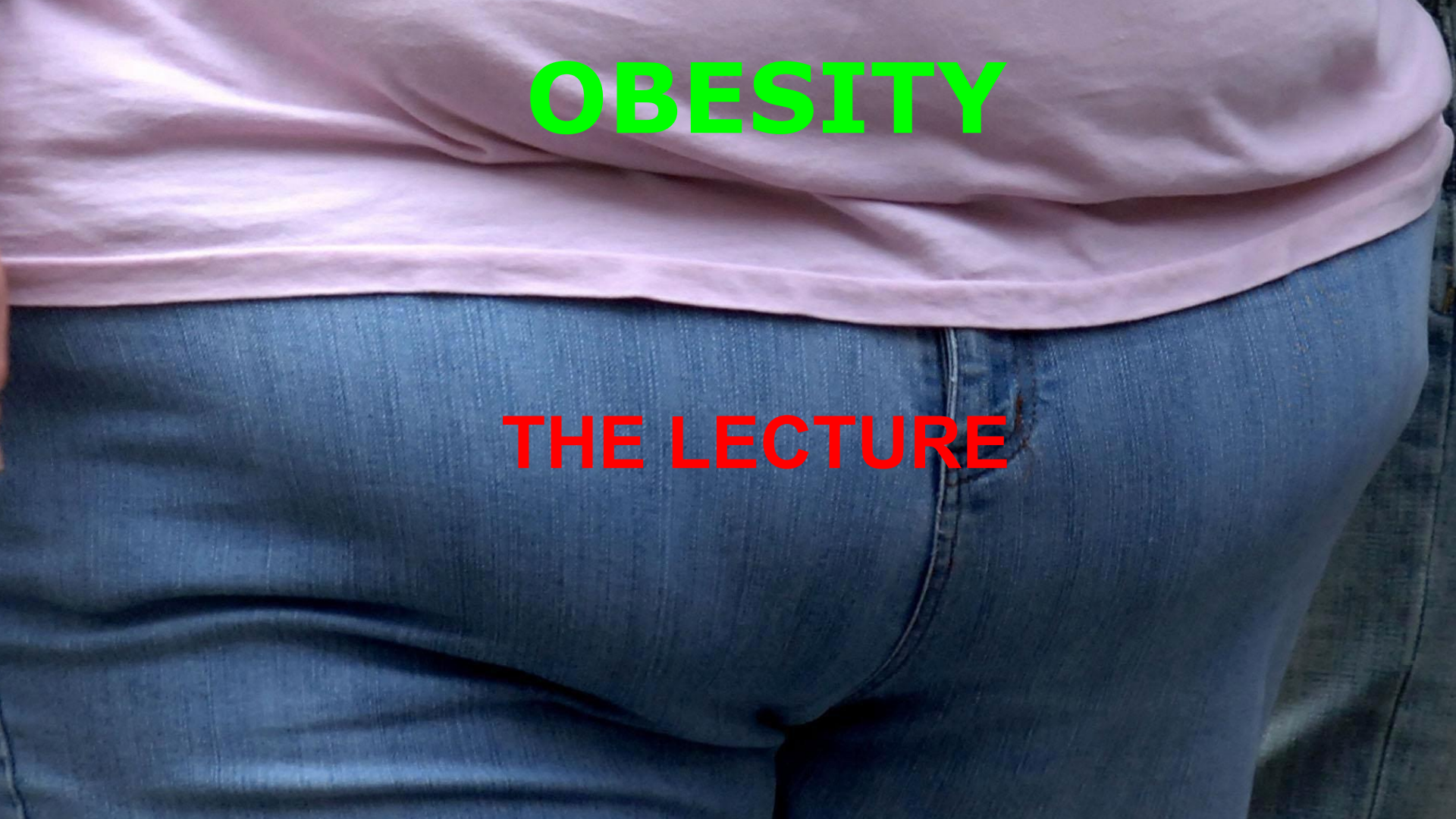
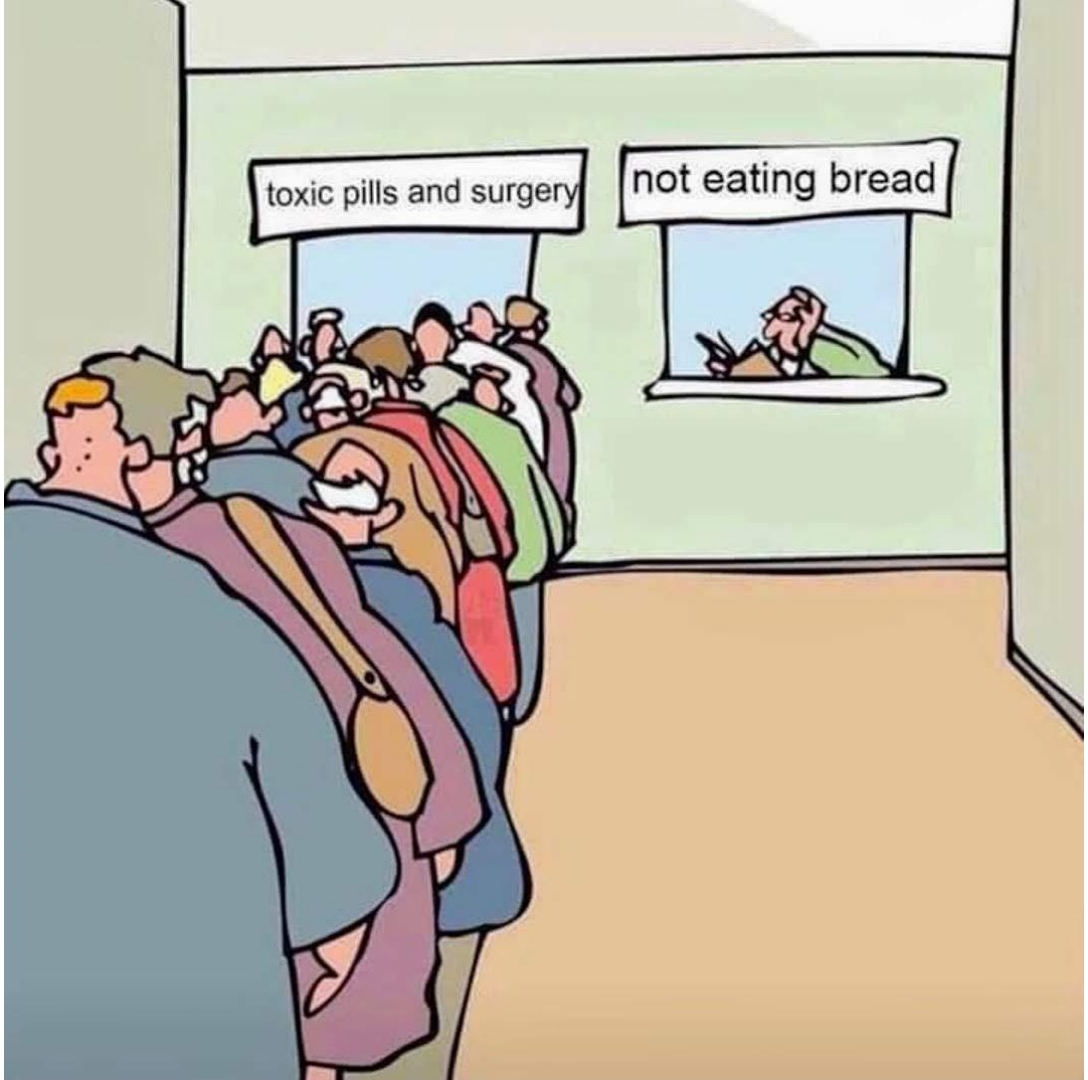

OBESITY
THE LECTURE


toxic pills and surgery
not eating bread

Obesity Causes other than Metabolic Syndrome

- Hypothyroidism
- Cushing’s Syndrome
- Prater-Willi Syndrome
- Insulinoma


Metabolic
Syndrome

Only 12% of Americans are Metobolically Healthy

Changing from ATP III (Adult Treatment Panel III) guidelines to more recent cut points decreased the proportion of metabolically healthy Americans from 19.9% (95% confidence interval [CI]: 18.3–21.5) to 12.2% (95% CI: 10.9–13.6).

Araujo J, Cai J, Stevens J. Prevalence of Optimal Metabolic Health in American Adults: National Health and Nutrition Examination Survey 2009-2016. Metab Syndr Relat Disord. 2019 Feb;17(1):46-52.

1. Obesity is not a moral failing
2. Obesity is not a simple matter of “Calories In - Calories Out” or “Eating Less and Moving More”
3. Calorie Restricted diets give short term results, are unsustainable and can permanently lower the BMR
4. Exercise contributes very little to weight loss
5. Ketogenic diets are sustainable and effective
6. How you can “reset” the body’s weight set-point
7. Ketogenic Diets Have a favorable effect on the Cardiac Risk Profile

Obesity is not a “moral failing” unless bad luck with the genes you inherited qualifies as one.

Here was the conclusion of the lead investigator in this large study of identical twins done in Holland. **“We conclude that genetic influences have an important role in determining human fatness in adults, whereas the family environment alone has no apparent effect.”** Dr. Stunkard calculated: Approximately 70 percent of the variance in obesity is familial.

Stunkard AJ et al. The body-mass index of twins who have been reared apart. N Engl J Med. 1990 May 24; 322(21):1483-7

In a 2012 online poll, 61% of US adults believed that “personal choices about eating and exercise” were responsible for the obesity epidemic.

Begley S. America’s hatred of fat hurts obesity fight. Reuters [internet] 2012 may 11. Available from http://www.reuters.com/article/2012/05/11/us-obesity-stigma-idUSBRE84A0PA20120511.

The False assumptions you must accept to believe the Calories in / Calories out (CICO) Theory

Assumption 1: Calories In and Calories Out are independent of each other.

Assumption 2: Basal metabolic rate is stable.

Assumption 3: We can reliably exert conscious control over Calories In.

Assumption 4: Fat stores are essentially unregulated.

Assumption 5: A Calorie is just a Calorie.

Assumption 1: Calories In and Calories Out are independent of each other.

FALSE! If you decrease your calorie intake the body responds by decreasing both Total Energy Expenditure and Resting Energy Expenditure and we've known that for a long time. Here are a couple of famous studies on that.

In 1919 five volunteers consumed a semi-starvation diet of 1400-2100 calories (30% lower than usual intake).

The patients experienced a 30% decrease in total energy expenditure from an initial caloric expenditure of roughly 3000 calories to approximately 1950 calories/day

Benedict F. Human Vitality and efficiency under prolonged restricted diet. Carnegie Institute of Washington; 1919 Available from https://archive.org/details/humanvitalityeff00beneuoft

The Minnesota STARVATION experiment

- 36 young healthy men
- 3200 kcal/day for the first 3 months then
- For 6 months starting at 1570 calories/day continually adjusted to reach a target total weight loss of 24% baseline. Some got less than 1000 kcal/day
- They averaged 1.1 kg (2.5 lbs) weight loss per week
- Diet potatoes, turnips, bread and macaroni. Meat and dairy were rare.
- Walked 22 miles/week with an expected calorie expenditure of 3009 kcal/day

Benedict F. Human Vitality and efficiency under prolonged restricted diet. Carnegie Institute of Washington; 1919 Available from https://archive.org/details/humanvitalityeff00beneuoft

Results

- Resting metabolic rate dropped by 40% and average strength dropped 21%
- Resting heart rate dropped from 55 to 35 and stroke volume decreased 20%
- Average body temperature dropped to 95.8°F
- “I’m cold. In July I walk downtown on a sunny day with a shirt and sweater to keep me warm. At night my well fed room mate, who isn’t in the experiment, sleeps on top of his sheets but I crawl under two blankets.”
- The men experienced a complete lack of interest in everything except for food, which became an object of intense fascination to them. Some hoarded cookbooks and utensils. They were plagued with constant, unyielding hunger. Some were unable to concentrate , and several withdrew from their university studies. There were several cases of frankly neurotic behavior.
    - One subject amputated 3 fingers of his hand with an axe.
    - Sexual interest was drastically reduced
- Patients should have lost 35.3 kg (78 lbs) according to the CICO calculations but lost only 16.8 kg (37 lbs) .

Assumption 3: We can reliably exert conscious control over Calories In for long periods.

In the Women's Health Study of 50,000 middle aged women the intervention group received dietary counseling and were encouraged to eat a low fat, high carb diet and to reduce calories.

- They managed to reduce their average calorie intake from 1788 to 1446 for over 7 years.
- They reduced their percent calories from 38.8% to 29.8%
- They increased their physical activity by 14%

Howard BV et al. Low fat dietary pattern and weight change over 7 years: the Women's Health Initiative Dietary Modification Trial. JAMA 2006:an4;295(1):39-49

Results of the Women's Health Initiative Study

By the end of the first year the weight began to go up in the intervention group. By the end of the 7th year there was no significant difference between the intervention group and the control group in terms of weight or waist circumference.

You can't willpower yourself thin in the long term.

Assumption 2: Basal metabolic rate is stable.

Not only is it not stable as we clearly saw in the Cambridge and Minnesota starvation studies but it can be permanently down regulated by prolonged severe calorie restriction.

In this Study, over a 20 year period, >100 patients were helped to lose 10% of their body weight on a 500 calorie liquid diet (Optifast). After the initial weight loss they were given a low glycemic diet with enough calories to maintain at the new weight, then they were followed for a year. After 1 year on the new diet the total energy expenditure was still 500 kcal/day below baseline.

Rosenbaum et al. Long-term persistence of adaptive thermogenesis in subjects who have maintained a reduced body weight. Am J Clin Nutr. 2008 Oct; 88(4):906-12


BIGGEST LOSER
Where are they now?

16 participants in the Big Loser Competition which uses a Low Fat, High Carb diet augmented by intense exercise had dexa-scan and resting metabolic rate (RMR) testing at baseline, immediately post weight loss and then 6 years later.

- Mean weight loss 58 kg (128 lbs).
- After 6 years 41 kg (90 lbs) had been regained.
- There was a persistent decrease in RMR of -499 kcal/day ($P<0.0001$).

Fothergill e et al. Persistent Metabolic Adaptation Years After "The Biggest Loser" Competition. Obesity: 24(8)1612-19

Assumption 3: We exert conscious control over Calories In.

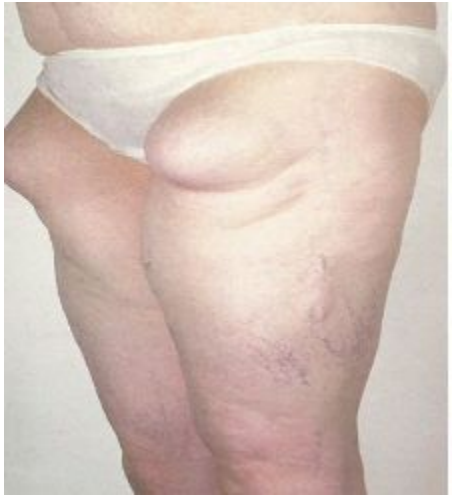
In this study 6 obese patients achieved a 10% weight loss and then were given twice daily subcutaneous doses of Leptin or placebo. The were then placed a functional MRI and shown images of desirable foods.

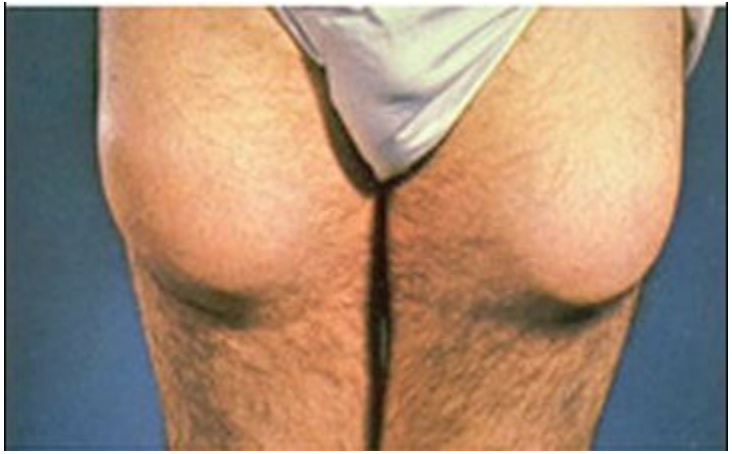
- The areas of the brain controlling emotion and cognition light up in response to food stimuli.
- Areas of the prefrontal cortex involved with restraint show decreased activity.
- Many of the changes were reversed in the patient who received Leptin rather than placebo.

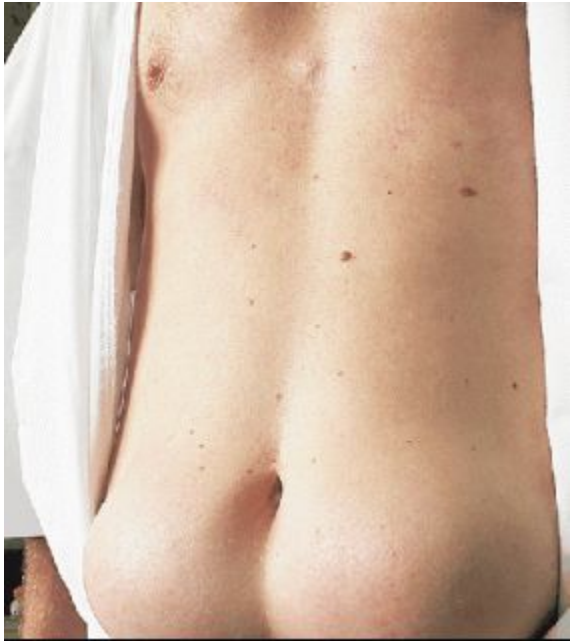
Rosenbaum M, Sy M, Pavlovich K, Leibel R, Hirsch J. Leptin reverses weight loss induced changes in regional neural activity responses to visual food stimuli. J Clin Invest. 2008 Jul 1; 118(7):2583-91

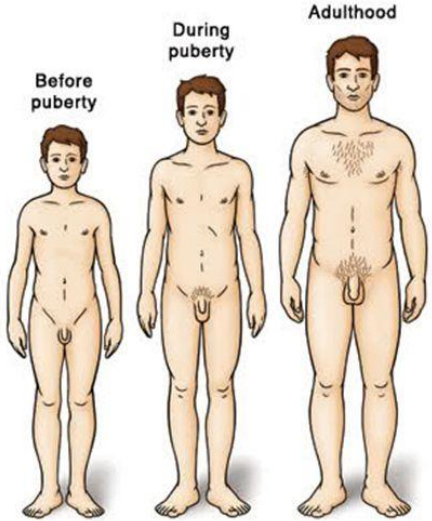
Assumption 4: Fat stores are essentially unregulated.

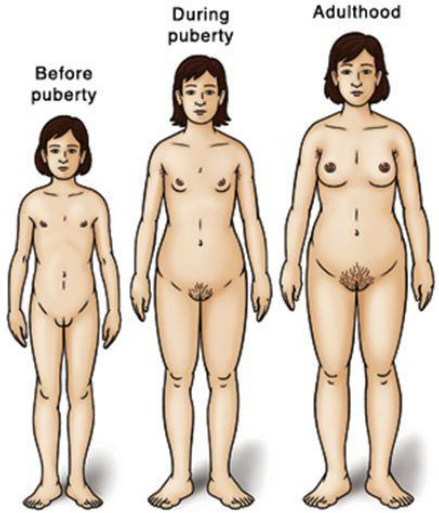
How much fat you store is directly related to the level of Insulin in your body. One of the best way to visually see that is what happens at the sites where diabetics regular inject insulin.








Before puberty
During puberty
Adulthood


Before puberty
During puberty
Adulthood

Assumption 5 - A calorie is just a calorie

It’s well known that

- a calorie of carbohydrate causes the release of a fair amount of insulin
- A calorie of protein causes the release of 50-75% as much insulin as a carb
- A calorie of fat causes the stimulation of very little insulin

Now let's talk about another fallacy that Exercise is a good way to lose weight.

Doubly Labeled Water to calculate Total Energy Expenditure

- Discovered in 1949
- Water molecules contain a Deuterium atom and an Oxygen-18 stable isotope atom
- Patients are given a known dose
- As the burn energy Oxygen-18 is lost in the breath, urine and sweat
- Deuterium is lost only with water losses
- The levels of Deuterium and Oxygen-18 are measure in the urine before and after the period in question and CO_2 production can be accurately calculated.

The Hadza People of Tanzania

Do the thin Hunter-Gatherers Really move more?

In this study Doubly Labeled Water was used measure TEE in 3 populations, Hadza, U.S. City dwellers and Farmers.

- No statistically significant Differences were found between the 3 groups
- U.S. city dwellers on average burned slightly more calories than the Hadza

Pontzer, H et al. Hunter-Gatherer Energetics and Human Obesity. PLOS One. 2012 Jul;7(7):e40503

Table 1. Population characteristics, energy expenditure, and body composition.

	HADZA		WESTERN		FARMING	
	Women	**Men**	**Women**	**Men**	**Women**	**Men**
N	17	13	186	53	14	11
Age (yr)	39.9±19.4	33.2±14.5	41.1±8.8	44.2±8.9	43.9±21.8	49.1±20.9
	18–75	*18–65*	*21–61*	*25–61*	*14–79*	*17–80*
Mass (kg)	43.4±6.4	50.9±5.4	74.4±12.8	81.0±11.1	48.1±6.9	54.7±2.9
	34.0–55.0	*42.5–58.2*	*49.5–117.7*	*57.2–101.3*	*39.0–62.8*	*49.5–58.7*
BMI (kg/m^2)	20.2±1.7	20.3±1.3	27.5±4.5	25.6±2.7	20.7±3.2	21.2±1.6
	17.0–23.9	*19.1–23.4*	*19.5–39.4*	*19.5–30.0*	*17.2–28.9*	*19.5–24.0*
Body Fat %	20.9±4.6	13.5±4.2	37.9±7.0	22.5±5.0	27.3±5.3	16.0±3.3
	12.4–27.7	*7.4–23.1*	*11.9–53.3*	*10.2–32.9*	*18.8–36.9*	*9.8–21.1*
TEE (kCal/day)	1877±364	2649±395	2347±360	3053±464	2469±315	2855±435
	1459–2596	*2008–3363*	*1351–3978*	*2211–4682*	*1972–3202*	*2212–3374*
PAL (TEE/BMR)	1.78±0.30	2.26±0.48	1.68±0.22	1.81±0.21	2.11±0.30	2.08±0.26
	1.44–2.53	*1.67–2.96*	*1.21–2.54*	*1.56–2.42*	*1.44–2.63*	*1.65–2.51*

Values shown are means, ±standard deviations, and *ranges*. See Text S1 for details on comparative data sources. PAL for the Hadza was calculated using estimated BMR [27].

doi:10.1371/journal.pone.0040503.t001

Has activity declined during the Obesity Epidemic?

In this 2008 Dutch study they examined Daily Energy Expenditure trends 1980-2008 and found it had continuously increased.

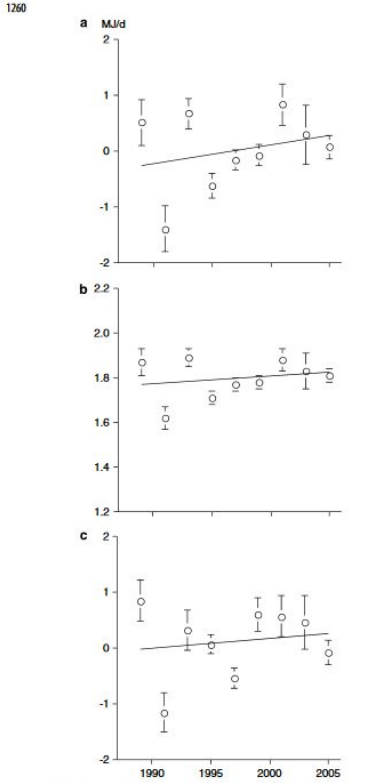


Figure 1 Trends in physical activity energy expenditure (MJ per day, mean ± s.e.) over time (year of publication) for a population in Northern Europe (Maastricht). (a) The residual of the regression of daily energy expenditure (DEE) on basal energy expenditure (BEE); (b) physical activity level (PAL) which is the ratio of DEE to BEE_2 (c) the residual of the regression of DEE on body mass, sex and age.

Westerterp KR, Speakman JR. Physical Activity Energy Expenditure has not declined since the 1980s and matches Energy Expenditure of Wild Mammals. Int J Obes (Lond). 2008 Aug; 32(8):1256-63

Is exercise a long term solution to obesity?

In this Meta-Analysis 31 studies from 1966 to 2000 were examined and divided into 2 groups - studies lasting more or less than 16 weeks.

- There is an initial modest weight loss in studies lasting less than 16 weeks
- For studies lasting longer than 16 weeks there was little to no permanent weight loss

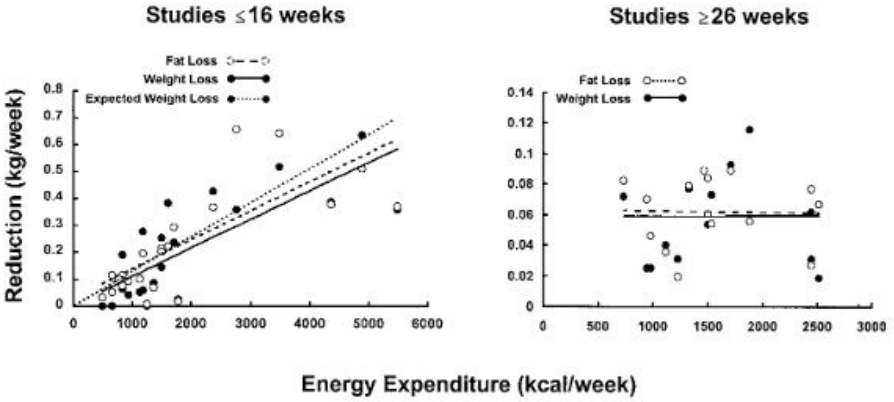


FIGURE 1—Illustration of the relationship between energy expenditure expressed as kcal per week, fat loss, weight loss, and expected weight loss expressed in kilograms lost per week. Studies with a duration of 16 wk or less are shown in the left panel, whereas the relationships for studies 26 wk or longer are shown in the right panel.

What is the best weight loss I can expect from exercise?

In this 10 month study, 141 overweight and obese patients (BMI 25-40) were randomized to no exercise, 400 kcal and 600 kcal supervised aerobic (at least 70% max HR) sessions 5 days per week and they were dropped from the study if they didn't complete 90% of the sessions. They were told to eat ad libitum and not make changes in their diet.

- The biggest weight loss was in the men on the 600 kcal program who lost a whopping 5.9 kg (13.0 lb) averaging 0.6 kg (1 lb) per month
- The women on this intense program lost 4.4 kg (9.7 lb) or 0.44 kg/month.
- The predicted weight loss from the extra calories they burned was 16 kg (35.2 lbs).
- So in this study the Males went from an average initial weight of 102.0 kg (225 lbs) to 96.1 (212 lbs)

Donnelly JE, Honas JJ, Smith BK, Mayo MS, Gibson CA, Sullivan DK, LeeJ, Herrmann SD, Lambourne K, Washburn RA, Aerobic exercise Alone Results in Clinically Significant Weight Loss: Midwest Exercise trial 2. Obesity (Silver Spring). PubMed. 2013 Mar; 21(3):E219-28

Why getting children more active at school doesn't help with weight loss.

Children from 3 schools were studied. One provided an hour a day of supervised, physical education(PE) with vigorous activity, the other 2 providing no PE. They gave 206 children Actigraphs to measure total physical activity (TPA) and Moderate -Vigorous Physical Activity (MVPA).

- the children from the school with PE had much higher levels of TPA and MVPA during the hours of school
- the children from the other schools had much more of both after school than the children in the school with PE
- over the course of the 2 week study, all the children had the same levels of TPA and MVPA.

Fremeaux AF et al. The Impact of School-time Activity on Total Physical Activity: the Activitystat Hypothesis (EarlyBird 46). Intern J Obes (2011) 35:1277-1283

Are Americans getting fatter because they are eating more calories? Here are a couple of studies to prove that's not the case.

- In fact Data from the National Health and Nutrition Examination Survey (NHANES) in the United States from 1990 to 2010 finds no association between increased calorie consumption and weight gain. While obesity increased at a rate of 0.37 percent per year, caloric intake remained virtually stable.
- From 1976 to 1996, the average fat intake decreased from 45 percent of calories to 35 percent. Butter consumption decreased 38 percent. Animal protein decreased 13 percent. Egg consumption decreased 18 percent. Grains and sugars increased.
    - USDA Factbook. Chapter 2: Profiling food consumption in America. Available from www.usda.gov/factbook/chapter2.pdf

- In the British experience, neither increased caloric intake nor dietary fat correlated to obesity—which argues against a causal relationship. In fact, the number of calories ingested slightly decreased, even as obesity rates increased.
    - Griffith R, Lluberas R, Luhrmann M, Gluttony in England? Long-term change in diet, The Institute for Fiscal Studies. 2013. Available from: http://www.ifs.org.uk/bns/bn142.pdf

The Weight “Set-Point” Theory

First proposed in 1984. Here how Drs Keesey and Corbett states it.

“This is because a rise in weight from the normal level causes energy needs to increase at a faster rate than the relationship would predict, whereas declines in weight from this level produce greater than predicted decreases in energy expenditure. We thus propose that an animal's body weight set-point be taken as the weight at which its daily energy needs can be accurately predicted from its metabolic body size. It is only at this one body weight that the animal is normometabolic.”

Keesey R, Corbett S. Metabolic Defense of the Body Weight Set-point. Res Publ Assoc Res Nerv Ment Dis. 1984; 62:87-96

Ethan Allen Sims (1916–2010)

Judith S. Stern

doi:10.1038/oby.2010.334

Ethan Allen Sims was born in 1916 in Newport, Rhode Island. He was the great-great-great grandson of Green Mountain Boys leader Ethan Allen and wrote a booklet called *Ethan Allen, the Philosopher*. He graduated from Harvard College (1938), obtained his MD from Columbia College of Physicians & Surgeons (1942), and became a house officer (1946) and later an instructor at Yale–New Haven Hospital. He spent his entire academic career at the University of Vermont (1950–2010) as a professor of medicine. In 1991, the university named its metabolic research unit the Sims Obesity/Nutrition Research Center.

relationship between "calories in" and "calories out" and the fact that a pound of fat gained is equivalent to 3,500 kcal do not explain the amount of weight gained by a particular individual. His December 2001 report in *Metabolism* led to his being featured in a *New York Times* article, "Is Obesity a Disease or Just a Symptom?," published 16 April 2002.

Ethan published many papers with his wife, Doro. In 1990, to celebrate their collaborative research, they were both given honorary doctor of science degrees by the University of Vermont. He was also honored for his extensive contributions to clinical research through the establishment by the National Institutes of Health of the Ethan Sims Clinical Research Feasibility Fund Award. The Obesity Society has honored Sims by creating The Ethan Sims Young Investigator Award.

Ethan was a true clinical investigator, and his Vermont study on experimental weight gain opened up new ways of thinking about obesity.

He recruited prisoners as subjects. He took thin prisoners and had them eat enough calories to become mildly overweight and took fat prisoners and had them calorie restrict enough to be just overweight about the same weight as the naturally thin prisoners he had “fattened up” and he measured the Basal Metabolic Rate of all the prisoners. The BMR of the “naturally fat” subjects was half that of the “Naturally thin” subjects. The “Naturally thin” subjects BMR rose from 1800 kcal/d to 2700 kcal/d. And after the experiment almost all the “naturally thin” subjects returned to their normal weight within a few months.

Source: Kolata, G. “Rethinking Thin: The New Science of Weight Loss -- And the Myths and Realities of Dieting. Farrar, New York

How to reset the Set-Point

- The Hypothalamus is the Thermostat
  - In 1890 Dr Alfred Frohlich at the University of Vienna treated a young boy with the sudden onset of obesity who turned out to have a lesion in the hypothalamus. This established the hypothalamus as a key regulator of energy balance and gave the first indication that obesity was a hormonal problem.
- Leptin can make the thermostat increase or decrease BMR in people w/o the metabolic syndrome but most obese people have higher than normal Leptin levels and have become Leptin resistant. Injecting Leptin does not cause weight loss.
- Ghrelin (the hormone that is produced by ghrelinergic cells in the stomach when it is empty) and satiety generating hormones such as Cholecystokinin and peptide YY have a role in weight control but cannot be the cause of obesity because injecting them into humans and other animals does not make them get fat.

Insulin levels turn out to mirror nicely the body mass set-point. Insulin goes higher after a meal in the obese

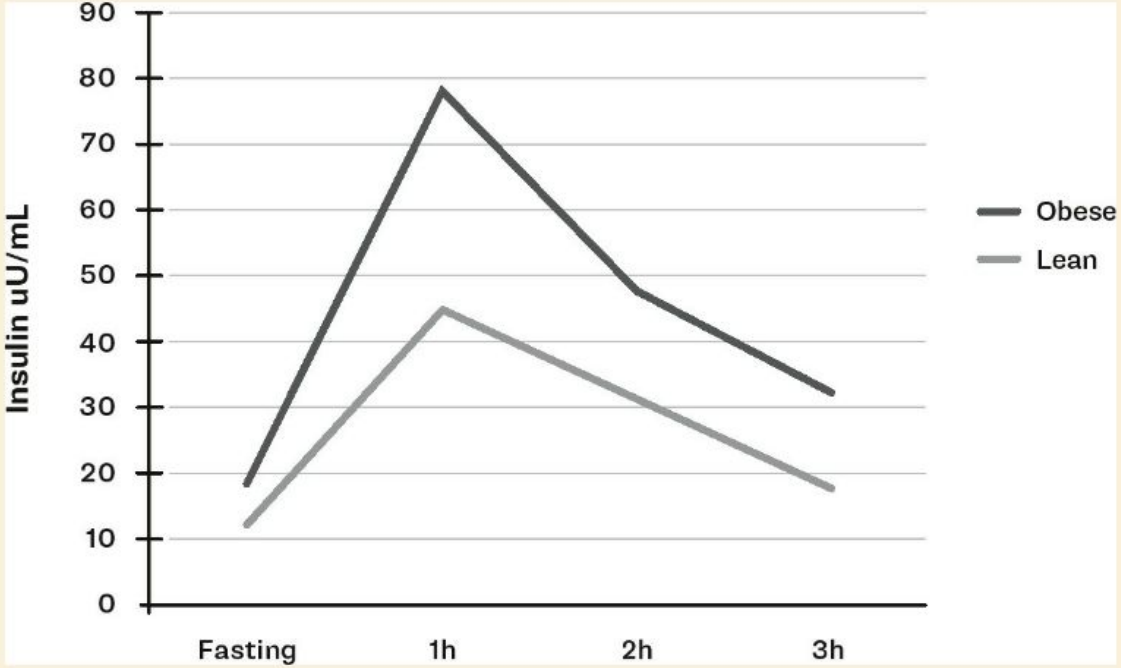
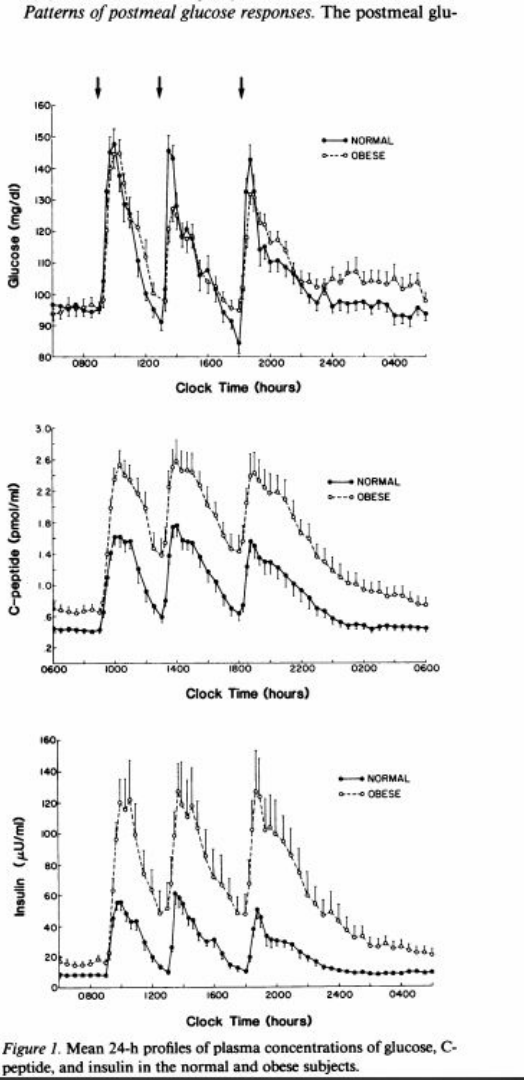


Figure 6.1. Different insulin responses in lean and obese people.

Tentolouris N, Pavlatos S, Kokkinos A, Perrea D, Pagoni S, Katsilambros N. Diet-induced thermogenesis and substrate oxidation are not different between lean and obese women after two different Isocaloric meals, one rich in protein and one rich in fat. Metabolism. 892008 Mar; 57(3):313-20

Insulin levels go higher and return to baseline slower in obese people than in normal weight individuals.



Polonski K, Van Cauter E. Twenty four hour profiles and pulsatile patterns of insulin secretion in normal and obese subjects. J Clin Invest. 1988 Feb; 81(2):442-8

The Higher the BMI, the higher the Insulin Level

- Black bar - hyperinsulinemia
- Light gray - insulin resistance
- Dark gray - hypersecretion of insulin

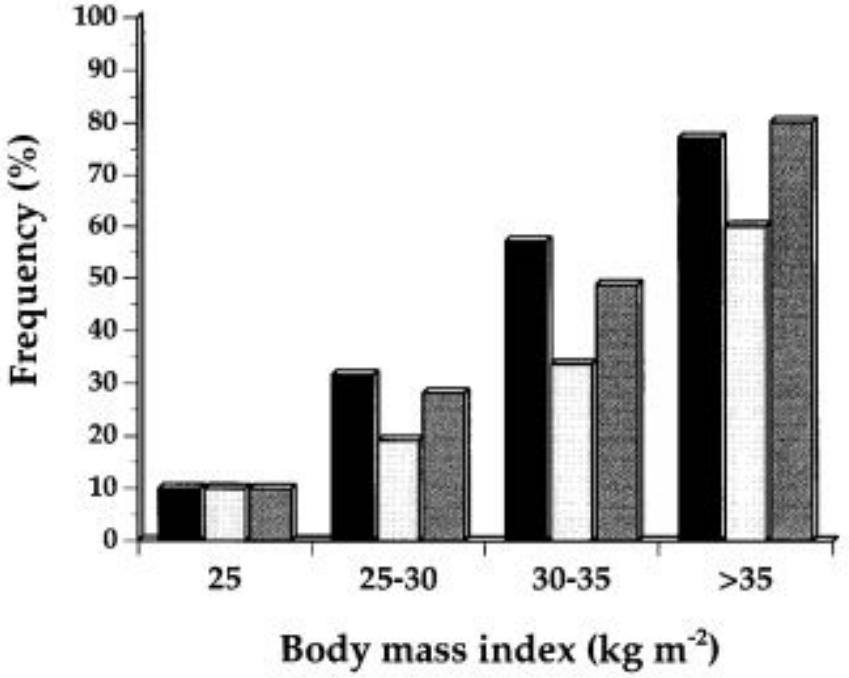


Figure 2. Prevalence rates of insulin resistance, hyperinsulinemia, and insulin hypersecretion (all defined as the top decile of the respective distributions in lean subjects) as a function of the BMI. *Black bars*, hyperinsulinemia; *light gray bars*, insulin resistance; *dark gray bars*, hypersecretion.

Ferrannini E, Natali A, Bell P et al. Insulin resistance and hypersecretion in obesity. J Clin Invest. 1997 Sep1; 100(5):1166-73

Pushing the “UP” button by giving Insulin increases weight

Russell-Jones D, Khan R. Insulin Associated weight gain in diabetes: Causes, effects and coping strategies. Diabetes, Obesity and Metabolism. 2007 Nov;9(6):799-812

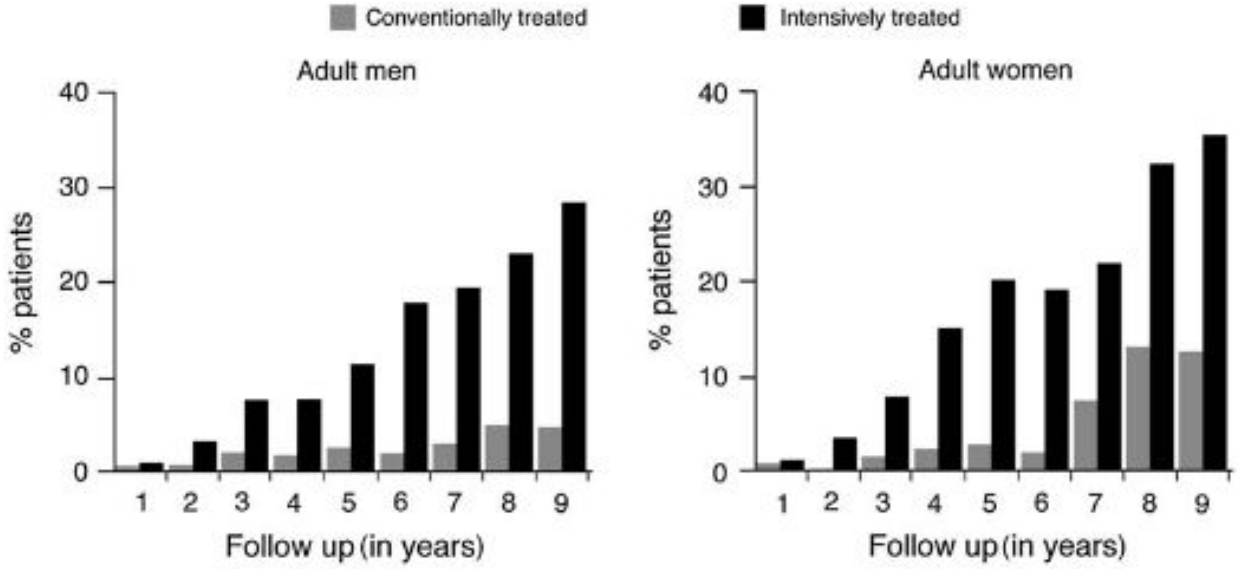


Fig. 2 Proportion of adult patients with major weight gain (>5 kg/m^2 increase in body mass index) occurring during the Diabetes Control and Complications Trial. Copyright © 2001 American Diabetes Association from DCCT Research Group [7]. Reproduced with permission from The American Diabetes Association.

Taking Insulin Away pushes the “DOWN” button

One clear illustration of this is Type 1 diabetes. They produce no insulin and unless exogenous insulin is given they will lose all their body fat.

The other big player - CORTISOL

- Secreted by the Adrenal Gland in response to stress
- Causes glucose levels to rise precipitously (triggering insulin release)

People taking Cortisol related steroids get fat and when you take it away they lose weight.

- Cushing's syndrome is like taking cortisol and obesity is a Hallmark of the disease.
- In this study patients who had been on prednisone for years for kidney transplants were weaned off. They had a 25% drop in plasma insulin, a 6% weight loss and 7.7% decrease waist girth.
    - Lemieux I et al. Effects of prednisone withdrawal on the new metabolic triad in cyclosporine-treated kidney transplant patients. Kidney International. 2002 Nov; 62(5): 1839-47

Cortisol levels highly correlate with finding of MetS

In this study of 439 Scottish adults living in North Glasgow a close correlation was found between urine cortisol excretion, BMI and other markers of the metabolic syndrome.

TABLE 5. Correlations With Cortisol (THF+allo-THF+THE)

Variable	Men (n=238)	Women (n=201)
Waist	0.29 (0.01)	0.27 (0.01)
Hip	0.31 (0.01)	0.14
BMI	0.34 (0.001)	0.23 (0.02)
Cholesterol	0.05	0.12
HDL cholesterol	−0.27 (0.01)	−0.22 (0.05)

Values are r^2 ($P<$).

Fraser R et al. Cortisol effects on body mass, blood pressure and cholesterol in the general population. Hypertension 1999 Jun; 33(6)1364-8

CORTISOL and Sleep Deprivation

24 hours of sleep deprivation raises cortisol levels by 100%

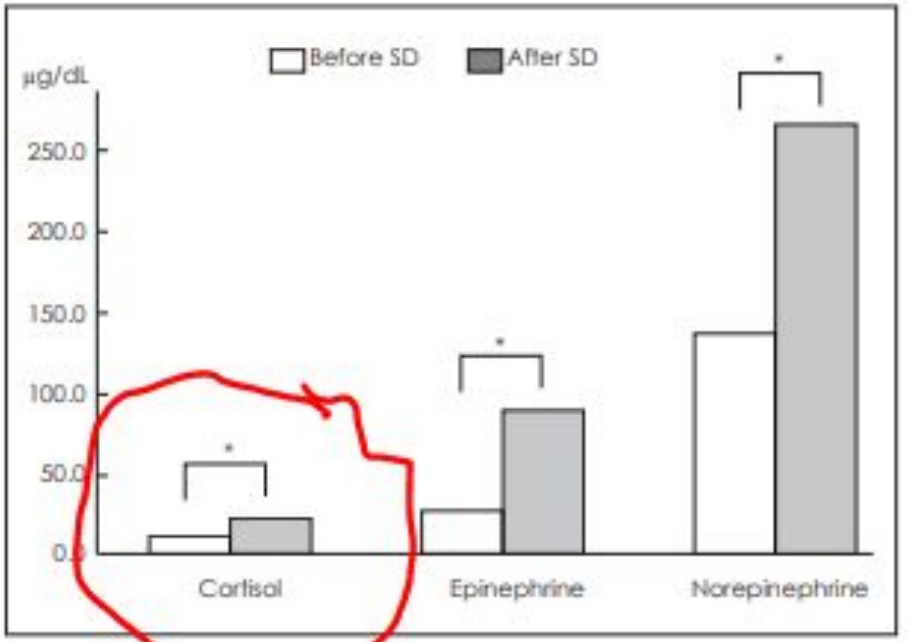


Fig. 1. Comparison of serum concentrations of stress hormones before and after 24 h of SD. Mean serum concentrations of cortisol, epinephrine, and norepinephrine were significantly increased after SD. *p<0.05 (Wilcoxon signed-rank test with multiple comparisons). SD: sleep deprivation.

Joo EY et al. adverse effects of 24 hours of sleep deprivation on cognition and stress hormones. J Clin Neurol. 2012 Jun; 8(2):146-50

How can patients push the “DOWN” button?

Decrease Carbohydrate intake!

The Last Laugh

In 2000 Dr. Atkins and Dr. Ornish held a national debate on CNN called:

“Who Wants to be a Millionaire Diet Doctor?”

	Atkins (n = 77)	Zone (n = 79)	LEARN (n = 79)	Ornish (n = 76)
Body mass index§				
2 mo	−1.60 (0.98)	−0.76 (0.99)	−0.99 (1.00)	−0.95 (0.90)
6 mo	−2.16 (2.14)	−0.73 (0.90)	−1.13 (1.91)	−0.85 (1.60)
12 mo	−1.65 (2.54)[a]	−0.53 (2.00)[b]	−0.92 (2.00)[a,b]	−0.77 (2.14)[a,b]
Body fat, %				
2 mo	−2.1 (1.8)	−1.8 (2.0)	−1.5 (1.8)	−1.2 (1.5)
6 mo	−3.6 (4.1)	−1.7 (3.1)	−2.0 (3.2)	−1.4 (2.7)
12 mo	−2.9 (4.8)	−1.3 (3.4)	−1.0 (3.4)	−1.5 (4.0)
Waist-hip ratio				
2 mo	−0.019 (0.016)	−0.012 (0.019)	−0.012 (0.022)	−0.009 (0.019)
6 mo	−0.021 (0.023)	−0.014 (0.023)	−0.010 (0.022)	−0.010 (0.023)
12 mo	−0.019 (0.026)	−0.013 (0.023)	−0.009 (0.024)	−0.012 (0.024)
LDL-C, mg/dL				
2 mo	2.3 (23.5)	−5.3 (17.8)	−7.3 (20.8)	−10.1 (19.8)
6 mo	1.7 (22.3)	0.5 (14.9)	−2.4 (19.4)	−3.2 (19.9)
12 mo	0.8 (22.6)	0.0 (17.6)	0.6 (17.0)	−3.8 (19.0)
HDL-C, mg/dL				
2 mo	−0.4 (7.7)	−0.5 (5.4)	−3.8 (6.1)	−5.3 (9.0)
6 mo	5.1 (9.6)	3.3 (6.9)	2.1 (6.7)	0.0 (9.2)
12 mo	4.9 (9.1)[a]	2.2 (6.1)[a,b]	2.8 (7.7)[a,b]	0.0 (6.3)[b]
Triglycerides, mg/dL				
2 mo	−52.3 (66.8)	−24.8 (53.1)	−17.4 (48.9)	10.9 (55.0)
6 mo	−35.6 (64.4)	−21.3 (58.9)	−16.1 (50.1)	−7.6 (54.4)
12 mo	−29.3 (59.0)[a]	−4.2 (48.5)[b]	−14.6 (60.8)[a,b]	−14.9 (46.2)[a,b]
Non–HDL-C, mg/dL				
2 mo	−8.0 (26.3)	−10.2 (21.7)	−10.7 (19.0)	−7.8 (17.8)
6 mo	−4.7 (23.1)	−3.7 (18.8)	−5.6 (18.6)	−4.7 (22.1)
12 mo	−5.1 (22.5)	−0.5 (20.0)	−4.0 (19.7)	−6.8 (20.3)
Insulin, μU/mL				
2 mo	−3.0 (3.9)	1.0 (6.0)	−1.9 (4.7)	−1.1 (3.3)
6 mo	−2.8 (4.1)	0.1 (8.9)	−2.1 (5.4)	−0.1 (3.6)
12 mo	−1.8 (4.8)	−1.5 (4.9)	−1.8 (5.1)	−0.2 (3.8)
Glucose, mg/dL				
2 mo	−0.4 (6.8)	−1.6 (10.6)	−0.8 (8.3)	−1.4 (6.9)
6 mo	0.2 (7.6)	−1.7 (9.6)	−0.9 (9.9)	−0.6 (7.3)
12 mo	−1.8 (13.4)	−1.6 (6.5)	0.5 (9.2)	−0.8 (7.9)
Systolic blood pressure, mm Hg				
2 mo	−6.8 (8.0)	−3.2 (8.2)	−3.6 (6.9)	−1.6 (6.3)
6 mo	−6.4 (9.5)	−3.6 (8.0)	−4.3 (7.6)	−1.7 (7.0)
12 mo	−7.6 (11.0)[a]	−3.3 (8.1)[b]	−3.1 (9.3)[b]	−1.9 (7.7)[b]
Diastolic blood pressure, mm Hg				
2 mo	−2.9 (6.2)	−2.1 (5.6)	−1.4 (4.4)	−0.4 (5.5)
6 mo	−3.3 (6.9)	−1.8 (5.6)	−2.5 (5.8)	−1.0 (5.6)
12 mo	−4.4 (8.4)[a]	−2.1 (5.8)[a,b]	−2.2 (6.7)[a,b]	−0.7 (6.0)[b]

Gardner CD et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women. JAMA. 2007 Mar 7;297(9):969-77

What about low carbohydrate diets making your LDL Cholesterol go up?

This was looked at in a subreview of the First Year Virta results. LDLc went up about 9% but that was the only negative marker. Here's what went right:

- Weight down 13%
- A1c down 16%
- Syst. BP down 5%
- Diast. BP dnow 4%
- Triglycerides down 24%
- HDL-C up 18%
- hs-CRP down 38%
- WBC count down 9%
- Hypertensive medication use down 18%
- Diuretic use down 24%
- LDL particle size up 1.1%

10 Year Atherosclerotic Cardiovascular Disease (ASCVD) risk score decreased by 11.9%

Bhanpuri, N, et al. Cardiovascular disease risk factor responses to a type 2 diabetes care model including nutritional ketosis induced by sustained carbohydrate restriction at 1 year: an open label, non-randomized, controlled study. Cardiovasc Diabetol (2018) 17:56

- Obesity is not a moral failure
- The Calories in - Calories Out theory cannot be supported by scientific evidence
- Calorie Restriction gives short term results that are not sustainable, makes patients miserable and can permanently lower the Basal Metabolic Rate.
- Exercise contributes very little to weight loss and “eat Less, Move More” is a losing strategy
- The only way to reset the body’s weight set-point is to decrease the insulin level there are 3 main ways to do that:
    - Low carb - fasting - stress reduction - medications (metformin, acarbose, orlistat, SGLT1 inhibitors, GLP-1 agonists, glitizones)
- Ketogenic diets are sustainable and effective.
- Ketogenic diets have a favorable effect on the cardiac risk profile.


You need to start taking an anti-depressant in addition to your statin medication.
Okay. No Problem.


You need to cut out grains and start eating animal protein and fat at every meal.
Sounds Dangerous.