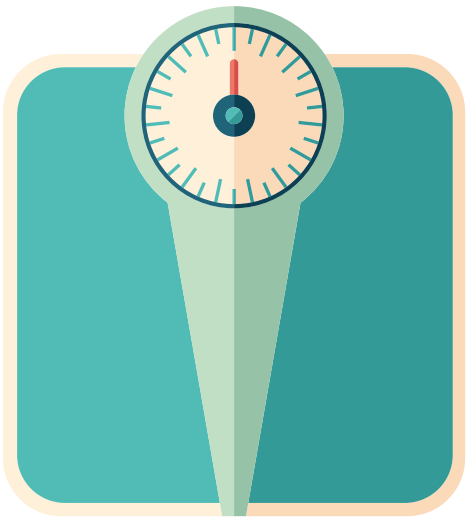
Center for Creative Leadership®

The Care and Feeding of the Leader's Weight



"When unproven science becomes a sales pitch, some people get rich and the rest of us get ripped off".

~spokesperson for the American Institute for Cancer Research

The Obesity Epidemic and How Executives Stack Up

Unless you've been living under a rock for the last few decades, you know that there is a global obesity epidemic underway. This was highlighted as early as 1998 in a report published by the World Health Organization (WHO), which documented the rapid increases in the incidence of obesity across various countries.[1] The sad truth is that since 1980, obesity rates have nearly doubled worldwide.[2]

But obesity is not a recent phenomenon. Artifacts of corpulent women from the Stone Age have been found in several sites across Europe. The first diet book, entitled *Letter on Corpulence Addressed to the Public*, was published in the 19th century. However, the rise in the prevalence of obesity has never reached such epidemic proportions as it has in these last few decades.

While obesity arises as a result of an energy imbalance where intake exceeds output over a period of time, numerous and complex factors can give rise to this imbalance and is the result of the interaction between a multitude of influences, rather than a single factor acting alone.[1] We will explore a number of these factors in this chapter.

Who is the fattest?

The country with the highest rates of obesity also happens to be one of the smallest countries in the world, Nauru, an island nation in the South Pacific. According to the WHO, over 90% are overweight or obese, with 78% qualifying as being obese. Of the top ten countries in the world with the highest rates of obesity, the islands of the South Pacific now occupy the top seven spots.[3] This is notable for reasons that will be discussed in more detail later, but has to do with an unfortunate combination of genetics and dramatic dietary shifts away from a traditional starch-based diet to one of imported western foods.

The saddest statistic, however, is that in 2013 42 million children **under the age of 5** were overweight or obese worldwide.[4] Worldwide in 1990, 4.2% of preschool children were overweight or obese. In 2010 it increased to 6.2% and is predicted to reach 9.1% in 2020.[5] Childhood obesity is a growing and devastating problem and leads to compromised health into adulthood.[6]

In developed countries the US and Mexico lead the way with the highest rates of obesity. Of interest is that in 1990, no state in the US had an obesity prevalence that was > 15%, in fact most were less than 10%. By 2010, a scant 20 years later, no state had an obesity rate less than 20%. Outside of the US, between half and two-thirds of men and women in 63 countries across five continents were overweight or obese in 2006.

The Story of Mississippi and Colorado

Since 1990, Mississippi has been one of the fattest states in the US while Colorado has enjoyed the reputation of being the state with the lowest rates of obesity. Indeed, in a recent comedic article entitled 'What Bad Coloradoans Say', one is "I am fat".

Fast forward to 2013, Mississippi still has the claim to fame as having the highest rate of obesity (along with West Virginia) where >35% of the population are obese. In 2013 CO is still the lowest in the country with an obesity prevalence of 21.3%. But all things are relative, as CO now has a higher rate of obesity than Mississippi did in 1990 or even in 2000 for that matter.[7]

What these data illustrate is that in less than three decades we have seen gargantuan (no pun intended) and unprecedented increases in obesity rates. Of interest is that obesity is highest in African Americans and lowest in Asian-Americans. It is also highest (39.5%) among middle-aged adults, 40-59 years of age. This is the typical age range of senior executives that have attended the Leadership at the Peak program at CCL. So how have they fared over this same time period?

Obesity Rates in Executives

Among executives, rates of obesity have remained remarkably stable. We have been collecting health data on hundreds of executives since the 1990s. Our data show that in the 1990s, 14.3% were obese and in the 2010s, 16.4% were obese (as defined by a BMI greater than 30). Average BMIs since 1990 have increased slightly from an average of 26.7 to 27 (for men). Percent body fat has also increased slightly (statistically significant) from an average of 22.7% to an average of 23% for men. For women, BMI has increased slightly from an average of 23 to 25.1 while percent body fat has stayed at a constant 30% average over the years.

But here is where it gets interesting. While few are obese, only 30% of the men are in the ideal range for BMI and 54% are overweight (5,100 surveyed). For female executives, the picture is quite different. Sixty-eight percent of female executives were in the ideal range, 20% were overweight, less than half as compared to men, and only 12% were obese (850 surveyed).

So for reasons that remain obscure, obesity rates haven't gone up in this group as much as it has in the general population. And the majority of female executives are in the ideal range while the majority of males are overweight. Relatively few of either gender are obese.

There are a number of hypotheses that could explain this. Certainly higher socioeconomic status could be one. But this does raise some questions regarding perceptions and the stigma that being overweight or obese may pose. Is being overweight more tolerated in males than in females, i.e. are females less likely to be promoted if they are overweight or obese than their male counterparts? Is obesity bad for executive image in general?

Obesity: Bad for Executive Image?

Some of our research hints that this is the case. Data that we collected from health examinations and multi-source evaluation surveys of 757 CEOs, vice presidents, and upper managers showed that higher waist circumferences, an observable cue of obesity, was negatively associated with evaluations of leaders across hierarchical levels, even after controlling for BMI, physical activity, personality, and demographic characteristics. Hierarchically based status characteristics are insufficient in overcoming the stigma of obesity. Thus, even CEOs are subject to the pernicious effects of obesity stigma.[8]

In other words, even though being an executive comes with a certain degree of authority, power and status, being obese or overweight is still seen as a negative.

Is Obesity Harmful to Health?

Unfortunately when obesity is the issue, people automatically focus on weight loss as the solution. This unparalleled focus on weight loss has led to some unintended consequences, not the least of which are the plethora of 'flavor of the month' diets and weight loss programs—on any given day, more than 25% of men and 45% of women in the US are on a diet. Sadly, many of these diets are not health promoting and may even be disease promoting, even when weight loss occurs. Weight loss at the cost of long-term health is not the solution. Yet, it is a billion dollar industry and feeds on people's desire to meet cultural norms for body image and health. Crowded out of this fad-diet culture is the message that a diet rich in fruits, vegetables, legumes, seeds and whole grains is helpful in preventing and even reversing chronic conditions like hypertension[9,10], cardiovascular disease[11,12,13], diabetes[14], and certain cancers[15,16]. The good news is that this same diet can help to prevent and reverse obesity as well.

But just how detrimental is it to one's health? Does obesity play a causative role in chronic disease, or is it more of a co-morbidity, i.e. is it guilty by association?

I think there is evidence it does both. There are health problems that are made worse by being obese. There are some conditions in which obesity plays more of a causative role, like cancer and diabetes. However, the same lifestyle factors (e.g. poor dietary habits and lack of exercise) that lead to heart disease, cancer and diabetes can also lead to obesity. The root cause is the same.

We often make assumptions about a person's health based on how they look. We assume skinny people are fit and healthy and overweight people are unfit and less healthy. We are surprised when someone who is lean gets a heart attack or cancer. We immediately attribute it to bad genetics or bad luck. We are less surprised when an overweight or obese person has those same health problems. But poor dietary and exercise habits are not just the domain of the obese; many thin people eat poorly and suffer the consequences.

A 2008 review article suggested that increasing cardio respiratory fitness is associated with reduced risk of CHD, even in the absence of weight loss.[17] The authors concluded that, while weight loss is associated with marked reductions in obesity-related risk and remains a desired outcome, we need to look beyond weight loss as the only indicator of success. Another study found that obese vegans had half the rates of diabetes than obese omnivores, after adjusting for other lifestyle factors.[18] Research by Steven Blair and colleagues out of the Cooper Clinic has repeatedly shown that those who are overweight or obese, but are fit, carry a lower risk of heart attack than those who are lean but unfit, suggesting that fitness level is a stronger predictor of risk than being overweight.[19,20] Even in those with established or suspected CHD, fitness greatly attenuates the risk associated with being obese.[21]

To be clear, I do think it is helpful to not carry around a lot of excess body fat. But weight loss should not be the only criteria by which we measure the success of a particular dietary change or exercise program. Weight loss at any cost is not the goal. After all, smoking cigarettes can assist with weight loss, crack addicts are quite thin and eating a high-fat ketogenic diet can result in substantial weight loss. But these strategies are not helpful when it comes to long-term health outcomes.

There is an additional problem when people set weight loss goals (and sometimes unrealistic ones). If the goal is to lose 20 pounds then a 20 pound loss is how success is defined. However, the individual may be really disciplined and only end up losing 10 pounds. A ten-pound weight loss is then seen as failure (and by definition, the dietary or exercise change a failure, therefore why stick with it?).

A better goal is say "I need to eat to be as healthy as I can; I need to exercise to get/stay fit, to feel and function better." This is also more of a long-term, higher order endeavor—indeed it is a life-time endeavor. Who doesn't want to stay healthy for life? Who doesn't want to be fit and functional into the later years of life? Likely there are some that don't care about that as much, but hopefully if you are reading this you are not one of them.

The good news is that eating to be healthy and achieving a good body weight are not mutually exclusive; you can also achieve a body weight that is sustainable and healthy for you. And yes, we come in all shapes and sizes and for some a healthy and sustainable body weight will not always be what society considers ideal. So we need to stop chasing skinny and start chasing vibrant health.

Eat to Be Healthy (and to lose weight)

When it comes to losing weight, changing your diet will have a greater impact than increasing your exercise level (in spite of what the infomercials tell us).[22] There are reasons for this that will be discussed in the exercise section.

When it comes to eating for weight loss, there are some important criteria to consider. (1) Your diet must also improve health. (2) It (the diet) must be sustainable over the long-term. Counting fat or carb grams, or counting anything for that matter, is not a life-long solution. (3) It must not involve going hungry. The question is how to meet all of these requirements and still achieve weight loss and weight maintenance over time?

Just about every diet out there can result in weight loss in the short-term. Data from scientific studies indicate that a 15 week diet will typically result in a weight loss of about 5-11 kg. Yet when measured over the long-term, most diets come up dismally short. To put it in perspective, weight loss diets have a lower success rate than interventions for alcoholics or cancer

patients. While long-term follow up data are meager, the data suggest almost complete relapse (i.e. all the weight is regained) after three years.[23]

We are all familiar with the concept of calories in versus calories out. Indeed, the only way to lose weight is to shift the balance in favor of fewer calories in and more calories out. As far as I know, the first law of thermodynamics has not been revoked. This is one reason why many types of "diets", be they low-fat, low-carb, or high-fat, can result in weight loss (at least in the short term) purely because adherence to these diets results in a negative caloric balance (or in the case of low-carb diets a lot of lost water weight).

In the middle of the calorie balance equation, however, is a black box called the human body. What is becoming apparent is that not all calories taken in are **equally retained**. Different foods affect our genetics, the number of calories lost as heat, and the type of bacteria in our gut which in turn affects how many calories are retained. All these factors will be discussed in this paper.

In this paper I am going to review (a) cross-sectional and prospective studies to determine what types of foods or eating patterns are predictive of weight gain in populations, (b) examine the role of energy or caloric density and other mechanisms of satiation, (c) the role of macronutrients (fats, proteins and carbs), (d) the possible role of nutrient density, (e) the possible role of chicken and fish in weight gain, (f) the research on nuts and weight loss/gain, (g) the contribution of genetics to obesity and (h) the role of our gut bacteria.

Epidemiological Studies

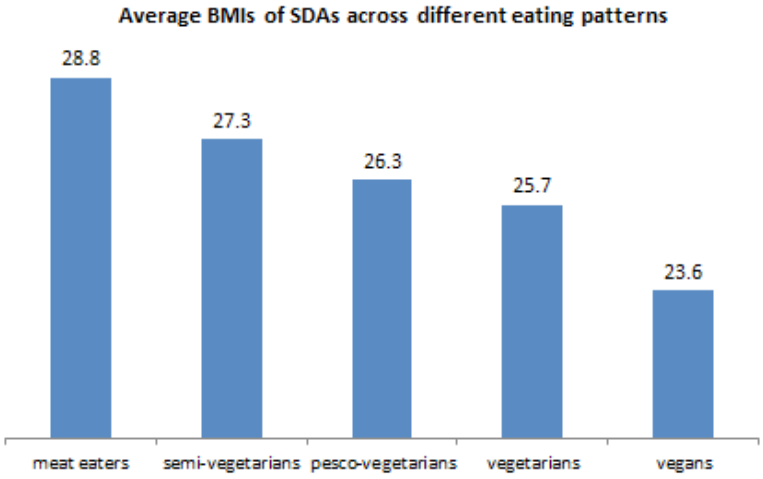
While epidemiological studies (cross-sectional, prospective or retrospective) don't prove causation, they do provide us with clues as to which dietary practices are most strongly associated with obesity and weight gain and/or which eating patterns are associated with being lean and thin in populations. These studies are good starting points. Once we have a general idea as to the foods and/or eating patterns that hurt or help, we can then start to look at mechanisms and interventions to explain these associations and tease out causative factors.

One of the best studies out there is the European Prospective Investigation into Cancer and Nutrition (EPIC). It is the largest detailed study of diet and health ever undertaken. It involves over 500,000 people in 10 European countries and is coordinated by the WHO. A UK subset of the study is the EPIC-Oxford which is a prospective cohort of 65,000 men and women in the UK. Of interest is this cohort includes thousands of vegetarians and vegans. Comparing meat-eaters to vegetarians to vegans is an easy way to slice the data as these are three very clear dietary demarcations and allows researchers to be less reliant on food intake surveys (which are notoriously unreliable).

What they found was that the age-adjusted BMIs were lowest in the vegans and highest for meat eaters, with pesco-vegetarians and lacto-ovo vegetarians falling in the middle. This was true for both men and women. Differences in lifestyle factors like smoking, exercise and education level accounted for less than 5% of the difference in BMI. Of note, high protein intake and low fiber intakes were the dietary factors most strongly associated with higher BMIs both between and within the different groups, i.e. the higher the fiber and lower the protein the lower the BMIs.[24]

These findings are not unique. Numerous studies have found that vegetarians are consistently lighter than non-vegetarians across a variety of ethnic groups (Asians, African-Americans, Africans, Caucasians), geographic regions and age-groups.[25,26] Vegans, in turn, tend to have lower body weights than vegetarians. BMIs were also lower among those vegetarians or vegans who had adhered to their diet for a longer period of time.
It is difficult, however, to control for all of the potential confounding factors in these diverse groups. Thus researchers have studied Seventh-Day Adventists (SDAs) because virtually all SDAs avoid tobacco and alcohol, limit caffeine, are generally well-educated and are encouraged to exercise. About half are vegetarian, some are vegan and the rest eat some meat. Those who do eat meat are selective in the type of meat they eat and tend to only eat moderate amounts. Certain meats, like pork or lobster, in fact, are not allowed. This represents a very neat experimental design. If there were ever a group of healthy meat eaters this is it, while also naturally controlling for a number of confounding variables.

Findings from these studies showed non-vegetarians as having significantly higher BMIs than their vegetarian or



vegan counterparts. A 2009 study on SDAs found that the average BMIs increased in a stepwise fashion from vegans, to lacto-ovo vegetarian, to pesco-vegetarians, to semi-vegetarians, to non-vegetarians.[27] The only group whose average BMIs were in the ideal range was the vegans[27].

But maybe vegans exercise more (actually in this study they exercised less), eat less junk food and are just more health conscious in general? Or is it a case of reverse causation, i.e. are skinny, health-minded people more likely to go vegan or vegetarian? These are legitimate questions. So let's take a look at prospective studies where they follow the same people over time.

In the EPIC-Oxford study they followed 21,966 men and women for an average of 5.3 years.[28] Over the course of the study, average weight gain went up by 400g/year for both men and women, not too surprising as people tend to gain weight over time. Those who exercised or started to exercise gained less weight. Smokers gained less weight

than non-smokers. Again, not too surprising and illustrating once again that not all habits that prevent weight gain are good for you. The dietary group that saw the least amount of weight gain, however, (25-50% lower) was the vegans (for both men and women). This was after adjusting for confounding variables (like exercise and smoking). Weight gains were similar for the meat-eaters, fish-eaters and vegetarians; although the starting weights were quite a bit lower for the vegetarians and fish-eaters than they were for the meat-eaters.

An even more interesting study, however, is the EPIC longitudinal study.[29]

In this study close to 500,000 people from 10 European countries were followed. After adjusting for confounding variables, they found that total meat intake was positively associated with weight gain after an average of 5 years of follow-up. Of interest is that this was **after adjusting for energy intake or calories**. In other words, those who ate meat gained more weight than those who didn't eat meat for the same intake of calories. The authors estimated that for every 250g/day of meat intake resulted in 2kg of weight gain after five years compared to the same calories from plant foods. Even more interesting was that the strongest association with annual weight change was observed for poultry (more on that later).

Several other prospective observational studies have also looked at meat consumption and weight gain. The majority showed increased weight gain with meat consumption, while only a couple studies did not.[30,31,32,33,34,35]

But just to confound things there are some studies that show that during calorie and fat restricted diets, diets high in protein showed a slightly greater weight loss than high-carbohydrate diets. One review concluded that higher protein intake was associated with improved weight regulation.[36] Apart from the fact that the authors of this review received funding from the dairy, beef and pork industries, is this true?

With regard to long-term weight loss, the results are actually quite mixed, with some showing reduced weight on high protein diets, while other studies didn't. Part of the problem is that the quality of the carbohydrate diets in many of these studies is either not reported or is rather poor.[37] Indeed, in one study, carbohydrate intake was increased by feeding subjects maltodextrin—a simple sugar.[38] A Spanish study found that eating more white bread was significantly associated with weight gain, while consumption of whole grain bread was not.[39] The type of carbs consumed is rather important and fiber intake is particularly important for aiding in weight loss.[40] In many of these low-carb/high protein vs. high carb/low protein studies, fiber intake was <20 grams, less than half of what is considered ideal (>50 grams).[41,42] Thus the quality of the carbohydrates being consumed is quite poor.

This is in fact a neat trick that is often used by low-carb advocates. If you compare a low-carb diet to a junky high-carb diet, the low-carb/high-protein diet often looks good by comparison. Of course, this is a very reductionist way

to look at diet and doesn't take into account the quality or the type of the foods consumed; a rather short-sighted approach in my opinion.

Additionally, often the increased protein was derived from other foods (like vegetables, protein powders or low fat dairy), not just meat.[43,44,45,46,47] Finally, in the study by Foster et. al., weight loss was only greater in the low-carb group after 6 months, but not after a year of follow up. Taken together, those studies that compare high-protein to high-carb diets don't tell us much about the contribution of meat per se, only that it suggests that in the absence of sufficient intakes of high fiber foods, high protein foods may be advantageous when it comes to weight loss, regardless of whether the type of proteins consumed are healthy or not.

What makes the EPIC study unique is that they controlled for underlying dietary patterns (like sugar, alcohol, cereals, vegetables, and fat intakes) and for total energy intake.

Other foods shown to be predictive of weight gain are sugar-sweetened soft drinks, hamburgers, pizza, and sausages.[48] In a US study which followed three different cohorts over time, foods most strongly associated with weight gain were potato chips (including fries), sugar-sweetened drinks, red and processed meats. Foods inversely associated with weight gain, i.e. weight loss, were vegetables, whole grains, fruits and nuts. Of interest in this study was that other factors like lack of sleep and exercise were also associated with weight gain over the 4 years of follow-up. Thus obesity is a multifaceted problem, albeit diet is the most significant.[49]

Food Trends

Food availability (sometimes called food disappearance) reflects total annual food production, imports, exports and nonfood uses. So while not perfect it is a good proxy for foods actually consumed (food waste and spoilage is also taken into account) and is useful for examining trends over time and where we are deriving the bulk of our calories.

Total available calories for the US population rose from 3200 calories per day in 1980 to 4,000 calories per day currently. It is estimated that actual caloric intake has increased by an average of 350 kcal.day^{-1} for children and 500 kcal.day^{-1} for adults. That is a big increase in calories. Incidentally this increase perfectly parallels the increase in rates of obesity[50,52]. Of interest, over the same time period, levels of physical activity have stayed about the same[51]. Thus, for the most part, the increase in obesity is attributable to eating too much, and too much of the wrong foods. So let's break down which foods contributed most to this increase in calories. This may surprise you.

Red meat availability declined slightly since 1970; however, total meat intake has increased significantly. This is due to a doubling of poultry intake from 34 lbs.yr^{-1} to 74 lbs.yr^{-1} and an increase in fish consumption. While milk consumption has gone down, cheese intake has increased from 11 lbs.yr^{-1} to 33 lbs.yr^{-1}. Processed fats and oils have also gone up from 56 lbs to 87 lbs, which represents a significant increase in calories. Grain availability has also increased by about 27 lbs. Most of this is from processed flour as only 2% of wheat grain is retained as whole wheat. Sweeteners, like high-fructose corn syrup, have increased slightly, but only by about 50 calories per day on average. What these data show is

that increasingly, a considerable proportion of our calories come from processed foods like oils and flour and from animal foods like chicken and cheese.[52]

Besides the fact that we are simply eating more calories, these types of calories and foods also make it very difficult to balance our calorie intake with expenditure. Our mechanisms of satiation (i.e. those signals which tell us we are full) were never meant to do battle with such calorie rich foods as cheese, chicken and oils. In addition, these foods play into our genetic tendency to gain weight (BTW most of us have this genetic tendency) as we will explore in the genetics portion of this chapter.

But first, here is a question to ponder. Why aren't wild animals fat?

I was born in Africa, Zimbabwe to be precise. My parents were South African thus I spent most of my childhood in South Africa. For just about every holiday we visited the game parks throughout Southern Africa. We never got tired of observing gazelles, elephants, various buck and giraffes in their natural habitat. If you have had the opportunity to visit an African game park you have likely had the same sense of awe and delight at seeing these animals. Yet, of all the hundreds (or even thousands) of animals we observed during that time, we never ever saw an obese giraffe, or eland, or springbok, even when food was in abundance. Why is that?

All animals have the ability to calibrate their caloric intake with caloric output; without counting calories or fat grams or anything for that matter. They have internal mechanisms of satiation that do this with great precision. Why don't we have this? Well, in actual fact we do.

Mechanisms of Satiation: The Role of Calorie Density (CD)

An important mechanism of satiation is stretch receptors in the stomach. When stretched they send a message to the brain to let us know that our stomachs are getting full.[53] Indeed, devices such as inserting balloons into people's stomachs are now being devised to trigger this mechanism in order to help people lose weight. How many times have you eaten to where your stomach is stretched to the point where it becomes painful? How many times have you eaten through the pain? Most of us have. Eating is pleasurable. This is a good thing as we likely wouldn't be here if it wasn't. This is why being satiated (i.e. having a full belly) is so important. Severely restricting food portions in an effort to lose weight is a short-lived strategy as doing this may fail to adequately engage those stretch receptors.

If you are eating high fiber foods like beans or high water content foods like fruit it is difficult to ingest excessive amounts of calories, even if you do eat until you are stuffed. This is Mother Nature's built in protection against obesity. Think about it. Could you eat a 3.5oz bag of potato chips? Most of us could. But, could you eat 4 large baked potatoes or 7 apples? Not so easy to do. But that is how many potatoes or apples you would have to eat to get the same number of calories as found in that small bag of potato chips.

Eating high fiber foods is an important weight loss strategy. The majority of studies show that an increase in fiber (either soluble or insoluble) increases post-meal satiety and decreases subsequent hunger. When calorie intake is ad libitum, published studies show that for every 14 g.day^{-1} increase in fiber consumed there is a 10% decrease in caloric intake and a weight loss of four pounds (1.9 kg) over 3 to 4 months. Of interest is that those who are obese tend to show a greater suppression of calorie intake and lose more weight by eating lots of fiber. On average, obese individuals reduced calorie intake[54] by 82% vs. 94% in lean individuals after increasing fiber intake. Extrapolating this further, eating 12 g per day of fiber means that one would be full on 2,000 calories; eating 40-50 g per day, one would feel full on 1500 to 1600 cal (all things being equal).

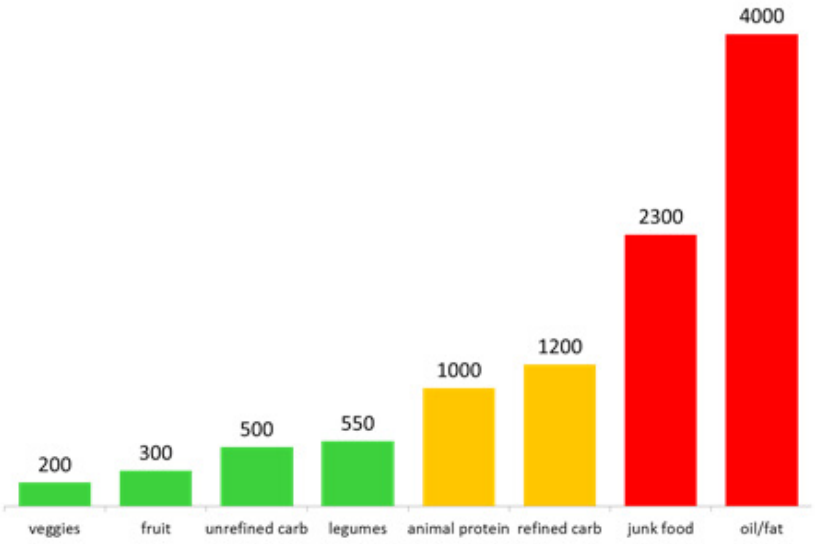
This brings us to one of the most important mechanisms of satiation, calorie density (CD). CD is a measure of the number of calories a food provides relative to its weight. It can be expressed as calories per gram or calories per pound. Why is this important?

Findings from several investigations have indicated that people tend to consume a constant weight of food day in and day out.[55,56,57] If you make even modest changes in CD, while keeping the total weight of food the same, this can significantly impact calorie intake. For example, on a typical day if an adult consumed 1200 grams (or 2.7 pounds of food) with an average CD of 817 cal.lb^{-1} (1.8 cal.gram^{-1}) the calorie intake for the day would be 2160. If the CD of the diet was decreased to 560 cal.lb^{-1} (1.25 cal.lb^{-1}) while the same weight of food was consumed, then the individual would ingest about 1500 calories, reducing intake by about 600 calories per day. This is significant and over time can add up.

What makes foods less calorie dense?

The two factors that provide bulk and weight yet don't contribute calories are fiber and water. When plant foods are processed, the water, fiber and most of the nutrients are removed and the foods become calorie concentrated. Sugarcane becomes sugar, wheat berries become white flour and olives become oil. Our mechanisms of satiation become overwhelmed with this degree of calorie concentration. Animal foods, like chicken, fish, beef, or pork also contain no fiber, very little water and few nutrients. Thus, by definition, they could be classified as processed foods. Animals eat the grain then poop out the fiber, pee out the water, store the fat, and you are left with a concentrated source of calories.

Below is a chart of foods and their average CD expressed as calories per pound (or per 500g). Foods with low to moderate calorie densities are fruits and vegetables, followed by cooked grains (like oatmeal), cooked root vegetables like potatoes, and beans. Foods that are very CD are fats and oils, processed foods like cakes and cookies, cheese, and meat. These are all above 900 calories per pound.



Research has shown that people can consume relatively large, indeed even unlimited, portions of foods that are <400 cal/lb and still lose weight. (To my knowledge, no research has shown

that we get fat by eating too many grapes or apples). People can consume relatively large portions of foods that are 400-800 cal/lb and still lose or maintain weight, depending on how active they are. Eating foods that are 800-1800 cal/lb should be limited as this can seriously undermine weight loss efforts. Foods above 1800 cal/lb should be severely restricted for the same reasons these very easily contribute to weight gain and obesity. Even elite athletes who are training many hours a day can gain weight if they eat large amounts of these foods.

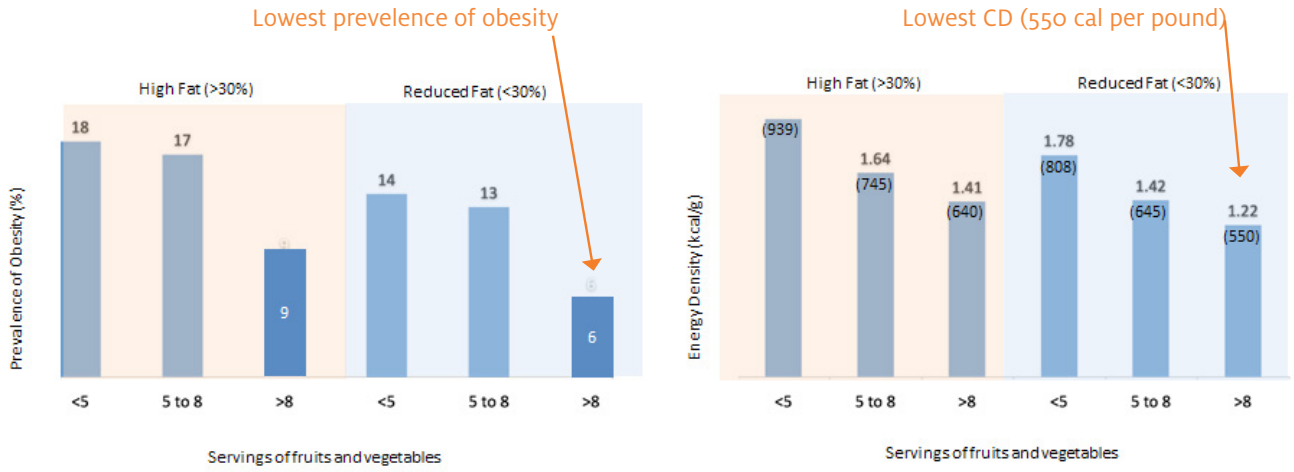
In their 2006 report, titled, *Food, Nutrition, Physical Activity and the Prevention of Cancer*, the World Cancer Research Fund recommended that in order to achieve an ideal body weight the average CD of one's diet should be around 1.25 cal.gram^{-1} (or 567 cal.lb^{-1})[58]. Not surprisingly, their other recommendation is to "Eat mostly foods of plant origin". These recommendations were created after an extensive review of thousands of studies.

Thus, if we tend to eat the same weight of food day in and day out, it would make sense from a weight management perspective to eat foods that are lower in CD in order to (a) be satiated and (b) not overeat on calories. Given that these foods are also higher in nutrients, the quality of the diet would be improved and lead to improved health outcomes.

But does the research support this approach?

Yes, it does. Eating a low CD diet does hold promise, both as a way to lose weight and/or prevent weight gain. A 2006 cross-sectional study compared the energy density of people's diets.[59] They found that those consuming a low CD diet had a much lower caloric intake (around 425 and 275 fewer calories per day for men and women, respectively) even though they consumed more food (about 300-400 more grams per day). Those eating a low CD diet were also thinner and more likely to be in the normal weight range. As fruit and vegetable intake increased from <5 to 5-8 to >8 per day the CD of the diet went down in a stepwise fashion as did the prevalence of obesity. The lowest CD diets were high in fruits and vegetables (>8 per day) and lower in fat and averaged 550 cal.lb^{-1} and had the lowest rates of obesity.

In another study where 50,000 middle-aged women were followed for an eight year period, a lower CD diet was



associated with less weight gain.[60]

But these studies don't indicate causality. It could be that thin people are more likely to eat lower CD diets.

Several interventional long-term trials, however, indicate that lower CD diets result in greater weight loss when compared to other methods of caloric restriction. In a study of 200 overweight men and women the energy density

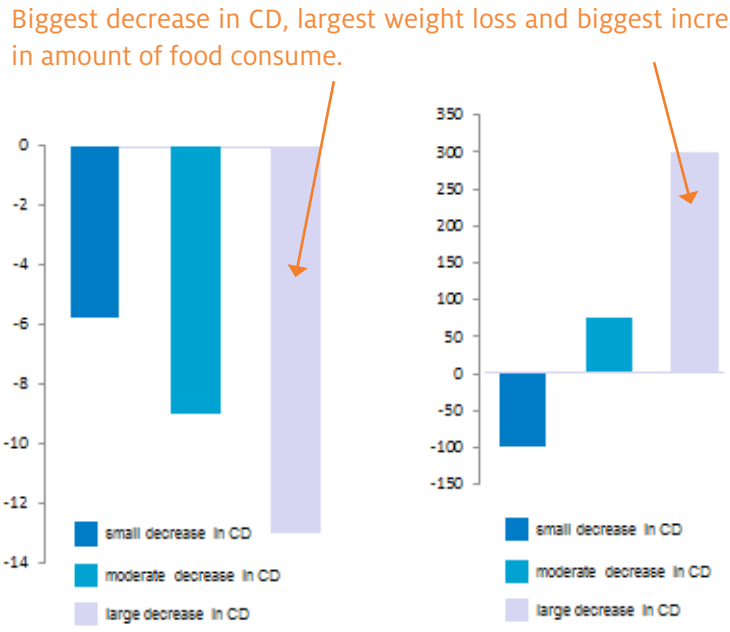
of the diet was found to be the main predictor of weight loss. Incorporating a low CD food (like vegetable soup) everyday increased the magnitude of the weight loss and helped people maintain the weight loss.[61]

In another trial of 97 obese women, one group was counseled to increase their intake of fruits and vegetables and reduce their fat intake while another group was counseled to restrict their portions. Both groups lost weight, however, after 12 months, the fruit and vegetable group had both a greater reduction in the CD (1.23 vs. 1.46 cal.g-1) of their diet and they lost more weight than the portion control group (17.4 lbs. vs. 14.1 lbs.).

Those eating the lower CD foods also reported eating 25% more food and having less hunger.[62] They also ate more total fiber. Of interest is that both groups decreased their total caloric intake by about the same amount, i.e. the increased weight loss could not be accounted for by the reduction in calories. Incidentally, both groups exercised (as measured by step counters) by about the same amount (average steps per day was 8,735 for both groups).

In another study with a large number of people, participants were classified into tertiles based on the magnitude of change in CD after six months of weight loss. Those with the largest reduction in CD lost more weight than those with only a moderate or slight reduction.[63] In addition to the weight loss, those eating the low CD diets were also shown to have improved diet quality.[64] Furthermore, those with large reductions in CD also increased the amount of food that they consumed by 300 g/day.

In a 2012, 3-month intervention study, those eating > 10 low CD foods per day (foods with a CD of less than 500 cal.



lb-1) and <2 foods that were greater than 1300 cal.lb-1 lost more weight (20 lbs.) than those restricting calories via reduced portions and fat intake (12 lbs.).[65]

Finally, another study looked at CD and weight change over a period of six years in 186 young women. What they found was that while the CD of the foods they consumed remained unchanged over the six years, body weights tended to go up. However, those eating a higher CD diet gained 2.5 times more weight (14 lbs) than those eating a lower CD diet (5.5 lbs.).[66] Those eating the lower CD diet achieved this by eating less fat and more fruits and vegetables.

Taken together, these studies show that eating a low CD diet improves weight loss outcomes, diet quality, sensations of fullness and allows for eating a higher volume of food. Now that sounds like a win, win, win to me. But what about varying the macronutrients, i.e. fat, protein and carbs?

Calorie Density and the Macronutrient Content of Foods

Intervention studies looking at CD have also manipulated the macronutrient content of the meals and found that CD is still **the most important predictor of satiety**. In one study on women aged 20-40, protein content was manipulated from low (10%) to high (30%) while the CD of the meals was kept constant. No differences in ad libitum calorie intake or ratings of fullness were observed between the low or high protein groups. The authors concluded that "When the appearance, taste, fat content, and energy density were controlled, simply adding meat to lunch and dinner entrees to increase the protein content within commonly consumed amounts was not an effective strategy to reduce daily energy intake."[67]

In another study, satiety, *ad libitum* calorie intake and appetite sensations were assessed 5h after meals with similar calorie densities and fiber, but that were either rich in protein, carbohydrate or fat. The researchers found no differences in measures of satiety following the different meals.[68] Several other studies have also found that when CD is controlled for varying the macronutrients does not significantly alter satiety or caloric intake.[68,69,70]

Preloading With Low CD Foods

Numerous studies have looked at preloading with low CD foods (like salads and soups) on subsequent *ad libitum* food intake and satiety. It works something like this. A fixed amount of food is consumed (the preload); after a short interval of time, subjects are fed a meal and the total caloric intake is measured. Satiety and ratings of fullness are also assessed.

Following a vegetable soup preload it was found that subjects reduced calorie intake at lunch by as much as 20%. Of interest is that the soups were prepared differently, i.e. as broth and vegetables served separately, as chunky vegetable soup, chunky-pureed vegetable soup, or pureed vegetable soup. All types of the soup had a similar affect in reducing subsequent intake.[72]

In another study, subjects were required to consume a first course salad, which varied in CD and in portion size on different days, followed by a main course of pasta. Compared to having no salad, a low CD salad resulted in a decrease in total energy intake at the meal; and the larger the salad the better. However, when a high CD salad was served, the total calorie intake for the meal went up 17% compared to no salad.[73] The moral of the story is to eat a large salad but to not add the cheese, chicken and heavy dressings that many of these salads come with.

Preloads with liquids such as soda, however, has been shown to have little effect on satiety and may contribute to increasing overall total calorie intake. In fact, as the consumption of soda went up, so did the total calories consumed at the meal.[74]

The question of whether calories in a liquid form affects satiety differently than in solid form is widely debated and not something I will fully review here. But one way to look at this is to use fruit, as it is high in water and but only moderately rich in fiber. For example, preloads using apples in different forms (whole apple, applesauce and apple juice with and without the fiber) have been studied. The whole apple did the best job of improving satiety and decreased total calorie intake by 15%. Applesauce decreased intake some but not as well as the apple, while the apple juice, even with added fiber, had little appreciable impact.[75]

A more recent study looked at the effect of vegetable and fruit juices on subsequent intake of a macaroni and cheese meal and found that the liquid forms of these foods did not significantly reduce hunger sensations, whereas the solid forms of these foods did. Of interest is that they tested this on both obese and lean subjects and found that obese subjects compensated less well with the liquid forms of these foods than did the lean subjects.[76]

To summarize, here are the main takeaways for successful weight loss and long-term weight maintenance:

1. Eat unlimited amounts of fruits and vegetables. Eat more beans, cooked whole grains and starchy vegetables. These help to fill you up.

2. Whenever you are hungry, eat until you are comfortably full. Don't starve or stuff yourself.

3. Start all meals with a large salad, vegetable or bean soup and/or fruit. All three at a given meal is even better.

4. Don't drink your calories. This includes alcohol, sodas and fruit juices. The only exception to this rule is if you make a green smoothie. If you do make a smoothie drink it over a period of time, don't chug it.

5. Dilute the calorie density of your meals by filling half your plate with intact whole grains, starchy vegetables and/or beans. Have the other half the plate be vegetables and/or fruit.

6. Oils are the highest in calorie density. Adding oils and fats to a meal will always raise the overall calorie density of a meal. Be careful.

7. Limit (or avoid) animal foods.

8. Limit plant foods that are higher in calorie density (breads, dried fruit, nuts) unless you have a higher metabolism and/or are exercising a lot. When you do eat these, incorporate them into meals that are made up of low calorie dense foods, i.e. like adding avocado to a salad.

Bonus Material: Does eating sugar (aka carbs) make us fat?

Recently it has become popular to demonize sugar (aka carbs) and blame it for all of our chronic health problems from obesity to heart disease to dementia to inflammation. Apart from the fact that this is a very reductionist approach to health, do the data support the view that sugar is the main culprit?

Humans are anatomically and physiological designed to seek out and eat sugar. Our brains use sugar almost exclusively as a source of energy. Our muscles preferentially burn glycogen or stored sugar during exercise, especially during short intense exercise. Other tissues like red blood cells and kidney cells can only use sugar for fuel.[77] When we eat high protein/low carb diets, we increase a process known as gluconeogenesis, or the production of sugar from amino acids, i.e. the body cranks up its glucose production. The tips of our tongue contain taste buds for sugar; it contains no taste buds for protein or fat. Consuming sugar is highly pleasurable and provides a reward to the person by producing opioid and dopamine-mediated responses which result in us experiencing pleasure.[78] This isn't necessarily a bad thing; rather it is nature's strategy for us to seek out more.

However, consumption of refined sugars heightens the intensity of that pleasure; similar to those derived from the use of narcotics. This can be intoxicating and addicting. Food manufacturers have taken advantage of this and have added highly-refined sugars to our foods leading us to over consume which of course is good for business and less good for health.[77]

As humans, we don't easily convert sugar or starches into body fat.[79] Converting sugar (or protein) into fat is known as *de novo lipogenesis*, or new fat production. Certain animals such as cows and pigs are really, really good at converting low-energy carbohydrates, like grass or grains, into body fat. However, human beings don't do this very efficiently. Under normal intakes of carbohydrates, *de novo lipogenesis* is limited, i.e. one would really have to over consume carbohydrates to gain fat.[77]

In one study, for example, both lean and obese women were overfed 50% more calories (compared to a control energy balanced diet), much of which (about 500 calories worth) came from refined sugars each day. De novo lipogenesis did occur, but the amount converted to fat was rather small. In this situation, the women produced less than 4 grams (or 36 calories) of fat per day from the extra sugars.[80] Thus in order to gain a pound of fat, they would have to be overfed by this amount for nearly 4 months.

In another study where subjects were fed large amounts of carbohydrate for 3 days, they found that de novo lipogenesis did not contribute to increasing body fat stores when up to 500g of carbohydrate were consumed. The authors concluded that it is only under conditions of 'massive' (their term) consumption of carbohydrate that fat synthesis starts to occur.[81] Part of the reason for this is that most of the consumed carbs are initially used to replenish liver and muscle glycogen stores. Additionally, when we increase our consumption of carbs, we also increase our oxidation rate (i.e. burning rate) of glucose.[82] In the latter study, subjects were fed a total of almost 1400 g of carbohydrate during the 96 hr trial and they oxidized (or burned) almost 1300 g. Of the 512 calories of fat ingested, 233g or about half, was oxidized. We are actually pretty good at compensating for the extra carbohydrate calories and less good at compensating for extra fat calories.

These were short-term studies, however, performed on a small number of people (they have to live in a metabolic chamber so for practical reasons it is hard to do this on large numbers of subjects). But these, as well as other studies, do demonstrate that the common belief that sugars are immediately converted to fat is only partially correct.
So, to answer the question, overeating calories of anything can result in fat gain, but eating fat does this more efficiently than eating carb calories. Dietary fat is easily converted to body fat, sugar less so. As Dr. McDougall likes to say, "*The fat you eat is the fat you wear.*" The biggest problem with sugar and high carb foods is that they are guilty by association. They most often come packaged with fat and little to no fiber.

Think about all those high carb foods you like to eat, most come with a nice amount of fat. Ice cream, cakes, cookies, pizza, desserts, donuts, candies or pastries are often high in both sugar and fat. It isn't too often, for example, that I see people eating plain bread. Thus, when people give up 'carbs' they are giving up a lot of these high-fat, CD foods and so health outcomes are often improved as a result.

This is not to say that sugar is blameless when it comes to health problems. It is devoid of nutrients and can be addicting. Simple sugars can increase blood glucose and consequently insulin levels. This in turn results in postprandial hypoglycemia (low blood sugar post ingestion) which results in increased hunger. Thus over the long-term high intakes of refined carbs and sugar may drive overeating and subsequent weight gain. In certain susceptible individuals it can also drive up triglyceride levels. High fructose corn syrup in particular can be harmful to health and promote weight gain as it metabolized differently than pure sugar.

In our natural environment sugars came from plant starches such as fruit, sweet potatoes, rice and other grains, and root vegetables. These sources of sugars are nicely packaged with fiber, nutrients and water. But when I tell people to eat more potatoes or fruit they are often concerned about "all that sugar".

To put this to the test, researchers put people on a 2-week diet which included about 20 servings of fruit a day (yeah, that's a lot). Caloric intake was such that weight was maintained. No adverse effects, like increases in triglycerides or blood glucose levels, were observed. Compared with an isocaloric low-fat diet, the fruit diet resulted in the greatest drop in LDL cholesterol (33%) and the greatest fecal output ever reported in a dietary intervention (that is a good thing).[83] As the saying goes, we need to eat like a bird and poop like an elephant.

So why do people sometimes lose weight when they switch to a low-carb, high protein diet? There are a number of reasons for this. As mentioned, carbohydrates are stored in the muscles and liver as glycogen. Glycogen holds on to 2-4 times its weight in water.[84] Thus under conditions of low carb intake, our glycogen stores quickly become depleted and much of that water is shed (up to a gallon in some people). High protein diets, particularly high meat protein diets, are quite acidic and have a strong diuretic effect. All this water weight precipitates quick and early weight loss and encourages dieters to continue the diet. As soon as they eat carbs again, glycogen is replenished, water is retained and up goes the weight. Now, over longer periods of time, a low-carb diet can result in some fat

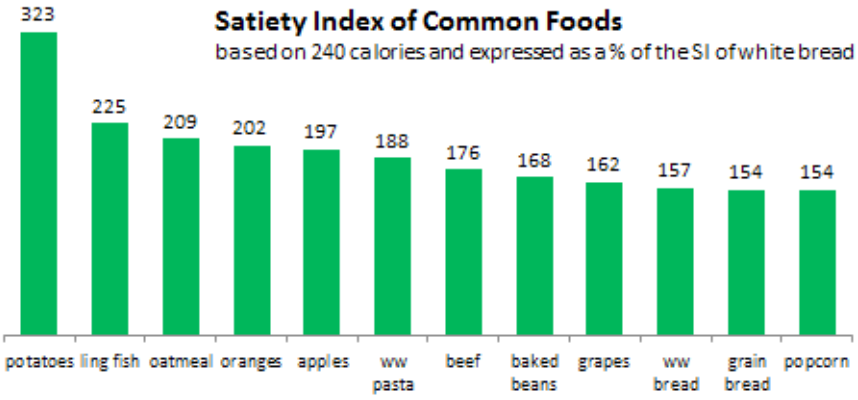
loss in addition to the water lost. However, these diets can be hard to maintain over the long-term and are risky, i.e. they can increase one's risk for a number of chronic diseases.[85,86]

Unless of course you are eating a low-carb diet that is high in **plant protein** but not animal protein.
Researchers from Harvard followed over a 100,000 people for 20-26 years (26 years for women and 20 years for men). They then looked at overall mortality in those eating an animal-based, low-carb diet, versus those eating a plant-based, low-carb diet. The animal-based low-carb diet was associated with increased risk of all-cause mortality, increased risk of cardiovascular mortality and increased risk of certain cancers. The plant-based low-carb diet was associated with reduced risk of all-cause mortality and heart and cancer deaths.[87]

To be clear I am not advocating a high-protein diet but as it turns out, the type of protein is important when it comes to our health.

The Satiety Index (SI)

Satiety is obviously quite complex and other factors can come into play. Another way to assess it is to have people eat a fixed number of calories of different foods and see which ones result in increased feelings of fullness as well as decreases in subsequent eating. A group of researchers did this for 38 common foods where 240 calories of each food was consumed.[88] They then expressed these as a percentage of the SI of white bread. Thus white bread scored 100 and foods that had greater satiety were some percentage greater than 100 and those with lower satiety scored some percentage less than 100. Of interest is that the food that scored the highest (by a lot) was potato (323 %). Of the tested foods, croissants scored the lowest (47%). Except for potatoes, they didn't include other vegetables in the test foods, likely because it would be difficult to eat 240 calories worth of say, kale in one sitting. Only two fruits were included (grapes and bananas) so it would be interesting to expand the list. Incidentally, foods with the



lowest satiety scores were found to be the fat-rich foods.

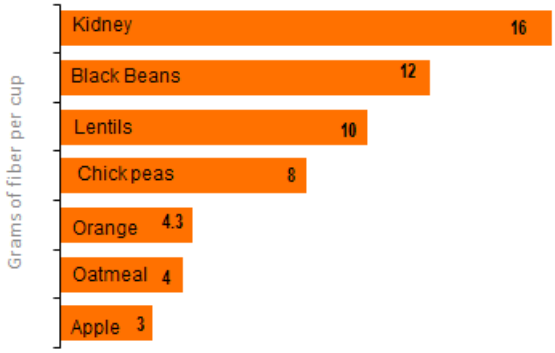
The most calorie dense food is fat. Vegetable oils, coconut oil, or olive oil are the most energy dense foods on the planet. They weigh in at 4,000 calories per pound. Yes, make no mistake, these are processed foods. The fiber, water and most of the nutrients have been removed and you end up with a very concentrated source of calories. And, contrary to popular belief, they are not health foods. Extracting the oil from olives or fat from coconuts is no different than extracting the sugar from sugar cane except you end up with a whole lot more calories per weight of food (pure sugar is 1800 calories/pound). From a CD perspective it is probably better to put sugar on your salad than oil. Actually, nuts and/or nut based dressings are best, but more on nuts later.

Thus, the best way to reduce your calorie density, increase satiety and increase your fiber intake is to strive to eat

eight or more servings of fruits and vegetables a day, along with a couple servings of beans, whole cooked grains and to reduce your intake of processed oils, meats and cheese.

Below is an example of what to eat to achieve 50+ grams per day of fiber.

1 cup black beans	**12**
2 cups brown rice	**8**
1 cup oatmeal	**4**
1/2 avocado	**3**
4 servings of fruit	**16**
2 cups of veggies	**16**
TOTAL g fiber	**59**



Mechanisms of Satiety: Hormones and Other Regulators of Energy Balance

A variety of hormones are released in response to food intake which signals satiety. These include cholecystokinin (Cck), glucagon-like peptide (GLP-1), ghrelin, insulin, and leptin. These are known as peripheral mediators as they are produced from various organs in the body, get into the blood stream providing feedback to the brain. There are other signaling molecules that are produced in the brain as neuropeptides; however, a discussion of these is beyond the scope of this paper.

Hedonistic and Homeostatic Drives

Homeostatic drives, or drives that seek to maintain calorie homeostasis, act in the short- or long-term to help induce satiety and maintain body weight. Higher concentrations of these hormones (with the exception of ghrelin) help to induce satiety to a greater or lesser extent. These homeostatic mechanisms of appetite regulation can be overridden by what is termed the hedonistic drives or reward pathways. Hedonistic drives occur when foods which are highly palatable and pleasurable are consumed and override homeostatic cues.[89] The foods that provide the most amount of pleasure tend to be foods with a high caloric density (as far as I know, no one drives to the mini-mart at midnight to get their salad fix).

The Brain and Homeostatic Drives

The drives to eat or the signals to stop eating are quite complex involving communication between the hypothalamus (brain), our gastrointestinal organs (like the stomach, pancreas and intestines) and fat tissue. Satiation or the process that causes one to stop eating may be initiated by neural input from the stretch receptors in the stomach to the brain signaling distension after food consumption. This is quickly followed by the release of various hormones and neuropeptides. They signal satiation and satiety either via the vagus nerve (which connects the gut to the brain) or via blood perfusing the hypothalamus.[90]

As mentioned, our signals to eat or stop eating primarily come from the brain. Insulin, produced in the pancreas binds to receptors in the hypothalamus. Binding to these receptors helps to induce satiation. It is believed that insulin resistance, as found in type 2 diabetics, is also mirrored in the brain which indicates an intriguing parallel between diabetes and obesity. Leptin, produced primarily by adipose tissues, also binds to receptors in the hypothalamus

signaling a reduction in food intake. Overweight and obese people are not leptin deficient, but they can be leptin resistant. **Cck** is released into the blood stream from intestinal cells and binds to receptors on the vagus nerve and helps to terminate feeding. A form of Cck is also produced in the brain. Finally, **ghrelin** is mainly released from the stomach, and binds to receptors on the pituitary gland and the hypothalamus.[91] Ghrelin tends to peak prior to eating and has appetite-stimulating properties and is the only gut hormone known to enhance appetite.

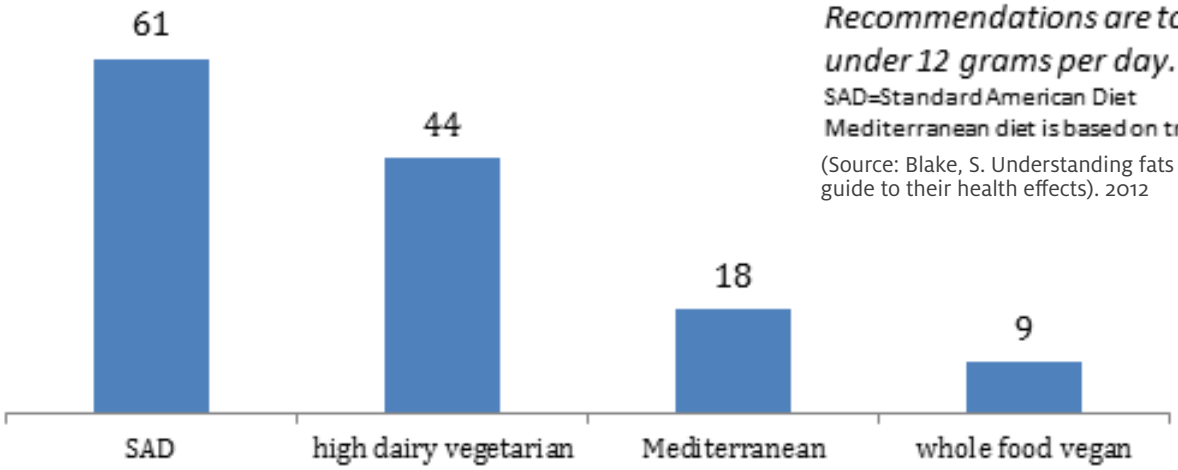
But here is where it gets interesting.

Our diet can profoundly affect the ability of our brains to provide good feedback, and thus our ability to regulate energy balance. Studies show that high-fat feeding (and especially high saturated fat feeding) induces the expression of several pro-inflammatory cytokines (like TNF and IL-6) and proteins (such as SOCS3 and IKK) in the hypothalamus, contributing to insulin and leptin resistance in the brain and thus an inhibition of peripheral feedback to the brain to stop eating.[92,93,94] An additional outcome of this inflammation is that it induces apoptosis, or cell death, of hypothalamic neurons.[95] Of further interest is that this inflammation is not the result of obesity, but rather occurs prior to weight gain.[96] In fact, animal studies show that within 24 hours of eating fat, markers of hypothalamic inflammation are elevated and within a week, markers of neuron injury also become evident. Of further concern is that recent studies have shown that insulin and leptin resistance in the brain regions may relate to neurological disorders, such as Alzheimer's and depression.[97,98]

To summarize, high fat diets, and especially diets high in saturated fats, damage and inhibit those parts of the brain that are involved in telling us when to stop eating. High fat consumption hurts us when it comes to our homeostatic mechanisms of energy regulation.

	Saturated Fat
1.	Cheese
2.	Dairy desserts (ice cream)
3.	Pizza
4.	Chicken and mixed dishes
5.	Desserts (cakes, cookies, donuts)
6.	Sausage, franks, bacon, ribs
7.	Reduced fat milk
8.	Burgers
9.	Mexican dishes
10.	Pasta dishes

Table 1. Top sources of saturated fat and in the US diet.
NHANES Survey 2005-2006



Grams per day of saturated fat intake in various eating patterns. *Recommendations are to keep intake under 12 grams per day.*
SAD=Standard American Diet
Mediterranean diet is based on traditional diet.
(Source: Blake, S. Understanding fats and oils: A scientific guide to their health effects). 2012

Mechanisms of Satiety: Exercise?

Many studies have shown that caloric intake does not increase acutely following exercise. One review found that only 19% of interventional studies (using a buffet, *ad libitum* approach) reported an increase in caloric intake, 65% showed no change and 16% showed a slight decrease in calorie intake following exercise.[99] Of correlational studies, half showed no relationship between energy expenditure and intake. Thus there is only a loose coupling of energy expenditure to increased appetite. Vigorous exercise, however, is more likely to lead to a temporary suppression of appetite than moderate exercise and this has been termed 'exercise-induced-anorexia'.[100]

A number of studies have examined the effect of exercise on gut hormones that are involved in appetite suppression. Plasma PYY (PYY is a hormone that has strong appetite-suppressing effects) has been shown to increase following exercise in both lean and obese subjects and to remain elevated for up to 5 h after exercise. Other gut hormones that suppress appetite (like GLP-1) have also been shown to increase following aerobic exercise.[101]

However, the bad news is that most of these effects have been primarily observed in men. A limited number of studies have looked at women and found that there are possible gender differences in these responses. For example, in one study, leptin concentrations in women were lowered after 12 weeks of training but weren't in men.[102] Thus for some women, exercise may serve to stimulate appetite and could explain why it is easier for men to lose weight via exercise then it is for women. Of course this does not mean that women should stop exercising for fear that it will make them eat more. This is still a limited area of study and, as will be discussed later, exercise does play an important role in weight management.
The data are also quite mixed and the results inconsistent when looking at responses to long-term exercise training. What the evidence suggests thus far is that increased physical activity causes at best

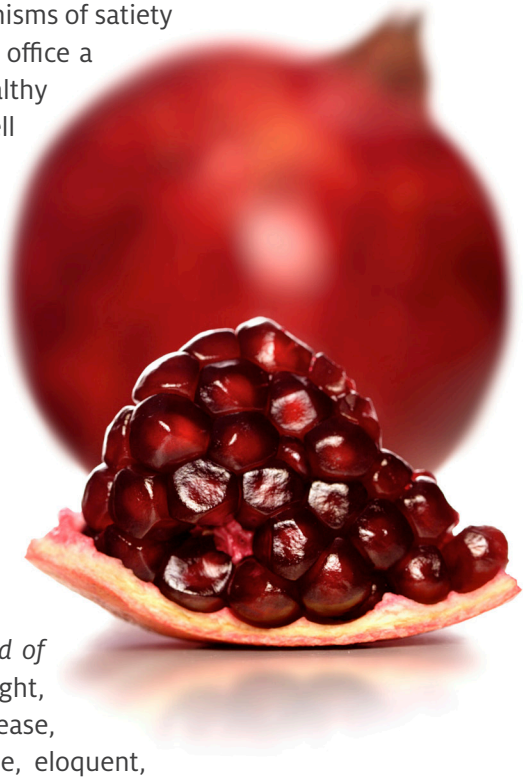
only a partial increase in caloric intake, i.e. we don't always fully compensate. Thus concerns that exercise might cause overeating are somewhat unfounded. However, the bad news is that when exercise is stopped or reduced, this is not accompanied by a reduction in caloric intake.[103] This is why exercising consistently is so important.

The Regulated Zone

Mayer and colleagues proposed that regulation of energy balance is very difficult to attain at low levels of energy 'throughput' (i.e. low energy expenditure), as is typical of most people living in urbanized cultures. Energy balance is easier to achieve at a high rate of energy expenditure or energy flux. Mayer observed that energy intake was better matched to energy expenditure when people are very physically active.[104] While his studies were cross-sectional in nature, studies on rats showed that energy regulation was poor at either very low levels of physical activity or when the rats were exercised to exhaustion. [105,106] Thus it appears that our physiology is better at caloric regulation when physical activity levels are high (called the regulated zone). Being in the regulated zone would thus mean having better sensitivity for matching energy intake to expenditure and living in the unregulated zone would mean being at much greater risk of positive caloric intake and weight gain. Mayer further hypothesized that there may be a minimum threshold of either physical activity or throughput above which expenditure and intake are more sensitive to changes in the other.[107]

Environment

Environmental conditions can also affect food intake. Exercising in hot and humid environments may suppress appetite, while exercising in the cold or in cold water, may stimulate it. Altitude, and especially exercise at high altitude, can also suppress appetite—unless you are chronically habituated to it.[108] Your food environment can also play a powerful role; food type and availability can override mechanisms of satiety or support them. Create a safe food environment at home and make your office a junk-free zone. The people that you socialize with (are they exercisers, healthy eaters?) can play a role. Pay attention to your network. If your friends eat well and exercise, that increases the odds that you will as well.



The take-home message in all of this is that exercise can contribute to weight loss and energy management, especially if accompanied by a low-fat calorie dilute diet. Exercisers who failed to lose weight, for example, had reduced their intake of fruits and vegetables.[109] Including some bouts of vigorous exercise may also be helpful as well as increasing your overall energy throughput. Additionally, exercising consistently is of primary importance (for lots of reasons).

Mechanisms of Satiety: The Possible Role of Nutrient Density

Dr Joel Fuhrman, author of the best selling books *Eat to Live* and *The End of Dieting*, uses the concept of nutrient density to help his patients lose weight, improve health and reverse many chronic illnesses, including heart disease, autoimmune and inflammatory diseases. The concept is relatively simple, eloquent, intuitively makes sense and is in fact, quite brilliant. A diet that is nutrient dense means optimizing micronutrient intake relative to the caloric intake. Micronutrients include vitamins, minerals, phytonutrients and antioxidants—of which there are thousands (estimates range are 10,000 to 100,000 micronutrients).

The macronutrients; fats, proteins and carbohydrates, comprise the calorie components of food. It is no wonder then that many weight loss diets are so laser focused on trying to manipulate the macronutrient component of the diet. There is still a prevailing belief that there is some magic combination of these three that will prove to be the dietary elixir of weight loss. Unfortunately this is completely misguided and overly simplistic. Carbohydrates come in a vast array of types and composition. Blackberries and black jelly beans, both high in carbs, are not the same foods. Additionally, whole plant-foods are never completely one or the other (even fruit and potatoes have some protein).

This is also a very reductionist approach to nutrition. Reductionism is when we eat foods based on isolated nutrient content, e.g. we drink milk for calcium, fish for omega-3s, or meat for protein, forgetting that there is a whole package that comes along for the ride. Thus we tend to classify foods according to a macronutrient label. Therefore chicken is a "protein", while fruits, grains and root vegetables are "carbs". But as Dr. Fuhrman says, it is far better to consider the nutrient content of food, i.e. we need to eat nutrient dense protein, nutrient dense fat and nutrient dense carbohydrate foods. It is how these macronutrients are packaged that is important.

Another way to think if it is this: if you eat 2,000 calories per day, you are better off getting more nutrients for those calories as opposed to eating 2,000 nutrient poor calories. The typical western diet is high in calories and low in nutrients. We are in a very real sense, overfed and undernourished.

The most nutrient dense foods in order are: leafy greens, vegetables, berries, other fruits, root vegetables, whole grains, tofu, beans, and seeds. Those with low nutrient density scores are processed foods, meats, dairy, sodas and alcoholic drinks.[110]

Nutrient Density

Source: Fuhrman, Nutrarian Handbook, 2012

Kale	1000	Tofu	86	Low fat yogurt	28
Collards	1000	Sweet Potato	83	Chicken Breast	24
Bok Choy	824	Apple	76	Eggs	27
Chinese Cabbage	704	Peaches	73	Lean turkey	26
Spinach	739	Green Peas	70	Low fat milk	23
Cabbage	481	Cherries	68	Ground beef	20
Red Pepper	420	Lentils	68	French Bread	18*
Romaine	389	Fava beans	61	Fruit yogurt	16
Carrots (ck)	336	Mango	51	Swiss cheese	15
Green Peppers	310	Cucumber	50	Fries	12
Artichoke	244	Oatmeal	55	Olive Oil	10
Asparagus	234	Red Potato	43	Ice Cream	9
Strawberries	212	Brown Rice	41	Cola	1
Tomato(ck)	190	Salmon	39		
Blueberries	130	Avocado	37	*Artificially inflated score due to fortification with vitamins and minerals	
Iceburg Lettuce	110	White potato	31		
Orange	109	WW bread	30		
Cantaloupe	100	Walnuts	30	ck = cooked	

But while this makes sense for better health, what does it have to do with weight loss?

While it is not the strongest factor, research suggests eating more nutrient dense foods can play a role in satiety and weight loss.

In a study by Dr. Fuhrman, participants who had switched to a nutrient dense way of eating were asked about their sensations of hunger (emotional, physical and location) and how these compared to their previous way of eating. Most reported a big shift in how they experienced hunger. For example, hunger was less unpleasant on the nutrient dense diet, even when meals were skipped. Frequency of hunger pains was dramatically reduced, and most reported being less irritable when they were hungry. The authors concluded that "*...it is not simply the caloric content, but more importantly, the micronutrient density of a diet that influences the experience of hunger. It appears that a high nutrient density diet, after an initial phase of adjustment during which a person experiences 'toxic hunger' due to withdrawal from pro-inflammatory foods, can result in a sustainable eating pattern that leads to weight loss and improved health.*"[111]

While this study was exploratory in nature and needs to be replicated, I think it has some merit. Certainly, many of his patients have not only experienced dramatic weight loss, but also the reversal of many chronic diseases. In a retrospective study of his patients, the average weight loss of 33 patients was 31 pounds after one year. Of the 19 patients who were tracked after two years, the mean weight loss was 53 pounds.[112] This is almost unheard of in weight loss studies. Certainly, it is likely patients lost weight in large part because switching to a nutrient dense diet also dramatically lowered the CD of the diet. But the idea that more nutrients could help with weight loss is intriguing. One mechanism could be that higher intakes of polyphenol rich foods (like fruits and vegetables) help to create more bacteria in the gut that are less thrifty, i.e. are less capable of harvesting energy from the food and more calories are pooped down the toilet; but more on that later.

In a double blind study, overweight individuals were randomly assigned to drink two cups of grape flavored drink or two cups of Concord grape juice. Both drinks had the same number of calories and were matched for flavor and smell. The study was blinded, so presumably the subjects didn't know whether they were drinking the fake juice or the real thing. After 12 weeks, those drinking the grape juice did not gain weight (in spite of an extra 173 calories per day) while those drinking the fake juice did gain weight (about 3 lbs. on average). Those drinking the grape juice also saw reductions in their waist circumference while those drinking the sugar drink reported feeling less satiated.[113]

The authors suggested that the flavonoids, found in abundance in grapes and grape juice, helps with weight control as they have been shown to increase thermogenesis (the heat lost through digestion of food) and to increase fat oxidation. This has also been shown to be true for tea extracts.[114] Flavonoids may also affect energy balance by reducing glucose and fat absorption via **inhibition** of GI enzymes involved in nutrient digestion. This theory was supported by evidence of increased fecal lipid excretion, i.e. less of the fat from foods was absorbed and more was pooped out.[115] (For the record, I do recommend that you eat the grapes rather than the grape juice but for obvious reasons it is easier to do a blinded study with juice).

What are these GI enzymes?

Orlistat is the only anti-obesity drug that has been approved for use in Europe. It acts by inhibiting pancreatic lipase (PL), a key enzyme involved in the digestion of fat. Use of this drug has been shown to enhance weight

loss of energy restricted diets. It also helps to reduce intra-abdominal fat and has been shown to modify risk of obesity-related comorbidities like hypertension.[116] While its effects are small, they are significant. However, there are unpleasant side effects associated with this drug, including bloating, oily spotting, fecal urgency and incontinence. The good news is that certain plants have been identified as containing PL inhibitors yet without the side effects of the drugs. These include pistachios, cabbage, radish, cinnamon, lemon thyme, potato, yam, oats and other cereals, lime, berries, ginseng, beans, mango, black and green tea, tomato, kiwi, apple and oregano (to name a few).[117]

While clinical trials need to study the efficacy of these foods for weight loss, some have undergone extensive study. Green tea, for example, has been extensively studied and found to aid in weight loss. Green tea extracts have been shown to increase thermogenesis and to inhibit PL and has been shown to aid weight loss in obese subjects.[118]

Nut Consumption and Weight: A Paradox?

Nuts are a CD food. Chestnuts are lowest coming in at 900 cal.lb^{-1} while macadamia nuts are highest coming in at around 3100 cal.lb^{-1}. That is a lot of calories for not much food. Yet, in spite of this they haven't been shown to promote weight gain, at least not when eaten in moderate amounts. In cross-sectional studies, nut consumption is associated with less weight gain over long periods of time and consumption of nuts, especially walnuts, has been associated with lower diabetes risk.[119]

In another isocaloric intervention, subjects were fed roasted peanuts or candy to the tune of 20 cal.kg^{-1} of body weight in extra calories per day. Dietary analysis showed that both groups significantly increased their caloric intake by about the same amount. After two weeks, body weight and waist circumference increased in the candy group but not in the peanut group. Basal metabolic rate also increased in the peanut group, but not in the candy group.[120] Other studies on nuts have also shown that increased caloric intake from nuts does not result in the weight gain one would expect from the increased calories.[121] (Note: technically peanuts are a legume, but are similar to nuts in terms of their CD).

Nut consumption in both short and long-term studies has consistently proven to not promote excessive weight gain in spite of the extra calories ingested. One paper which reviewed clinical trials on nuts, found that most studies reported no effect of nut consumption on body weight[122], while three of these studies reported weight loss over the study period with nut consumption. Mechanistic studies indicate that nuts have a high satiety and low metabolizable energy (i.e. inefficient calorie absorption). Nuts may also elevate resting energy expenditure and increased heat lost. Additionally weight loss regimens that include nuts indicate improved compliance and greater weight loss when nuts are permitted.[123]

Nut consumption has also been associated with a longer life span (after controlling for other factors).[124] And it is not just because those who eat nuts might eat less meat as vegetarians who consume nuts have reduced risk and better health outcomes compared to those who don't eat nuts.[125] Walnuts, in particular, are one of the healthiest nuts there are, and have been shown to improve endothelial function and to lower blood pressure.[126]

In conclusion, both nuts and seeds are quite nutritious and are associated with numerous beneficial health outcomes. Both nuts and seeds (note seeds are more nutrient dense than nuts) can thus be integrated into ones diet; albeit in small to moderate amounts. Notice that the studies don't suggest that unlimited nut consumption will promote weight loss, they simply show that there is less or no weight gain for some amount of calories from nuts. Given that our nuts are shelled for us, it is pretty easy to eat them by the handful and subsequently ingest more calories than

we can easily compensate for. Think back to the days when you had to crack and shell the nuts yourself, it took a bit more work. Thus for those trying to lose weight the recommendation is to limit nut intake to one to two handfuls a day. Nut butters, like peanut or almond butter, can also be consumed as long as intake is limited. For those trying to gain weight or who struggle to maintain weight, nuts can be an easy way to increase caloric intake and can thus be eaten more liberally.

Other Foods that May Promote Weight Gain: Why chicken and fish are not vegetables

Chicken: obesity promoting?

One of the questions we ask our executive participants is "what are the healthy aspects of your diet?" What surprises me (and maybe it shouldn't) is how often people will include eating chicken as being healthy. Since when did chicken become a health food? I think we can all agree that vegetables are healthy, but chicken? It contains few antioxidants to speak of (iceberg lettuce, a nutrient poor food, has 3x the antioxidants), no fiber (a nutrient that 97% of Americans are deficient in) and provides no vitamins of note. More concerning is that chicken consumption has increased 204% over the last few decades while vegetable consumption has declined. In the US we eat about 10 billion chickens per year--that is a lot of chickens. Not only is chicken a nutrient poor food, it can also be harmful to our health, especially when eaten to the degree that we do in western countries.

But can chicken consumption lead to weight gain or loss?

The Netherlands Cohort Study collected data on 5,000 elderly individuals for 14 years and examined the association between intakes of various types of meat and subsequent changes to BMI. Meat consumption was higher for men (no surprise there), but chicken consumption was similar for both men and women. The major finding of the study was that increased chicken consumption was strongly associated with weight gain in both sexes.[127]

In another prospective study, poultry consumption was most closely tied to increases in waist circumference in women but not men.[128]

And finally data from close to 90,000 men and women across five European countries showed that higher intakes of animal but not plant protein was associated with subsequent weight gain for both men and women. The strongest association was for chicken, then red and processed meats, followed by fish and dairy products.[129] Chicken in fact was associated with 40% more weight gain compared to red meat.

Now there are obvious limitations to these studies. They don't show causality and dietary surveys are notoriously unreliable. It is also difficult to adjust for all the confounding factors. However, there are some possible reasons as to why poultry consumption could promote weight gain.

1. Chicken is NOT a lean meat

We are often told to eat more "lean meat" of which chicken is considered to be--or is it? Contrary to popular belief it is not. This is in part because chickens aren't free to roam (even grass fed chickens have very limited roaming space) but it is mostly because they have been selectively bred to be obese. A study from the UK compared chickens for their fat and protein content over the years. In 1896 the fat content of chicken was 1.8 g per 100 grams. In 2004 it was 23.2 g per 100 g (17 g for grass-fed), that is over a 10-fold increase (see table).[130] And while skinless chicken does have slightly lower levels of saturated fat than red meat, it does have similar levels of cholesterol to beef.

year	Fat g/100g	Protein g/100 g	Kcal per 100 g
1896	1.8	22.8	107
1940	10.37	26.2	198
1953	12.6	20.2	194
2002	16.9	20.9	236
2004 (organic)	17.1	18.2	227
2004	23.2	16.1	273

2. An Obesity Promoting Virus?

But another potential explanation is that most chickens are now infected with an adenovirus, a virus which promotes obesity. Birds infected with this virus have been shown to gain 50% more abdominal fat than uninfected birds in spite of eating the same amount of food.[131] This virus is easily transmitted in crowded chicken pens via nasal, oral and fecal means. Researchers started looking to see if this virus had been transmitted to humans. What they found was that one in five were infected and those who were infected were, on average, 33 pounds heavier than those who tested negative.[132]

Of recent interest to researchers is adenovirus-36 (Ad-36). With the exception of two studies, multiple studies from the US, Italy and South Korea have reported a significant association of Ad-36 infection with obesity in children and adults.[133] In human twin studies, results have shown that those twins who test positive for the virus were fatter than their twin who tested negative.[134] A 2013 longitudinal study which followed 1,400 Hispanic men and women for 10 years found that those infected (14.5%) had greater obesity at the beginning of the study as well as increased obesity in the follow up period.[135] Animal studies unequivocally show that this virus induces fat accumulation. Paradoxically, infection with this virus is also associated with lower blood lipid levels and improved glycemic control, in spite of the increased weight.[136]

Scientists think that this virus (or family of viruses) does its dirty work by increasing the number of fat cells (by mobilizing fat stem cells) and by increasing uptake of fat into fat cells. Thus, those infected, are more likely to put on fat for the same caloric intake.[137]

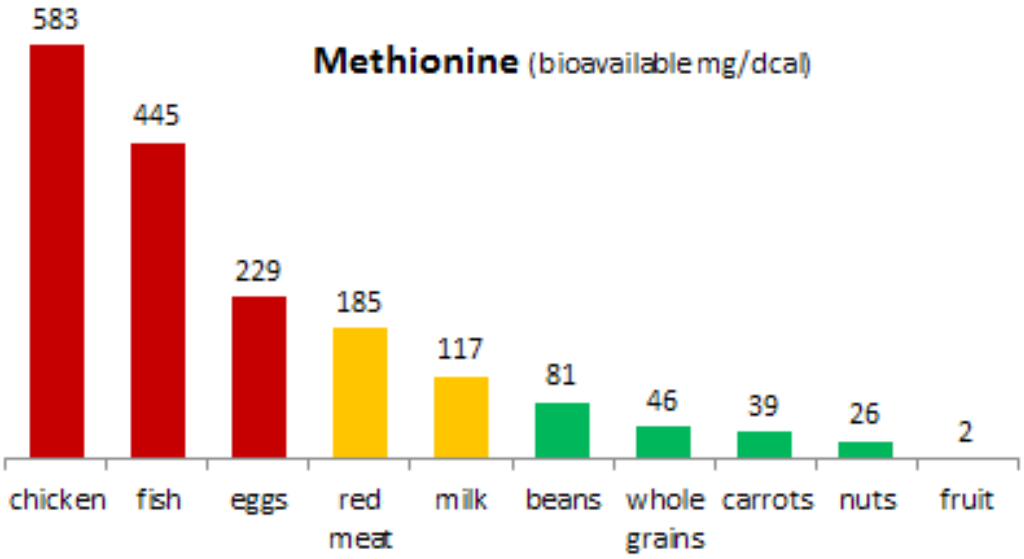
However, it is still unclear as to the causative role these viruses may play in the development of human obesity. According to Dr. Dhurandhar, a leading researcher in the area, "... additional evidence is required... and the question of whether Ad-36 contributes to human obesity has remained incompletely answered." Part of the difficulty is that, for ethical reasons, you can't knowingly infect humans with the virus while infecting a matched group with a placebo virus and then watch and see what happens. Then again, that level of evidence was never attained for cigarette smoking. Either way, these data are provocative.[138]

3. Other Concerns with Poultry

Contamination: Regardless of whether poultry (chicken and/or turkey) promotes obesity, it is most definitely NOT a health food. It is one of the dirtiest meats and the presence of salmonella and e-coli in chicken, an indicator of fecal contamination, is common; over 80% of poultry in the US from 2003 to 2008 tested positive, for example.[139] Two-thirds of beef, by comparison, were positive. In another study using laser imaging, fecal residue was found in 90% of chicken carcasses.[140] How does it get there? When chickens are gutted in the slaughter house, the digestive tract is ruptured and intestinal contents are spilled out. Thus, even organic chicken is not immune.

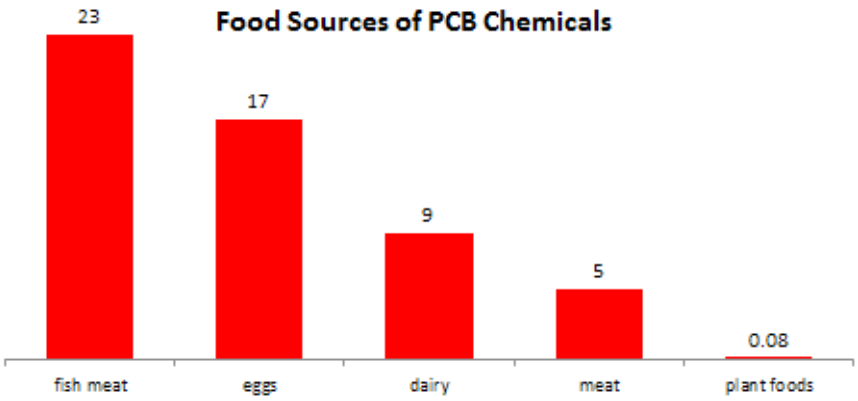
Arsenic: Arsenic, a known carcinogen, is also fed to poultry; it helps to control parasites and gives the meat that nice pink color. Sampling of chickens has found that nearly three-quarters of raw chicken breasts, thighs and livers from conventional producers tested, carried detectable levels of arsenic. Of certified organic or other premium chicken parts tested, about one-third had detectable levels.[141] Arsenic can also contribute to heart disease, diabetes and mental decline. No amount is deemed safe. (Rice is also often contaminated because of this practice of feeding it to chickens. It gets into the environment as run off from the chicken farms and rice is particularly adept at absorbing arsenic).

Methionine: Chicken meat is also very high in the amino acid methionine (plant proteins are quite low). Some types of cancer, including tumors of the colon, breast, ovary, and prostate, have what scientists call an absolute methionine dependency.[142,143] Indeed, several animal studies utilizing a methionine restricted diet have reported inhibition of cancer growth and extension of life-span.[144] The authors of this review concluded that "In humans, vegan diets, which can be low in methionine, may prove to be a useful nutritional strategy in cancer growth control." Methionine also has a pro-oxidant effect, i.e. it promotes formation of free radicals.[145] Oxidation or free radical formation is implicated in accelerating the aging process.



Heterocyclic Amines (HCAs): Because we need to cook chickens at high temperatures (i.e. due to above mentioned e-coli and salmonella contamination) cooked chicken meat has some of the highest levels of HCAs and polycyclic aromatic hydrocarbons (PAH).[146] These are potent carcinogens and are produced when muscle meats such as beef, pork, fish or chicken are cooked at high temperatures (although chicken is unique in that the temperature doesn't have to be that high in order for these to form).[147] High consumption of these meats, especially when grilled, is associated with increased risk of aggressive prostate cancer,[148,149] as well as other cancers.[150]

Advanced Glycation Endpoints (AGEs): Finally, as discussed in the brain paper, grilled, broiled, fried and barbequed chicken are among the highest dietary sources of AGEs.[151] These are implicated as playing a causal role in Alzheimer's disease and in promoting inflammation and oxidation.[152]



Thus, when it comes to our health, there are a lot of good reasons to not eat chicken besides its association with increased weight gain.

Fish and Obesogens

In addition to chicken, executives often include fish as being a healthy aspect of their diet. Unfortunately, similar to chicken, fish is not a health food. It has more cholesterol than beef or chicken (except for salmon, which is only a tiny bit lower) and fish is high in saturated fat.

Fish are also packed with persistent organic pollutants (POPs) like DDT, PCBs, dioxins, and methyl mercury, to name a few. These are endocrine-disrupting chemicals that might predispose us to obesity. Scientists think that consumption of these POPs leads to adipocyte differentiation (or increased fat cell formation).[153] Hence they are described as obesogens.

According to one review, "Consumption of food is considered as the major source of non-occupational exposure to

PCDD/Fs with foodstuffs from animal origin accounting for more than 90% of the human body burden."[154] Fish is the worst culprit, however.[155] According to one Finnish study, fish had by far the highest levels when compared to other foods.[156] In another study, organic and regular farmed fish were found to have the highest levels (this is most often what is served in restaurants) however; even wild caught fish can have significant amounts as well.[157] Finally, in one of the largest studies to date, which tested over 11,000 food samples from 18 countries, the highest mean contamination level of non-dioxin like PCBs was observed in fish and fish derived products, followed by eggs, milk and meat. Plant foods were the lowest.[158]

Yes, fish does have DHA and EPA omega-3 fatty acids, but these come packaged with a host of unhealthy chemicals and fats. People who are struggling to lose weight yet who are trying to eat healthy will often, and rightly so, choose fish over red meat. Yet, if one eats fish 2-3 times per week, over the course of a year that adds up to ingesting a lot of 'obesegens'. In light of these data, it could very well be that all that their 'healthy' fish consumption is only serving to sabotage their weight loss efforts.

Soy: A good substitute?

One way to transition away from chicken or meat is to include soy (or wheat) based meat substitutes. Many of the fears around soy consumption touted on the internet are misleading and unscientific. Whole soy foods are nutritious and are associated with reduced risk of breast cancer and recurrent breast cancer as well as other health benefits (which we don't have time to explore here). [159,160]

Additionally, according to a review paper, "an increasing body of evidence suggests that soy protein and its isoflavones may have a beneficial role in obesity. Several nutritional intervention studies in animals and humans indicate that consumption of soy protein reduces body weight and fat mass in addition to lowering plasma cholesterol and triglycerides. In animal models of obesity, soy protein ingestion limits or reduces body fat accumulation." One mechanism is that genistein, a soy isoflavone, inhibits fat accumulation in cells and increases lipolysis (or fat breakdown) in a dose dependent manner.[162] In one study on postmenopausal women, daily soy supplementation (administered in a double blind manner) resulted in a reduction in subcutaneous and total abdominal fat compared to an isocaloric casein (cow's protein) supplementation, i.e. for the same caloric intake cow's protein increased abdominal fat, while soy reduced it.[163] While the fat loss effects are small, substituting soy milk for cow's milk or soy meat for regular can be helpful. But meat substitutes should also be the side dish or condiment and not the main meal. Whole soy foods, like tofu, tempeh or edamame are best.

Bonus Material: The Glycemic Index, Insulin and Obesity?

Recently it has become popular to promote consumption of low glycemic index (GI) foods to promote weight loss. The glycemic index is a measure of how much a particular food increases blood glucose levels. This is based on 50 grams of ingested food and is expressed relative to the GI of 50 grams of white sugar (or sometimes white bread). The glycemic load (GL) is the product of the GI of a particular food and the amount of available carbohydrate content. For example, cooked carrots have a high GI but you have to eat a lot of carrots to get a big spike in blood glucose, thus they have a low GL.

It is thought that rapid spikes in blood glucose (produced by high GI foods) causes hyperinsulinemia (high insulin levels). This in turn results in rapid drops in glucose producing hypoglycemia which in turn results in hyperphagia--abnormally increased appetite. Chronically elevated insulin levels are not good for a number of reasons, but from a weight loss prospective it acts to inhibit fat oxidation and promote fat deposition.

David Jenkins, a Canadian researcher who came up with the GI, intended it be a tool for diabetics. The GI is now being used in ways that it was never intended, i.e. as a weight loss tool and/or a way to determine what foods are "good" and which foods are "bad". The example of the carrots comes to mind, a very healthy food but with a high GI, and not likely to cause weight gain even if eaten to excess. Meat, on the other hand, has a low GI but isn't the most nutritious of foods.

Thus, as with many tools, it has its strengths and limitations.[164] It can be useful for diabetics, for example, or for those with high blood lipids (like triglycerides). Limitations are that we don't eat foods in isolation. Cooking, processing, degrees of ripeness and the type of starch found in foods varies and will affect the GI responses.[165] The glycemic response to a given food can also differ widely between individuals. Individuals who have higher levels of cardiorespiratory fitness, for example, show lower blood glucose levels post-meal compared to unfit individuals.[166]

When it comes to appetite and weight management, studies on single foods have shown suppressed intake of calories following low GI foods.[167,168] However, long-term studies on adults using mixed meals of varying GI (as is how we normally eat) have found little to no effect of GI on appetite or on subsequent *ad libitum* intake or weight loss benefit.[169,170,171,172,173,174] It is my conclusion that GI is not a helpful tool for weight loss.

What about the ability of carbohydrates to induce increases in insulin? This is the whole theoretical construct upon which many low-carb diets are based. Insulin promotes fat deposition and carbohydrates trigger insulin release, therefore carbs are obesity promoting, right? Hence the admonition is to reduce fruit intake (because fruit is high in sugar) and to completely cut out grain, bean and potato intake.

Hopefully by now you realize this is an over simplistic and reductionist approach to diet, and doesn't take into account the nutrient content or CD of foods. It paints all carbohydrate foods with the same brush. No one is arguing that eating white sugar, white flour or white rice is good for you. But lentils and lollipops are not the same foods. Eating lots of meat in place of grains and beans is playing Russian roulette with your health. Can people lose weight eating this way? Yes, but the long-term health outcomes are scary.

But back to insulin. Yes, high GI foods trigger insulin production, **but so do high protein foods**. If you feed people a steak with no accompanying carbs your insulin levels go up.[175] Yes, you read that correctly, meat or complete proteins can stimulate insulin production as much as or even more than carbohydrate rich foods. In 1997 an insulin index of foods was published which measured the insulin area under the curve for 38 different foods using isocaloric amounts. White bread was used as the reference. What they found was that protein rich foods can also trigger significant insulin production.[176] Pasta for example had an insulin score of 40% and beef a score of 51%. A subsequent study found that isocaloric intakes of beef, pork and chicken resulted in similar insulin responses.[177] A study on type 2 diabetics found that 50 g of meat protein and 50 g of sugar triggered the same insulin response.[178]

When comparing fasting insulin levels of omnivores to vegetarians eating high starch diets, vegetarians were found to have significantly lower insulin levels (35.3 vs. 50.6 $pmol.l^{-1}$).[179] Put people on a whole-food vegan diet for just three weeks and LDL goes down, blood pressure drops, fasting glucose drops, insulin sensitivity improves and insulin levels drop (7.92 to 5.76).[180] Conversely when young people were put on an *ad libitum* high-meat, Paleo diet along with 10 weeks of cross-fit training, blood lipid levels get worse (LDL increased, HDL decreased) in spite of improvements in fitness and some loss of body fat.[181]

Combining processed carbohydrates with meat protein is particularly good at stimulating insulin production. Eat white rice, yes insulin will go up. Add Tuna or chicken to that white rice and insulin levels will double. At the end of the day, the best way to limit insulin production is to eat high fiber foods and limit or avoid animal foods.

Insulin-like Growth Factor (IGF-1), Glucagon and Protein Type

Animal proteins increase levels of IGF-1. This is not a good thing when it comes to cancer risk (it increases it), but it could also be bad for weight loss. Why? IGF-1 has an anabolic (or growth) effect on human fat cells. Plant-based diets which are low in 'complete' proteins actually help to down-regulate IGF-1 which in turn down-regulates the growth of fat cells.[182]

Plant-based diets not only reduce insulin production, they also stimulate glucagon production. Glucagon, in addition to down-regulating cholesterol production by the liver, may also increase thermogenesis. This may be another reason why those eating plant-based diets tend to be leaner for the same caloric intake. Carter *et al*. have stated, "The mean weight of vegans is 20lbs less than that of ovo-lactovegetarians and non-vegetarians, despite similar caloric intakes and physical activity, which suggests that calories of vegan diets may be used inefficiently".[183]

Physical Activity and Obesity

The word sedentary comes from the Latin word 'sedere' or to sit. As office bound professionals, leaders spend a lot of time sitting; whether it be in cars, meetings, offices, airplanes, airports or at home in front of the television. Sitting for prolonged periods is not good for a lot of reasons, but in particular it is associated with increased risk of being overweight and obese. In one study of Australian adults, those sitting for 7 or more hours per day were about 68% more likely to be overweight or obese than those sitting for <4.7 hours per day.[184] In another study, men who sat for >6 hrs per day were almost twice as likely to be overweight compared to those who sat for <45 min.[185]

While we didn't measure sitting behavior in senior executives we did measure levels of physical activity.

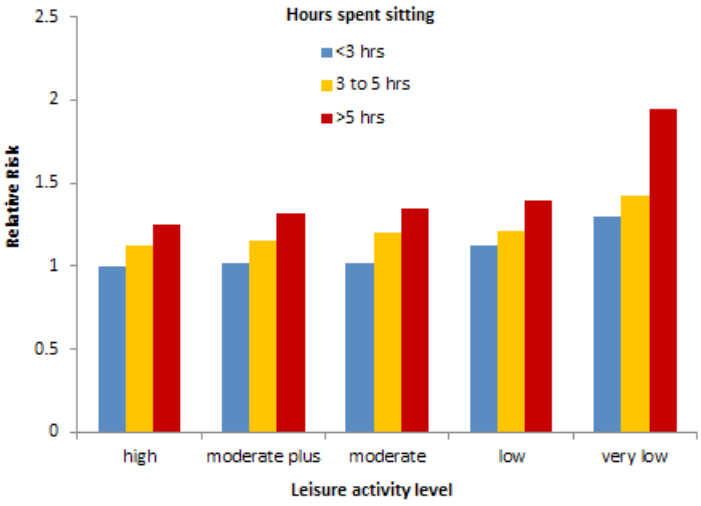
Levels of physical activity were significantly inversely associated with indices of overweight and obesity (BMI, percent body fat and waist circumference) i.e. those who reported exercising consistently for six months or longer (maintenance stage) had significantly lower waist circumference, BMI and percent body fat scores as compared to those who didn't exercise or only did so sporadically. This is not too surprising as those who exercised regularly reported expending more calories per week in exercise than those who didn't. Women in the maintenance stage (who were in the ideal range for BMI, %BF, waist circumference) reported expending about 2,000 calories per week in exercise, 1200 calories more than the non- or sporadic exercisers. Men in the maintenance stage reported expending around 3,000 calories per week in exercise, 1700 more calories than the non- or sporadic exercisers.

Large scale cross-sectional and longitudinal studies also indicate that those who are habitually more active tend to be less obese.[186]

It should be noted that these data don't imply causality, i.e. it could be that those who are leaner are more likely to exercise. Regular exercise helps with weight maintenance, lower body weights makes it easier to exercise. Indeed, when asked what their motivations are to exercise, executives ranked weight control as being an important motivator (behind 'health benefits', 'exercise makes me feel better' and 'exercise increases energy levels').

The Active Coach Potato

It is important to distinguish *too much sitting* from *too little exercise* and to consider both types of behavior when making recommendations and considering the overall impact of physical activity on obesity. There is potential for high sedentary time and being physically active to co-exist, i.e. the *Active Couch Potato* phenomenon.[187] There are data to suggest that higher amounts of time spent sitting poses increased risk for all-cause mortality even when regular exercise is performed.[188] (See bar chart)



Ultimately from both a weight and health perspective, the goal is a two pronged one: 1) to be active (i.e. sit less) as much as possible during the day and 2) to incorporate daily structured exercise time. Given that there is limited time for lengthy structured workouts, it is likely that one can expend as many or more calories by standing and walking more during the work day. Consider that sitting burns 50-60 calories and hour and standing and walking burns 100-400 calories an hour, thus more movement and less sitting over the course of a nine hour work day will add up.

Structured Exercise and Weight Loss

I remember when I trained for my first marathon back in college. I had high expectations that all that running was going to turn me into a lean, mean machine. Alas, it did not. My weight stayed stubbornly the same. It wasn't that I was very overweight; my percent body fat at the time was around 25%, typical for most female college students. I just wanted to lean up a bit, be more like those elite runners I read about in Runner's World magazine. It wasn't until I was in graduate school when I started training for Ironman triathlons that I was able to get quite lean (12-14%) but it took about 20 hours (or more) a week of exercise to achieve that.

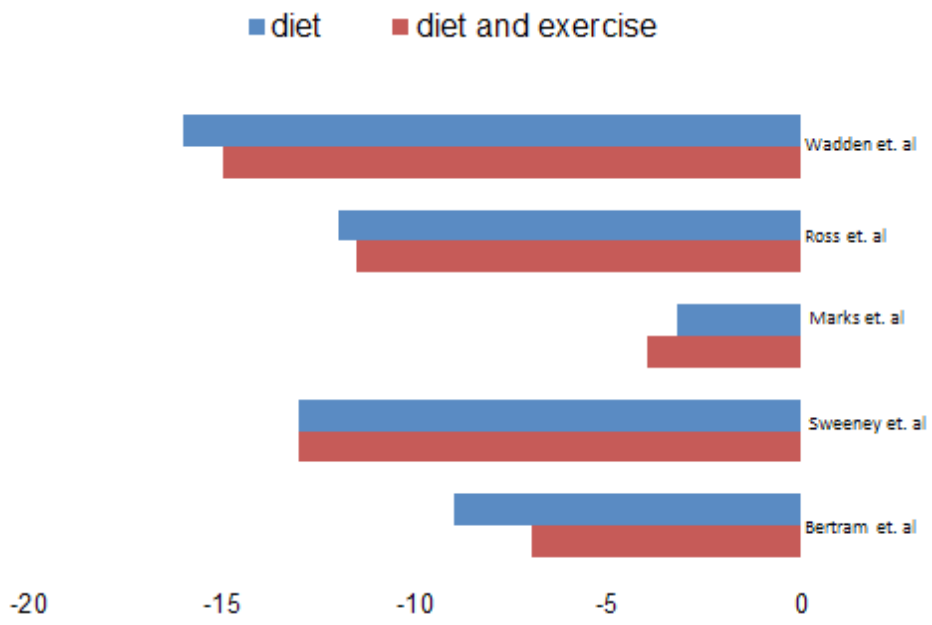
Years later at the age of 44, I was still training and racing as an endurance athlete, in fact at the time I was racing at the pro level on the mountain bike. As I entered my 40s, I noticed that my winter weight kept creeping up and was getting harder and harder to lose. At the start of the training season I would ramp up my training hours (about 10-15 hour per week) and track everything I ate in an effort to drop the weight. I would manage to drop a few pounds, but invariably it was an exercise in frustration as, in spite of all this effort, I just couldn't seem to get back to what I considered to be my ideal racing weight.

A couple of years later I decided not to race as seriously and co-incidently I started delving into the science of nutrition. As a result, I switched to eating a plant-based, nutrient-dense, calorie-dilute, vegan diet. I quit counting calories and just ate until I was full (stuffed in fact) as it became more about health than it did about weight loss. Given how much I was eating, I was sure I was not losing any weight and thought I might even be gaining some. So about a month after changing my diet, I got on the scale to check how bad the damage was. To my surprise I had lost about seven pounds and had achieved my "ideal racing weight", a weight I hadn't been able to achieve counting all those calories. This in spite of exercising less! Since then I have dropped another five pounds and have stayed at a constant weight for the last eight years, in spite of fluctuations in the amount of exercise that I do. I continue to eat until I am full and have lost many of the food cravings I used to have.
My experience is similar to a lot of people in that a) the weight starts to creep up after the age of 40 and b) there are high expectations of weight loss when starting an exercise program (soon followed by discouragement when the expected loss didn't occur). What I ultimately learned was that the type of foods I was eating was more important than the number of calories or portions that I was eating.

Exercise interventions, at least in the short-term, have proven to be disappointing when it comes to weight loss. Data from randomized controlled studies suggest that adding exercise to dietary changes does not significantly increase short-term weight loss compared with diet changes alone. The figure below shows the results from 6 studies that compared short-term (4-6 months) dietary interventions along with diet changes plus exercise. Only one study found a statistically significant, but small, improvement in weight loss with diet changes plus exercise versus dietary changes alone.[189,190,191,192,193,194,195,196]

There could be a number of reasons as to why exercise alone doesn't always result in significant weight loss.

1. **Difficult to induce large calorie deficits:** For most people it is difficult to exercise long and hard enough to induce sufficient caloric expenditures to induce weight loss. Consider that walking 30 minutes only results in



a caloric expenditure of 150-200 calories. Even running for 30 minutes expends only 300 to 400 calories. Add to this, if you are sitting all day the total caloric output is relatively small.

2. **Dietary compensation:** It is easy for people to 'justify' intake of extra treats (i.e. calories) as a reward for their exercise. Consider that it takes 30 sec to eat a 400 calorie cookie or donut and 60+ minutes of walking to expend those calories, it really is an unfair battle.

3. **We exist in a state of low metabolic flux:** Metabolic flux is the combination of calories in and calories expended. When lots of calories are expended and ingested that is a state of high metabolic flux or throughput, common for those involved in heavy physical labor or elite athletes. But most of us operate in an environment of low flux, even when we do regular exercise. As previously discussed, trying to lose or even regulate weight in a state of low flux is quite difficult, especially when there is little time for exercise combined with lots of time spent sitting.

Yet, exercise is not without its merits when it comes to weight loss and maintenance. More recent studies have shown small (2-7kg) but not insignificant reductions in weight using exercise alone without caloric restriction.[197] A 2006 Cochrane review of 43 studies reported that exercise improved weight loss marginally compared with control groups, but that weight losses were more significant when combined with dietary changes.[198] Of interest was that vigorous exercise was more effective at inducing weight loss than moderate or light exercise, especially when there were no accompanying dietary changes.[199] When diet was also changed, however, exercise intensity did not affect the amount of weight lost, likely because the exercise effect is outweighed by the effects of dietary changes.

What is also important to note is that research does support the efficacy of exercise to prevent weight gain, or regaining weight that is lost via dietary changes. Thus, exercise is still critical when it comes to matters of weight.

What about the fat burning zone? At low intensities of exercise a greater proportion of the calories burned will be from fat (depending on how long you go and how well trained you are). So there is some truth to there being a "fat burning zone". However, if you go at higher intensities, while the proportion of calories derived from fat goes down, the absolute calories from fat could be higher. At the end of the day it is more about creating a calorie deficit and trying to optimize caloric expenditure during exercise than it is about which zone you are in. However, there is some benefit to going longer at lower intensities on occasion to train that metabolic system. It should also be noted that most of the fat that we burn during exercise comes from intramuscular fat (fat stored in the muscles) not subcutaneous fat.

What about weight training and building muscle to increase metabolism? Again, this is something of a half-truth. Yes, muscle is more metabolically active then fat. Those with higher proportions of muscle will burn more calories at rest than those with less muscle. So if I weight train and gain more muscle will that help? Maybe. Unfortunately 1 kg of muscle (or 2 lbs.) only results in about 25 more calories expended per day in increased metabolic rate. Yes, this can add up over the long-term, but can easily be offset by eating 2-3 potato chips. Incidentally, 1 kg is what most people gain on average after starting a resistance training program, although it is generally is easier for men to gain muscle than women.

Don't get me wrong, I think resistance training is important for a lot of reasons. But I think its biggest value as a weight loss tool is in preventing muscle loss as we age as well as the other benefits it brings like stronger bones and maintenance of functionality. Another reason it is important is that when we lose weight we often lose some muscle tissue in addition to fat tissue. This is why losing weight then regaining it then losing it and regaining it is a dangerous cycle. We don't tend to regain the muscle during the cycles of weight gain, but we do regain the fat. Thus resistance training is helpful in maintaining muscle mass, both as we age and during periods of weight loss.

So where does this leave us?

The goal of exercise is to get fit, feel better, improve energy and reduce risk for chronic diseases like cancer and heart disease. If you need to lose weight then it is important to engage in daily exercise that is either of a longer duration (an hour or more) and/or is fairly vigorous, i.e. it is good to mix it up. It is also important to be active (standing and moving more) throughout the day. Combine this with eating a whole-foods, high fiber, plant-based diet and your chances of weight loss success will be enhanced significantly.

Ultimately, the best formula is this: Whole, calorie dilute, plant-foods + aerobic endurance exercise (>60 min 1-2x per week) + vigorous aerobic exercise (> 30 min 2-3x per week) + resistance training (1-3x per week) + more daily movement = weight loss success (and better health and feeling better).

But not everyone responds equally to the same program of diet and exercise. There are genetic differences.

Genetics and Obesity

A tale of two populations

At the beginning of the chapter I mentioned that of the top ten fattest countries in the world, seven were Islands of the South Pacific. Traditionally many of these people were large people, yet they were muscular and large rather than fat and large. They were described by early explorers as "a singularly tall, muscular and well-proportioned people."[200] Given that many had to travel long-distances by boat and that there were periods of famine, it is likely that a genetic predisposition to retaining calories represented a survival advantage. The traditional diets of these islanders was predominantly vegetarian (one estimate was that they were vegetarian 85% of the time). Given limited land and resources, raising beef wasn't an option and chickens were rarely eaten. The diets consisted of root vegetables like taro and sweet potatoes, fruits, greens, and coconuts. Fresh and dried fish also supplemented their diets.

Today many of these islands rely on food exports of low-nutrient, energy-dense western foods. Chicken, canned fish, oils, dairy, meat, sugar and white flour now make up a large proportion of their diets.[201] Superimpose these calorie dense foods onto a genetically susceptible population combined with lower levels of physical activity and it is no wonder that obesity rates in many of these island nations is over 70%.

The Pima Indians are another example of a population who have a strong genetic predisposition to obesity and type 2 diabetes. Yet the Pima Indians who live in Mexico and who follow their traditional diets of beans, flour and corn tortillas and potatoes, diets that are both low in fat and high in carbohydrates and fiber (>50g per day), have low rates of obesity and diabetes.[202] Their rates of obesity and diabetes, in fact are similar to the non-Pima Indians living in the same area.[203] However, the Pimas living in Arizona who are genetically similar and who eat a low-fiber, high-fat diet, yet one that is lower in calories, have among the highest reported prevalence of obesity and type 2 diabetes of any ethnic group in the US. The US Pima Indians are described as being extremely obese.

The lesson in all this is that people do have genetic predispositions but these need not determine one's fate. Diet and lifestyle can limit the expression and the negative impact of genetics. Genetics loads the gun, lifestyle pulls the trigger. If you do have a strong predisposition toward weight gain then you will have to be extra careful about eating a very low CD diet, one that is high in fiber, water and nutrients and is lower in fat. The low in fat part actually turns out to be quite important when it comes to genetics.

Thrifty Genes

There are a number of genes that have been identified as increasing one's risk for obesity. FTO region genes otherwise known as the *fat mass and obesity-associated gene* was one of the first to be identified. Exactly how it influences human body mass remains somewhat elusive. In animal studies FTO genes are involved in governing appetite and energy expenditure. In humans it appears to be more related to food intake and impaired satiety.[204,205] What we do know is that those deficient in the FTO gene are somewhat protected from obesity.[206] Those who are positive for this gene have about a 1.7 times increased risk of obesity (at least in Caucasians) and are on average 3kg heavier.[207] One study found that about 16% of Caucasians have the homozygous form of this gene. The homozygous form represents a stronger predisposition.

Another gene is PPAR*gamma*. This is known as a thrifty gene. It is a transcription gene that mediates the expression of other genes. This gene plays a role in hypertrophic obesity (this is where the fat cells increase in size, most commonly the cause of adult obesity) and in insulin resistance. When a high fat diet is consumed, this gene and those downstream from it help to facilitate fat storage and to inhibit the expression of leptin, a hormone which promotes satiety. Most people have this gene.[208,209]

Polymorphisms, or variants, of another gene, APOA5 have also been identified as increasing risk for obesity.[210] Genetic variations of this gene are associated with increased triglyceride levels, metabolic syndrome and risk of obesity.[211,212,213]

The Genes and Diet Interaction

In animal studies, APOA5 variant mice fed a low-fat chow showed no increases in food intake or in body fat. However, when those same APOA5 variant mice were fed a high-fat diet, increases in body fat did occur.[214] In humans, those with an APOA5 major allele variant (-1131C) showed increases in body fat when they ate a high-fat diet (>25%), whereas those with the minor allele didn't.[215] In another study on diabetic Koreans, those positive for this variant who were fed a low-fat diet rich in whole grains and beans, showed decreases in fasting glucose and triglycerides.[216]

In the Framingham Heart Study, researchers found that when fat intake was less than 30% for carriers of the -1131C allele the risk for obesity was low. However, in those eating a high fat diet (>30%), obesity risk was much greater.[217] When carriers of this variant were fed a fat restricted diet, they lost more weight than when non-carriers were fed the same diet, suggesting that the carriers benefited more from a fat restricted diet than did the non-carriers.[218]

In 1993 a gene called FABP2, or fatty acid binding protein, was identified (as part of the Pima Indian studies) as being associated with obesity, metabolic syndrome and increased insulin resistance. This gene makes an intestinal fatty acid *binding protein* using one

of two amino acids. When the gene makes the protein with threonine, the body seems to absorb more fatty acids from the fat in meals. It has been shown that this gene increases small intestinal lipid absorption without affecting glucose uptake or metabolism.[219] A 12-week exercise program on middle-aged women, however, has been shown to improve indices of obesity, blood lipids and insulin resistance in those who were positive for the gene.[220]

The study of the genetic contribution to obesity is complicated and ongoing. There is much that we don't fully understand. However, of interest is that many (if not most) of these genes affect dietary fat metabolism and storage. There is compelling evidence to suggest that eating a low-fat, high-fiber diet, as well as being physically active can blunt the expression and negative effects of these genes.[221] Eating a high-fat diet, in turn, seems to bring out the worst of these genes.

As far as I can tell, there are no obesity genes associated with carbohydrate metabolism. It is also interesting to note that those with "skinny" genes (yes we all know people like that) are in fact the exception, not the rule. Most people have variations of these obesity genes. This is good news when stranded on a desert island, but not good news when you are surrounded by CD foods and exercise is limited. Thus, for most of us, we are programmed to gain weight, not lose it. Make no mistake; weight loss can be tough for some people to achieve, even when they eat a healthy diet. As previously mentioned, I do believe chasing skinny can be detrimental; chasing good health is always the ultimate goal.

Our Gut Microbiome and Obesity

Thrifty Bacteria

The human gut (or colon) has been described as a "lush microbial ecosystem containing about 100 trillion microorganisms..."[222] Now that is impressive. Scientists are just starting to examine the impact that these microorganisms have on our health. Accumulating evidence suggests that these gut bacteria can play a significant role in the development of obesity, obesity-associated inflammation, immune function and insulin resistance. There are a number of proposed mechanisms by which these bacteria play a role, including how they impact eating behavior, energy harvest, energy expenditure and fat storage. [223]

Diet, genetics and lifestyle can profoundly affect the gut bacteria, but diet is likely the factor that has the most significant impact. An interesting study compared the gut flora of African children in a remote village to children living in the EU. The African children's diet consisted mainly of cereals (millet and sorghum), legumes and vegetables. Fiber intakes were high and consumption of animal protein was very low. The diets of the EU children were high in fat, animal protein and sugar and low in fiber.

The researchers found that the gut flora of these children were quite different. Firstly the African children had a more rich and diverse flora. Reductions in biodiversity and richness of the gut flora is one of the undesirable effects of eating a Western diet rich in fat, protein and sugar and is associated with an increase in the incidence of non-infectious intestinal diseases (like IBS). They also found that the makeup of the gut flora was quite different.[224]

There are four broad types or classes of bacteria, *Actinobacteria*, *Bacteroidetes*, *Firmicutes* and *Proteobacteria* that makeup of the majority of human gut microbiota.[225] The African children had more of the *Bacteroidetes* then the European children (57.7% vs. 22.4%). This is significant, as some studies have found that lean individuals have more *Bacteroidetes* while obese individuals have more *Firmicutes*.[226,227] It has been suggested that higher amounts of *Firmicutes* improves the ability of the host to extract energy (in particular from fat) and to store this energy as fat.[228] *Bacteroidetes* on the other hand are not good at harvesting energy from fat, i.e. they are less thrifty.

Colonization of animals with more *Firmicutes* strains of bacteria, for example, resulted in increased uptake of fatty acids.[229] Interestingly, monitoring of obese participants during a weight loss program linked an increase in the levels of *Bacteroidetes* to weight loss, independent of caloric intake.[230] Thus from a weight maintenance perspective is likely better to have more *Bacteroidetes* (think B for boney) than *Fimicutes* (think F for fat).

An interesting series of experiments have been done on mice. In one study, mice were colonized with fecal bacteria from human twins discordant for obesity, i.e. one group of mice was colonized with bacteria from the obese twin and another group with bacteria from the lean twin (for obvious reasons this type of study couldn't be done on humans). Using flora from twins of course reduces any variability associated with genetics. Both groups of mice were then fed the same diet. What they found was that the mice receiving the bacteria from the obese twin gained significantly more body fat than those mice that were colonized with the lean twin's gut bacteria, in spite of eating the same food.[231]

They then placed the lean mice with the obese mice in the same cage. Mice are coprophagic, which means that they eat each other's feces (yumm). The obese mice, after eating the feces of the lean mice, consequently lost weight. However, when all the mice were subsequently fed a high saturated-fat and a low vegetable and fruit diet, all of the mice gained weight, including the mice with the lean flora, albeit, not as much as the mice with the obese flora.

One distinguishing characteristic was that the lean mice showed a greater capacity to breakdown and ferment polysaccharides. A number of studies have shown that increased fermentation of starches is associated with decreased body fat and that failure to ferment dietary resistant starch results in less body fat loss, at least in mice.[232,233]

Another group of researchers looked at the microbiome of vegetarians and found that vegetarians had more of the 'lean' type bacteria suggesting a "smaller capacity for energy gain from food in vegetarians".[234] Now to be fair, this smaller capacity is relatively small but can add up over time, about five pounds of fat over a year, which equates to the average weight gain of adults in mid-life. [235]

One dietary factor that has been proposed as a way to switch gut bacteria to the less thrifty kind is to eat foods high in polyphenols. Phenolic compounds suppress growth of *Firmicutes*. *Bacteroidetes* growth, on the other hand, prevails following intake of polyphenol-rich foods. These would include foods like grapes, green tea, berries, wine vinegar and other nutrient rich plant foods.[236]

What affects our gut bacteria? Certainly genetics, physical activity, antibiotics and dietary factors can all play a role. Dietary manipulations on mice colonized with human fecal bacteria revealed that the composition of their human gut microbial communities changed dramatically within a single day after the animals were switched from a plant-rich chow to a high-fat, high-sugar western style diet.[237] Another study in which the same group of people were put on a plant-based diet for 5 days followed by a meat-based diet for 5 days, found that the gut microbiome was quite different between those two dietary interventions.[238] Another finding of this study that is worth mentioning is that the meat-based diet resulted in an increase of *Bilophila wadsworthia* which supported a link between dietary fat and the outgrowth of microorganisms capable of triggering inflammatory bowel disease.

Thus diet likely plays a significant, if not the most significant role in determining the makeup of our gut flora. Eating more plants with fiber and less fat appears to change the makeup of the gut flora in a more positive way.

Conclusion

Solving the Obesity Crisis

According to the World Health Organization, on an individual level people need to limit fats (especially fats of animal origin) and sugars, increase consumption of fruits, vegetables, legumes, whole grains and nuts, and engage in regular exercise.[2] Yes, that is their recommendation. It really is as simple as that, but hopefully, you now understand some of the science behind this recommendation.

Unfortunately this message has been crowded out by a lot of dietary 'myths' that appeal to our primal instincts; that high-fat, energy dense, high-protein animal foods are good for weight loss and not harmful to long-term health. I fear that we will pay a heavy price for such dietary advice. Switching to a whole-foods, plant-based diet is better for overall health, better for the environment, and also helps with weight loss. I think the science is quite compelling on all of those fronts. It is also not as difficult to make the switch as you might think.

On a societal level we need to treat calorie dense foods like we treat tobacco; limit advertising to children, tax unhealthy and CD foods and stop subsidizing the meat and dairy industries. Conversely, we need to do a better job of marketing healthy food, creating safe food environments, and subsidizing healthy options like fruits and vegetables. Apples need to cost a dime and hamburgers $25. Admittedly, these would be tough measures to pass. But if we are to solve this crisis, it will take the combined efforts of private industry, government, health care providers and individuals.
However, until such a time, the best place to start is with you.

i. A note about veganism or vegetarianism: Going vegetarian or even vegan will not necessarily or magically result in weight loss. It is possible to be a junk food vegan or vegetarian and still be obese or overweight. Junky foods like cookies and cakes (even if they are vegan) can be more calorie dense than chicken or meat or some dairy products. But there are aspects of eating vegan or vegetarian that helps promote weight loss as we have discussed. I would also say that the term vegan is quite black and white and as such, some might think it is an either/or proposition, i.e. "I can't be vegan so therefore I won't change anything". This is self-defeating. Yes I do think that giving up meat and dairy is a good thing for lots of reasons, but it is up to you to decide, based on the data presented here, how much you want to shift away from eating animal and other processed foods and how far towards eating more whole, plant foods you want to go. It doesn't have to be an all or nothing approach. However, if weight is something you really struggle with, I think eating a lower in fat, 100% plant based diet might be the way to go. If you really can't live without some animal foods, then try to get to a place where you only eat it 1-3x per week and think of it as a condiment, not the main dish, or better yet substitute in some faux meat.

References

1 "*Obesity: Preventing and Managing the Global Epidemic*" Report of a WHO Consultation on Obesity. Geneva, 3-5 June 1997.

2 http://www.who.int/mediacentre/factsheets/fs311/en

3 Obesity in the Pacific: Too big to ignore. WHO Regional Office for the Western Pacific. 2002.

4 http://www.who.int/dietphysicalactivity/childhood/en

5 Onis, M. Blossner, M and Borghi E. Global prevalence and trends of overweight and obesity among preschool children. *Am J Clin Nutr* 2010;92:1257-64.

6 www.who.int/mediacentre/facsheets/fs311/en

7 www.CDC.gov/obesity/data/adult.html

8 King, EB et . al. Waistlines and ratings of executives: does CEO status overcome obesity stigma? *Human Resource Management*, Dec, 2014. Published online

9 Berkow SE and Barnard ND. Blood pressure regulation and vegetarian diets. *Nutr Rev*. 2005;63:1-8.

10 Appleby PN, Key TJ, and Thorogood M. Mortality in British vegetarians. *Public Health Nutr.* 2002;5:29-36.

11 Thorogood M et. al. Relationship between body mass index and mortality in an unusually slim cohort. *J Epidmiol. Comm Health*. 2003;57:130-33.

12 Key T. et. al. Mortality in vegetarians and non-vegetarians: detailed findings from a collaborative analysis of 5 prospective studies. *Am J Clin Nutr.* 1999;70(suppl):516S-24S.

13 Esselstyn CB et. al. A way to reverse CAD? *J Fam Pract. 2014*;63(7):356-64b.

14 Jenkins, DJA et. al. Type 2 diabetes and the vegetarian diet. *Am J Clin Nutr.* 2003;78:610S-16S.

15 Mosby TT et. al. Nutrition in adult and childhood cancer: role of carcinogens and anti-carcinogens. *Anticancer Res*. 2012;32(10):4171-92.

16 Frattaroli, J et. al. Clinical events in prostate cancer lifestyle trial: results from two years of follow-up. *Urology*. 2008;72(6):1319-23.

17 Ross R and bradshaw AJ. The future of obesity reduction: beyond weight loss. *J Nat Rev Endocrinol*. 2009;5:319-26.

18 Tonstad, S. et. al. Vegetarian diets and incidence of diabetes in the Adventist Health Study-2. *Nutr Metab Cardiovasc Dis*. 2013;23(4):292-9.

19 Lee CD, et. al. Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. *Am J Clin Nutr.* 1999;69(3):373-380.

20 Katzmarzyk, PT et. al. Cardiorespiratory fitness attenuates the effects of the metabolic syndrome on all-cause and cardiovascular disease mortality in men. *Arch Int Med*. 2004;164(10):1092-97.

21 McAuley, PA et. al. The obesity paradox, cardiorespiratory fitness, and coronary heart disease. *Mayo Clin Proc*. 2012;87(5):443-51.

22 Westerterp KR. Physical activity, food intake, and body weight regulation: insights from doubly labeled water studies. *Nutr Rev.* 2010;68(3):148-54.

23 Miller, WC. How effective are traditional dietary and exercise interventions for weight loss? *Med Sci Sports Exerc*. 1999;31(8):1129-34.

24 Spencer EA. et. al. Diet and body mass index in 38000 EPIC-Oxford meat-eaters, fish-eaters, vegetarians and vegans. *Int J Obes Relat Metab Disord*. 2003;27*6):728-34.

25 Berkow, SE and Barnard, ND. Vegetarian diets and weight status. *Nutr Rev* 2006;64(4):175-88.

26 Wang, Y and Beydoun MA. Meat consumption is associated with obesity and central obesity among US adults. *Int J Obes (Lond).* 2009; 33(6):621-8.

27 Tonstad, S et. al. Type of vegetarian diet, body weight, and prevalence of type 2 diabetes. *Diabetes Care*. 2009;32(5):791-6.

28 Rosell M et. al. Weight gain over 5 years in 21,966 meat-eating, fish-eating, vegetarian, and vegan men and women in EPIC-Oxford. *Int J Obes (Lond)* 2006;30:1389-96.

29 Vergnaud, AC at. al. Meat consumption and prospective weight change in participants of the EPIC-PANACEA study. *Am J Clin Nutr* 2010;92:398-407.

30 Bes-Rastrollo, M. et. al Perdictors of weight gain in a Mediterranean cohort: the Seguimiento Universidad de Navarra Study 1. *Am J Clin Nutr* 2006;83:362-70.

31 French, SA et. al. Predictors of weight change over two years among a population of working adults: the Healthy Worker Project. *Int J Obes Relat Metab Disord* 1994;18:145-54.

32 Kahn HD et. al. Stable behaviors associated with adults' 10-year change in body mass index and likelihood of gain at the waist. *Am J Public Health* 1997;87:747-54.

33 Spencer, EA et. al. Diet and body mass index in 3800 EPIC-Oxford meat-eaters, vegetarians and vegans. *Int J Obes Relat Metab Disord*.

2003;27(6):728-34.

[34] Stamler, J and Dolecek TA. Relation of food and nutrient intakes to body mass in the special intervention and usual care groups in the Multiple Risk Factor Intervention Trial. *Am J Clin Nutr* 1997;65:366-73S.

[35] Schulz M et. al. Food groups as predictors for short-term weight changes in men and women of the EPIC-Ptsdam cohort. *J Nutr* 2002;132:1335-40.

[36] Paddon-Jones, D. et. al. Protein, weight management and satiety. *Am J Clin Nutr* 2008;87(suppl):1558S-61S.

[37] Pesta, D. et. al. A high protein diet for reducing body fat: mechanisms and possible caveats. *Nutr Metab*. 2014;11(1):53.

[38] Claessens, M. et. al. The effect of a low-fat, high-protein or high-carbohydrate ad libitum diet on weight-loss maintenance and metabolic risk factors. *Int J Obes (Lond)*. 2009;33:296-304.

[39] Bautista-Castano, I. et. al. Changes in bread consumption and 4-year changes in adiposity in Spanish subjects at high cardiovascular risk. *Brit J Nutr.* 2013; 110:337-46.

[40] Howarth, Nc, Saltzman, E. and Roberts, SP. Dietary fiber and weight regulation. *Nutr Rev.* 2001;59(5):129-39.

[41] Clifton, Pm Keogh, JB and Noakes, M. Long-term effects of a high protein weight loss diet. *Am J Clin Nutr* 2008;87:23-9.

[42] Volek, JS et. al. Carbohydrate restriction has a more favorable impact on the metabolic syndrome than a low fat diet. *Lipids*. 2009; 44(4):297-300.

[43] Due, A et. al. Effect of normal-fat diets, either medium or high in protein, on body weight in oeverweight subjects: a randomized 1-year trial. *Int J Obes Relat Metab Disord*. 2004;28:1283-90.

[44] Foster, GD et. al. A randomized trial of a low-carbohydrate diet for obesity. *N Engl J Med* 2003;348-90.

[45] Lasker DA et. al. Moderate carbohydrate, moderate protein weight loss diet reduces cardiovascular disease risk compared to high carbohydrate, low protein diet in obese adults: A randomized clinical trial. *Nutr Metab (Lond)*. 2008;5:30.

[46] Layman DK et. al. A reduced ratio of dietary carbohydrate to protein improves body composition and blood lipid profiles during weight loss in adult women. *J Nutr* 2003;133:411-7.

[47] Skov AR, et. al. Randomized trial on protein vs carbohydrate in ad libitum fat reduced diet for the treatment of obesity. *Int J Obes Relat Metab Disord*. 1999;23:538-36.

[48] Bes-Rastrollo, M et. al. Predictors of weight gain in a Mediterranean cohort: the Seguimiento Universidad de Navarra study 1. *Am J Clin Nutr* 2006;83(2):362-70.

[49] Mozaffarian, D. et. al. Changes in diet and lifestyle and long-term weight gain in women and men. *N Engl J Med* 2011;364:2392-404.

[50] Swinburn B, Sacks G. and Ravussin E. Increased food energy supply is more than sufficient to explain the US epidemic of obesity. *Am J Clin Nutr.* 2009;90:1453-6.

[51] Westerterp KR and Speakman JR. Physical activity energy expenditure has not declined since the 1980s and matches energy expenditure of wild animals. *Int J Obes*. 2008;32:1256-63.

[52] Barnard, ND. Trends in food availability, 1909-2007. *Am J Clin Nutr* 2010;91(suppl):1530S-6S.

[53] Spetter MS et. al. The sum of its parts—effect of gastric distention, nutrient content and senroy stimulation on brain activation. *PL0S ONE*. 2014; 9(3).

[54] Howarth NC, Saltzman, E and Roberts SB. Dietary fiber and weight regulartion. *Nutr Rev.* 2001;59(5):129-39.

[55] Duncan KH, Bacon JA and Weinsier RL. The effects of high and low energy density diets on satiety, energy intake, and eating time of obese and nonobese subjects. *Am J Clin Nutr* 1983;37:763-7.

[56] Bell EA et al. Energy density of foods affects energy intake in normal-weight women. *Am J Clin Nutr.* 1998;67:412-20.

[57] Bell EA and Rolls BJ. Energy density of foods affects energy intake across multiple levels of fat content in lean and obese women. *Am J Clin Nutr.* 2001;73:1010-8.

[58] World cancer Research Fund/American Institute for cancer Research. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective. Washington DC: AICR, 2007.

[59] Ledikwe, JH et. al. Dietary energy density is associated with energy intake and weight status in US adults. *Am J Clin Nutr.* 2006;83:1362-8.

[60] Bes-Rastrollo, M. et. al. Prospective study of dietary energy density and weight gain in women. *Am J Clin Nutr.* 2008;88:769-77.

[61] Rolls et. al. Provision of foods differing in energy density affects long-term weight loss. *Obes Res.* 2005; 13:1052-60.

[62] Ello, M et. al. Dietary energy density in the treatment of obesity: a year-long trial comparing 2 weight-loss diets. *Am J Clin Nutr.* 2007;85:1465-77.

[63] Ledikew JH et. al. Reductions in dietary energy density are associated with weight loss in overweight and obese patients in the PREMIER trial. *Am J Clin Nutr.* 2007;85:1465-77.

[64] Edikwe JH. et. al. Low-energy-density diets are associated with high diet quality in adults in the United Sstates. *J Am Diet Assoc*. 2006;106:1172-80.

[65] Raynor, H. et. al. The effects of an energy density prescription on diet quality and weight loss: a pilot randomized controlled trial. *J*

Acad Nutr Dietetics. 2012;112(9):1397-02.

[66] Savage JS, Marini M. and Birch LL. Dietary energy density predicts women's weight change over 6 y. *Am J Clin Nutr*. 2008;88:677-84.

[67] Blatt AD, et. al. Increasing the protein content of meals and its effect on daily energy intake. *J Am Diet Assoc*. 2011;111(2):290-4.

[68] Raben, A et. al. Meals with similar energy densities but rich in protein, fat, carbohydrate, or alcohol have different effects on energy expenditure and substrate metabolism but not on appetite and energy intake. *Am J Clin Nutr.* 2003;77:91-100.

[69] Poppitt, SD, McCormack, D and Buffenstein, R. Short-term effects of macronutrient preloads on appetite and energy intake in lean women. *Physiol Behav.* 1998;64:279-85.

[70] Bell, EA et. al. Energy density of foods affects energy intake in normal-weight women. *Am J Clin Nutr*. 1998;67:412-20.

[71] Rolls, BJ et. al. energy density but not fat content of foods affected energy intake in lean and obese women. *Am J Clin Nutr.* 1999;69:863-71.

[72] Flood Je and Rolls BJ. Soup preloads in a variety of forms reduce meal energy intake. *Appetite*. 2007;49:626-34.

[73] Rolls BJ, Roe LD and Meengs JS. Salad and satiety: energy density and portion size of a first course salad affect energy intake at lunch. *J Am Diet Assoc*. 2004;104:1570-76.

[74] Flood JE, Roe LS and Rolls BJ. The effect of increased beverage portion size on energy intake at a meal. *J Am Diet Assoc*. 2006;106(12):1984-90.

[75] Flood-Obbagy Je and Rolls BJ. the effect of fruit in different forms on energy intake and satiety at a meal. *Appetite*. 2009;52(2):416-33.

[76] Houchins JA et. al. Effects of fruit and vegetable, consumed in solid vs. beverage forms on acute and chronic appetitive responses in lean and obese adults. *Int J Obes (Lond)*. 2013;37(8):1109-15.

[77] McDougall, J. Sugar, Coated with Myths, September 2006 5(9) *McDougall Newsletter.*

[78] Levine AS, Kotz Cm and Gosnell Ba. Sugars: hedonic aspects, neuroregulation and energy balance. *Am J Clin Nutr.* 2003;78(4):834S-42S.

[79] Bjorntorp P and Sjostrom L. Carbohydrate storage in man: speculations and some quantitative consideratins. *Metabolism*. 1978;27(suppl 2):1853-65.

[80] McDevitt RM. Et. al. De novo lipogenesis during controlled overfeeding with sucrose or glucose in lean and obese women. *Am J Clin Nutr.* 2001;74(6):737-46.

[81] Acheson KJ et. al. Glycogen storage capacity and de novo lipogenesis during massive carbohydrate overfeeding in man. *Am J Clin Nutr.* 1988;48:240-7.

[82] Thomas CD. et. al. Nutrient balance and energy expenditure during ad libitum feeding of high-fat and high-carbohydrate diets in humans. 1992;55:934-42.

[83] Jenkins DJ et. al. Effect of a very-high-fiber vegetable, fruit and nut diet on serum lipids and colonic function. *Metab*. 2001;50(4):494-3.

[84] Olsson KE and Saltin B. Variations in total body water with muscle glycogen changes in man. *Acta Physiol Scand*. 1970;80:11-8.

[85] Chao A. et. al. Meat consumption and risk of colorectal cancer. *JAMA*. 2005;293:172-2.

[86] Fung, TT. Low-carbohydrate diets and all-cause and cause specific mortality: Two cohort studies. *Ann Intern Med*. 2010;153(5):289-98.

[87] Fung, TT. Low-carbohydrate diets and all-cause and cause specific mortality: Two cohort studies. *Ann Intern Med*. 2010;153(5):289-98.

[88] Holt SH, et. al. A satiety index of common foods. Eur J Clin Nutr. 1995;49(9):675-90.

[89] Borer, KT: Nonhomeostatic control of human appetite and physical activity in regulation of energy balance. *Exerc Sport Sci Rev.* 2010;38:114-21.

[90] Stensel D. Exercise, appetite and appetite-regulating hormones: implications for food intake and weight control. *Ann Nutr Metab*. 2010;57(suppl) 2:36-42.

[91] Barsh GS and Schwartz MW. Genetic approaches to studying energy balance: perception and integration. *Nature Review Genetics*. 2002;3:589-600.

[92] De Souze CT et. al. Consumption of a fat-rich diet activates a proinflammatory response and induces insulin resistance in the hypothalamus. *Endocrinology*. 2005;146(10):4192-99.

[93] Milanski M. et. al. Saturated fatty acids produce an inflammatory response predominantly through the activation of TLR4 signaling in hypothalamus: implications for the pathogenesis of obesity. J Neurosci. 2009;29:359-70.

[94] Munzberg H. Flier JS, and Bjorback C. Region-specific leptin resistance within the hypothalamus of diet-induced obese mice. *Endocrinology*. 2004;145:4880-89.

[95] Moraes, JC et. al. High-fat diet induces apoptosis of hypothalamic neurons. *PLoS ONE*. 2009;4(4):1-11.

[96] Thaler, JP. Obesity is associated with hypothalamic injury in rodents and humans. *J Clin Invs*. 2012. 122(1):153-62.

[97] Pasinetti GM and Eberstein JA. Metabolic syndrome and the role of dietary lifestyles in Alzheimer's disease. J Neurochem.

2008;106:1503-14.

[98] Rintamaki R et. al. Seasonal changes in mood and behavior are linked to metabolic syndrome. *PLoS ONE*. 2008;3:e1482.

[99] Blundell JE, King NA. Physical activity and regulation of food intake: current evidence. *Med Sci Sports Exerc*. 1999;31:S573-S583.

[100] Bilski J et. al. Effects of exercise on appetite and food intake regulation. *Med Sport*. 2009;13:82-94.

[101] Stensel D. Exercise, appetite and appetite-regulating hormones: implications for food intake and weight control. *Ann Nutr Metab*. 2010;57(suppl) 2:36-42.

[102] Hickey MS et. al. Gender-dependent effects of exercise training on serum leptin levels in humans. *Am J Physiol Endocrinol Metab*. 1997;272-E562-E566.

[103] Stensel D. Exercise, appetite and appetite-regulating hormones: implications for food intake and weight control. *Ann Nutr Metab*. 2010;57(suppl) 2:36-42.

[104] Mayer J, Purnima R, Mitra KP. Relation between caloric intake, body weight and physical work: studies in an industrial male population in West Bengal. *Am J Clin Nutr.* 1956;4:169-75.

[105] Flatt JP. Issues and misconceptions about obesity. *Obesity*. 2011;19:676-686.

[106] Mayer J. et. al. Exercise, Food intake and body weight in normal rats and genetically obese adult mice. *Am J Physiol*. 1954;177:544-48.

[107] Hill JO, Wyatt, HR and Peters JC. Energy balance and obesity. *Circulation*. 2012;126(1):126-132.

[108] Stensel D. Exercise, appetite and appetite-regulating hormones: implications for food intake and weight control. *Ann Nutr Metab*. 2010;57(suppl) 2:36-42.

[109] Caudwell P et. al. Exercise alone is not enough: weight loss also needs a healthy (Mediterranean) diet. *Public Health Nutr.* 2009;12:1663-66.

[110] Fuhrman J. Nutritarian Handbook & ANDI Food Scoring Guide. 2012; Gift of Health Press, Flemington, NJ.

[111] Fuhrman, J et. al. Changing perceptions of hunger on a high nutrient density diet. *Nutr J*. 2010;9:51

[112] Sarter, BS, Campbell T. and Fuhrman, J. Effect of a high nutrient density diet on long-term weight loss: A retrospective chart review. *Altern Ther Health Med*. 2008;14(3):48-53.

[113] Hollis, JH et. al. Effects of Concord grape juice on appetite, diet, body weight, lipid profile and antioxidant status of adults. *Am Coll Nutr.* 2009;28(5):574-82.

[114] Venables, MC et. al. Green tea extract ingestion, fat oxidation, and glucose tolerance in healthy humans. *Am J Clin Nutr.* 2008;87:778-84. Rumpler, W. et. al. Oolong tea increases metabolic rate and fat oxidation in men. *J Nutr.* 2001;131:2848-52.

[115] Hsu TF. et. al. Polyphenol-enriched oolong tea increases fecal lipid excretion. *Eur J Clin Nutr.* 2006;60:1330-36.

[116] Drew B, Dixon, A and Dixon J. Obesity management: update on orlistat. Vasc Health Risk manag. 2007;3:817-21. Rubio M et. al. Drugs in the treatment of obesity: sibutramine, orlistat and rimonabant. P*ub Health Nutr.* 2007;10:1200-5.

[117] Garza AL et. al. Natural inhibitors of pancreatic lipase as new players in obesity treatment. *Planta Med* 2011;77:773-85.

[118] He, R. Beneficial effects of oolong tea consumption on diet-induced overweight and obese subjects. *Chin J Integr Med*. 2009;15:34-41.

[119] Jackson, CL and Hu FB. Long-term associations of nut consumption with body weight and obesity. *Am J Clin Nutr.* 2014;100(S):408S.

[120] Claesson AL. et. al. Two weeks of overfeeding with candy, but not peanuts, increases insulin levels and body weight. *Scand J Clin Lab Invest*. 2009;69(5):598-5.

[121] Natoli S and McCoy P. A review of the evidence: nuts and body weight. *Asia Pac J Clin Nutr.* 2007;16(4):588-97.

[122] Natoli S and McCoy P. A review of the evidence: nuts and body weight. *Asia Pac J Clin Nutr.* 2007;16(4):88-97.

[123] Mattes RD and Dreher ML. Nuts and healthy body weight maintenance mechanisms. *Asia Pac J Clin Nutr* 2010;19(1):137-41.

[124] Boa Y et. al. Association of nut consumption with total and cause specific mortality. *N Engl J Med*. 2013;369(21):2001-11.

[125] Sabate J. Nut consumption, vegetarian diets, ischemic heart disease risk, and all-cause mortality: evidence from epidemiologic studies. *Am J Clin Nutr.* 1999;70(3 Suppl):500S-3S.

[126] West, SG. et. al. Effects of diets high in walnuts and flax oil on hemodynamic responses to stress and vascular endothelial function. *J Am Coll Nutr.* 2010;29(6):595-3.

[127] Gilsing AMJ et. al. Longitudinal changes in BMI in older adults are associated with meat consumption differentially, by type of meat consumed. *J Nutr.* 2012;142(2):340-9.

[128] Halkjaer J et. al. Dietary predictors of 5-year changes in waist circumference. *J Am Diet Assoc*. 2009;109(8):1356-66.

[129] Halkjaer J et. al. Intake of total, animal and plant protein and subsequent changes in weight or waist circumference in European men and women: the Diogenes project. *Int J Obes (Lond).* 2011;35(8):1104-13.

[130] Wang, Y et. al. Modern organic and broiler chickens sold for human consumption provide more energy from fat than protein. *Public Health Nutr.* 2010;13(3):400-8.

[131] Dhurandhar NV et. al. Effect of adenovirus infection on adiposity in chicken. *Vet Microbiol*. 1992;31(2-3):101-7.

[132] Dhurandhar NV et. al. Association of adenovirus infection with human obesity. *Obes Res*. 1997;5(5):464-9.

[133] Ddhurandhar NV. A framework for identification of infections that contribute to human obesity. Lancet Infect. Dis. 2011;11(12):963-9.

[134] Atkinson RL et. al. Human adenovirus-36 is associated with increased body weight and paradoxical reduction of serum lipids. *Int J Obes (Lond)*. 2005;29(3):281-6.

[135] Lin WY et. al. Long-term changes in adiposity and glycemic control are associated with past adenovirus infection. *Diabetes Care*. 2013;36:701-7.

[136] Dhurandhar, NV Is obesity caused by an adenovirus? Expert Rev Anti Infect Ther. 2012;10(5):521-4.

[137] Pasarica M. et. al. Adipogenic human adenovirus Ad-36 induces commitment, differentiation, and lipid accumulation in human adipose-derived stem cells. Stem Cells. 2008;26(4):969-78.

[138] Dhurandhar, NV Is obesity caused by an adenovirus? *Expert Rev Anti Infect Ther.* 2012;10(5):521-4.

[139] Zho S. Comparison of the prevalences and antimicrobial resistances of Escherichia coli isolates from different retail meats in the United States 2002 to 2008. *Appl Environ Microbiol*. 2012;7(6):1701-7.

[140] Cho B. et. al. Dectection of fecal residue on poultry carcasses by laser-induced fluorescence imaging. *J Food Sci*. 2009;74(3):154.

[141] Wallinga, D. Playing chicken: avoiding arsenic in your meat. *The Institute for Agriculture and Trade Policy.* 2006.

[142] Halpern BC et. al. The effect of replacement of methionine by homocysteine on survival of malignant and normal adult mammalian cells in culture. *Proc Nat Acad Sci*. 1974;71(4):1133-6.

[143] Guo HY et. al. Expression of the biochemical defect of methionine dependence in fresh patient tumors in primary histoculture. *Cancer Res*. 1993;53(11):2479-83.

[144] Cavuoto P Fenech MF. A review of methionine dependency and the role of methionine restriction in cancer growth control and life-span extension. *Cancer Treat. Rev.* 2012;38(6):726-36.

[145] Lopez-Torres, M and Barja G. Lowered methionine ingestion as responsible for the decrease in rodent mitochondrial oxidative stress in protein and dietary restriction possible implications for humans. *Biocim Biophys Acta*. 2008;1780(11):1337-47.

[146] The Five Worst Foods to Grill. *A Report by the Cancer Project*, July 2010.

[147] Zaidi, R et. al. Rapid detection and quantification of dietary mutagens in food using mass spectrometry and ultra performance liquid chromatography. *Food Chem*. 2012;135;2897-3.

[148] Punnen S. et. al. Impact of meat consumption, preparation, and mutagens on aggressive prostate cancer. *PLoSOne*. 2011;6(11):e27711.

[149] Figg WD. How do you want your steak prepared? *Cancer Biol Ther.* 2012;13(12):1141-42.

[150] Turesky RJ. Formation and biochemistry of carcinogenic aromatic amines in cooked meats. *Toxicol Lett*. 2007;168(3):219-27.

[151] Uribarri, J. et. al. Advanced glycation end products in foods and a practical guide to their reduction in the diet. *J Am Diet Assoc*. 2010;110(6):911-16.

[152] Age- and stage-dependent accumulation of advanced glycation end products in intracellular deposits in normal and Alzheimer's disease brains. *Cereb Cortex*. 2005;15(2);211-20.

[153] Grun F and Blumber B. Environmental obesogens: Organotins and endocrine disruption via nuclear receptor signaling. *Endocrinolgy*. 2006;147(6Supp):S50-5.

[154] Srogi K. Levels and congener distributions of PCDDs, PCDFs and dioxin-like PCBs in environmental and human samples: a review. *Environ Chem Lett*. 2008;6(1):1-28.

[155] Schecter A et. al. Brominated flame retardants in US food. *Mol Nutr Food Res*. 2008;52(2):266-72.

[156] Rantakokka P et. al. Dietary intake of organotin compounds in Finland: a market-basket study. *Food Addit Contam*. 2006;23(8):749-56.

[157] Shaw SD. Et. al. PCBs, PCDD/Fs, and organochlorine pesticides in farmed Atlantic salmon from Maine, eastern Canada, and Norway, and wild salmon from Alaska. *Environ Sci Technol*. 2006;40(17):5347-54.

[158] European Food Safety Authority; Results of the monitoring of non dioxin-like PCBs in food and feed. *EFSA Journal*. 2010;8(7):1701.

[159] Korde LA et. al. Childhood soy intake and breast cancer risk in Asian American women. *Cancer Epidemiol Biomarkers Prev.* 2009;18(4):1050-9.

[160] Magee PJ and Rowland I. Soy products in the management of breast cancer. *Curr Opinion Clin Nutr Metab Care*. 2012;15(6):586-91.

[161] Velasquez MT and Bhathena SJ. Role of dietary soy protein in obesity. *Int J Med Sci*. 2007;4(2):72-82.

[162] Park HF et. al. Genistein inhibits differentiation of primary human adipocytes. *J Nutr Biochem*. 2009;20:140-8.

[163] Sites CK et. al. Effect of a daily supplement of soy protein on body composition and insulin secretion in postmenopausal women. *Fertil Steril*. 2007;88(6):1609-17.

[164] Jenkins D. et. al. Clycaemic index: did Health Canada get it wrong? Position from the International Carbohydrate Quality Consortium (ICQC). *Brit J Nutr.* 2014;111:380-2.

[165] FAO/WHO expert consultation on carbohydrates in human nutrition. Report of a Joint FAO/WHO Expert Consultation, 1998.

[166] Tokmakidis SP, et. al. Training, detraining, and retraining effects on glycemic control and physical fitness in women with type 2 diabetes. *Horm Metab Res*. 2014;36(13):974-9.

[167] Ludwig DS. The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. *JAMA*. 2002;287:2414-23.

[168] Roberts SB. High-glycemic index foods, hunger, and obesity: is there a connection? *Nutr Rev*. 2000;58:163-9.

[169] Flint et. al. Glycemic and insulinemic responses as determinants of appetite in humans. *Am J Clin Nutr.* 2006;84:1365-73.

[170] Reynolds RC et. al. Effect of the glycemic index of carbohydrates on day-long (10h) profiles of plasma glucose, insulin, cholecystokinin and ghrelin. *Eur J Clin Nutr.* 2009;63:872-78.

[171] Alfenas RC and Mattes RD. Influence of glycemic index/load on glycemic response, appetite, and food intake in healthy humans. *Diabetes Care*. 2005;28:2123-29.

[172] Aston LM, Stokes CS and Jebb SA. No effect of a diet with a reduced glycaemic index on satiety, energy inake and body weight in overweight and obese women. *Int J Obes (Lond).* 2008;32:160-5.

[173] Niwano Y et. al. Is glycemic index of food a feasible predictor of appetite, hunger and satiety? *J Nutr Sci Vetaminol (Tokyo).* 2009;55(3):201-7.

[174] Makris AP et. al. The individual and combined effects of glycemic index and protein on glycemic response, hunger and energy intake. *Obesity*. 2011;19(12):2365-73.

[175] Rabinowitz D et. al. Patterns of hormonal release after glucose, protein and glucose plus protein. *Lancet*. 1966;2(7461):454-6.

[176] Holt SH, Miller JC and Petocz P. An insulin index of foods: the insulin demand generated by 1000-kj portions of common foods. *Am J Clin Nutr.* 1997; 66(5):1264-76. Int J Med Sci. 2007;4(2):72-82.

[177] Charlton KE et. al. Pork, beef and chicken have similar effects on acute satiety and hormonal markers of appetite. *Appetite*. 201156(1):1-8.

[178] Nuttall FQ et. al. Effect of protein ingestion on the glucose and insulin response to a standardized oral glucose load. Diabetes Care. 1984;7(5):465-70.

[179] Hung CJ et. al. Taiwanese vegetarians have higher insulin sensitivity than omnivores. *Br J Nutr.* 2006;95(1):129-35.

[180] Trepanowski JF et. al. A 21-day Daniel fast with or without krill oil supplementation improves anthropometric parameters and the cardiometabolic profile in men and women. *Nutr. Metab (Lond).* 2012;9(1):82

[181] Smith M et. al. Unrestricted Paleolithic diet is associated with unfavorable changes to blood lipids in healthy subjects. *Int J Exer Sci*. 2014;7(2):128-39.

[182] Kern PA et. al. Insulinlike growth factor action and production on adipocytes and endothelial cells from human adipose tissue. *Diabetes*. 1989;38:710-17.

[183] Carter JP, Furman T and Hutchenson HR. Preeclampsia and reproductive performance in a community of vegans. *Southern Med J*. 1987;80:692-97.

[184] Brown WJ, Miller YD and Miller R. Sitting time and work patterns as indicators of overweight and obesity in Australian adults. *Int J Obes Relat Metab Disord.* 2003;27(11):1340-6.

[185] Mummery WK. et. al. Occupational sitting time and overweight and obesity in Australian workers. *Am J Prev Med*. 2005;29(2):91-7.

[186] Forety et. al. Psychological correlates of reported physical activity in normal-weight and obese adults: the Reno diet-heart study. *Int J Obes Rel Met Dis*. 1995;19(supple 4):S69-72.

[187] Owen, N et. al. Too much sitting: the population-health science of sedentary behavior. *Exerc Sport Sci Rev.* 2010;38(3):105-113.

[188] Patel AV. Et. al. Leisure time spent sitting in relation to total mortality in a prospective cohort of US adults. *Am J Epidemiol*. 2010;172(4):419-29.

[189] Wing RR. Physical activity in the treatment of the adulthood overweight and obesity: current evidence and research issues. *Med Sci Sports Exerc*. 1999;31(suppl)S547-S552.

[190] Bertram SR, Venter I, Stewart RI. Weight loss in obese women: exercise vs. dietary education. *S Afr Med J*. 1990;78:15-18.

[191] Blonk MC, Jacobs MA, Biesheuvel EH, et al. Influences on weight loss in type 2 diabetic patients: little long-term benefit from group behaviour therapy and exercise training. *Diabetic Med*. 1994;11:449-457.

[192] Marks BL, Ward A, Morris DH, et al. Fat-free mass is maintained in women following a moderate diet and exercise program. *Med Sci Sports Exerc*. 1995;27:1243-1251.

[193] Ross R, Pedwell H, Rissanen J. Effects of energy restriction and exercise on skeletal muscle and adipose tissue in women as measured by magnetic resonance imaging (MRI). *Am J Clin Nutr.* 1995;61:1179-1185.

[194] Ross R, Rissanen J, Pedwell H, et al. Influence of diet and exercise on skeletal muscle and visceral adipose tissue in men. *J Appl Physiol*. 1996;81:2445-2455.

[195] Sweeney ME, Hill JO, Heller PA, et al. Severe vs moderate energy restriction with and without exercise in the treatment of obesity: efficiency of weight loss. *Am J Clin Nutr*. 1993;57:127-134.

[196] Wadden TA, Vogt RA, Andersen RE, et al. Exercise in the treatment of obesity: effects of four interventions on body composition,

resting energy expenditure, appetite, and mood. *J Consult Clin Psychol*. 1997;65:269-277.

[197] Garrow J. and Summerbell C. Meta-analysis: effect of exercise, with or without dieting, on the body composition of oeverweight subjects. *Eur J Clin Nutr*. 1995;49:1-10.

[198] Shaw KA. et. al. Exercise for overweight or obesity (review). *Cochrane Databse Syst Rev*. 2006;18(4):CD003817.

[199] Shaw KA. et. al. Exercise for overweight or obesity (review). *Cochrane Databse Syst Rev*. 2006;18(4):CD003817.

[200] Houghton P. *People of the great ocean*. Cambridge, Cambridge University Press, 1996.

[201] Diet, food supple and obesity in the Pacific. World Health Organization, Regional Office for the Western Pacific, 2003.

[202] Ravussin E at. al. Effects of a traditional lifestyle on obesity in Pima Indians. Diabetes Care. 1994;17(9):1067-74.

[203] Schulz LO. et. al. Effects of traditional and western environments on prevalence of type 2 diabetes in Pima Indians in Mexico and the US. *Diabetes Care*. 2006;29(8):1866-71.

[204] Haupt A. et al. Variation in the FTO gene influences food intake but not energy expenditure. *Exp Clin Endocrinol Diabetes*. Apr 2009;117(4):194-7

[205] Tanofsky-Kraff M. et al. The FTO gene rs9939609 obesity-risk allele and loss of control over eating. *Am J Clin Nutr*. 2009;90(6):1483-8

[206] Fawcett KA and Barroso I. The genetics of obesity: FTO leads the way. *Trends in Genetics*. 2010;36(6):266-74.

[207] Frayling TM. et. al. A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. Science. 2007;316(5826):889-94.

[208] Kadowaki T. et. al. The role of PPARgamma in high-fat diet-induced obesity and insulin resistance. *J Diabetes* Complications. 2002;16(1):41-5.

[209] Kubota N. et. al. PPARgamma mediates high-fat diet-induced adipocyte hypertrophy and insulin resistance. *Mol Cell*. 1999;4:597-609.

[210] Smith CE et. al. Apolipoprotein A5 and lipoprotein lipase interact to modulate anthropometric measures in Hispanics of Caribbean origin. *Obesity (Silver Spring)*. 2010;18:327-32.

[211] Zheng, XY, Zhao, SP and Yan H. The role of apolipoprotein A5 in obesity and the metabolic syndrome. *Biol. Rev*. 2013;88:490-8.

[212] Martin S. et. al. Contribution of APOA5 gene variants to plasma trighlyceride determination and to the response to both fat and glucose tolerance challenges. *Biochem Bioph Acta*. 2003;1637:217-25.

[213] Ong KL et. al. Association of a genetic variant in the apolipoprotein A5 gene with the metabolic syndrome in Chinese. *Clin Endocrin*. 2011;74:206-13.

[214] Van den Berg SA. et. al. Apolipoprotein A5 deficiency aggravates high-fat diet-induced obesity due to impaired central regulartion of food intake. *FASEB J*. 2013;27:3354-62.

[215] Sanchez-Moreno C. et. al. APOA5 gene variation interacts with dietary fat intake to modulate obesity and circulating triglycerides in a Mediterranean population. *J Nutr*. 2011;141(3):380-5.

[216] Kang R. et. al. Consumption of whole grain cereals and legumes modulates the genetic effect of the APOA5-1131C variant on changes in triglycerides and apoplipoprotein A-V concentrations in patients with impaired fasting glucose or newly diagnosed type 2 diabetes. *Trials*. 2014;15:100.

[217] Corella D. et. al. APOA5 gene variation modulates the effects of dietary fat intake on body mass index and obesity risk in the Framingham Heart Study. *J. Molecular Med*. 2007;85:119-28.

[218] Aberle J. et. al. A polymorphism in the apolipoprotein A5 gene is associated with weight loss after short-term diet. *Clin Genetics*. 2005;68:152-4.

[219] Levy E. et. al. The polymorphism at codon 54 of the FABP2 gene increases fat absorption in human intestinal explants. *J Biol Chem*. 2001;276(43):39679-84.

[220] Han TK. Effects Ala54Thr polymorphism of FABP2 on obesity index and biochemical variable in response to a aerobic exercise training. *J Exerc Nutr Biochem*. 2013;17(4):209-17.

[221] Ahmad T. et al. Lifestyle interaction with fat mass and obesity-associated (FTO) genotype and risk of obesity in apparently healthy U.S. women. *Diabetes Care*. 2011;34(3):675-80.

[222] Tsai F and Coyle WJ. The microbiome and obesity: is obesity linked to our gut flora? *Curr Gastroenterol Rep*. 2009;11(4):307-13.

[223] Shen J Obin MS and Shao L. The gut microbiota, obesity and insulin resistance. *Mol Aspects Med*. 2003;34(1):39-58.

[224] De Filippo C et. al. Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa. *PNAS*. 2010;107(33):14691-96.

[225] Backhed F. et. Al. Host-bacterial mutualism in the human intestine. *Science*. 2005;320:1647-51.

[226] Santacruz A. et. al. Gut microbiota composition is associated with body weight, weight gain and biochemical parameters in pregnant women. *Brit J Nutr*. 2010;104:83-92.

[227] Ley T, et. al. Microbial ecology: human gut microbes associated with obesity. *Nature*. 2006;444(7122):1022-3.

[228] Turnbaugh PJ et. al. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature*. 2006;444:1027-31.

[229] Carmody RN and Turnbaugh PJ. Gut microbes make for fattier fish. *Cell Host Microbe*. 2012;12(3):259-61.

[230] Ley T, et. al. Microbial ecology: human gut microbes associated with obesity. *Nature*. 2006;444(7122):1022-3.

[231] Ridaura VK et. al. But microbiota from twins discordant for obesity modulate metabolism in mice. *Science*. 2013;341:1241214.

[232] Keenan MJ et. al. Effects of resistant starch, a non-digestible fermentable fiber, on reducing body fat. *Obesity (Silver Springs)*. 2006;14:1523-34.

[233] Zhou J. et. al. Failure to ferment dietary resistant starch in specific mouse models of obesity results in no body fat loss. *J Agric Food Chem*. 2009;57:8844-51.

[234] Liszt K. et. al. Characterization of bacteria, clostridia and bacteroides in faeces of vegetarians using qpcr and pcr-dgge fingerprinting. *Ann Nutr Metabl*. 2009;54(4):253-57.

[235] http://nutritionfacts.org/video/gut-flora-obesity/

[236] Rastmanesh R. High polypheol, low probiotic diet for weight loss because of intestinal microbiota interaction. *Chem Biol Interact*. 2011;189(1-2):1-8.

[237] Turnbaugh PJ et. al. The effect of diet on the human gut microbiome: a metagenomic analysis in humanized gnotobiotic mice. *Sci. Transl. Med*. 2009.:1(6):6ra14.

[238] David LA et. al. Diet rapidly and reproducibly alters the human gut microbiome. *Nature*. 2014;505(7484:559-63.

Center for Creative Leadership®

CCL - Americas
www.ccl.org
+1 800 780 1031 (U.S. or Canada)
+1 336 545 2810 (Worldwide)
info@ccl.org

CCL - Asia Pacific
www.ccl.org/apac
+65 6854 6000
ccl.apac@ccl.org

CCL - Europe, Middle East, Africa
www.ccl.org/emea
+32 (0) 2 679 09 10
ccl.emea@ccl.org