white paper

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EXECUTIVE SUMMARY:

Obesity rates are increasing around the world. Obesity raises the risk of many chronic diseases, including heart disease, diabetes, and cancer. We have been repeatedly told that the solution to the obesity crisis is decreasing food intake by daily calorie restriction. But numerous scientific studies have shown that calorie restriction does not work. So, what's the answer? Intermittent fasting. Intermittent fasting involves a period of fasting followed by a period of eating freely. There are two major types of intermittent fasting: fasting daily for short periods of time (also called 16:8 or time restricted feeding) or fasting on certain days of the week (5:2 or alternate day fasting). Studies of intermittent fasting continuously demonstrate that these diets are effective for weight loss and chronic disease risk reduction. For instance, recent trials indicate that 10% of study participants lose 15 kg and above, 15% lose 10 kg and above, and 40% lose 5 kg and above with various intermittent fasting protocols. These diets are also very sustainable. Results from long-term studies show that people can stick to these diets for extended periods of time and maintain their weight loss by incorporating fasting into their lifestyle. Intermittent fasting has also been shown to be protective against heart disease by reducing "bad" LDL cholesterol by 10-20%, triglycerides by 20-30%, and increasing "good" HDL cholesterol by 10-15%. Diabetes risk is also reduced with fasting. Results reveal impressive reductions in insulin, insulin resistance, and in some cases, complete reversal of type 2 diabetes. Fasting may also be effective for preventing cancer. Fasting slows the growth of tumors in animals and decreases the chance of breast cancer recurrence in humans. In addition, promising research suggests these diets may protect the brain from neurodegenerative diseases, like Alzheimer's and Parkinson's, while improving memory and mood. Intermittent fasting may also help you live longer. Early studies in animals show that fasted mice live longer than mice eating freely every day. In humans, it's been shown that fasting reduces several biomarkers for aging, which can help extend lifespan. In summary, intermittent fasting is a sustainable and simple diet plan that can be adjusted to fit into anyone's lifestyle. Fasting offers incredible health benefits, including weight loss and protection from several diseases including heart disease, diabetes, cancer, Alzheimer's and Parkinson's. Fasting should unquestionably be prioritized as a first line of therapy to combat obesity and obesity-related diseases.

1. THE BIG PROBLEM:

Obesity is rife. Obesity rates have almost tripled since the 1970s [1]. At present, 39% of adults are overweight and 13% are obese worldwide, with women being far more likely to be obese than men [1]. Being overweight or obese raises the risk of developing several diseases including, heart disease, diabetes, kidney disease, liver disease, sleep apnea, osteoarthritis, and some cancers [1-3]

Obesity is the number one killer of people worldwide. In fact, obesity is killing loads more people that wars, terrorism, and gun violence combined. Globally, 2.8 million adults die each year (and nearly 8000 die each day) as a result of being overweight or obese [3]. It's also been shown that 44% of the diabetes burden, 23% of the heart disease burden, and 40% of the cancer burden is attributable to being overweight or obese. The rising death toll has lead numerous countries and continents, such as Australia [4], America [2], Canada [5], Europe [6] Asia and the Pacific [7], to declare obesity a national health crisis [8].

Treating obesity and obesity-related diseases costs trillions of dollars per year [9]. Globally, 2 trillion dollars is spent on obesity, which is second only to what is spent on war and terrorism [9]. As a person's weight increases, so does the number of sick days and dollars spent on health care. In Australia, obesity was associated with over 4 million days lost from work and 4 billion dollars in lost productivity [10]. In addition, obesity is costing Australia 4 billion dollars annually in health care costs [10]. The same goes for the UK, where 10 billion dollars is spent annually on medical expenses to treat conditions related to being overweight or obese [11]. It's also been shown that in America, obese individuals spend 42% more on health care costs when compared to healthy weight individuals [12].

We have been repeatedly told that the solution to the obesity crisis is decreasing food intake by daily calorie restriction. But for the majority of people calorie restriction does not work. It works short-term, and it works in theory, but no one can do it in practice for long periods of time [13, 14]. Telling people to eat less and monitor calories every day is not sustainable. Exercising also doesn't work for weight loss [15, 16]. When people exercise, they tend eat more, so it's almost impossible to lose weight by exercising alone. The weight loss industry globally is failing miserably. And people are frustrated...understandably so! So, what's the answer?

2. INTERMITTENT FASTING IS THE ANSWER:

Intermittent fasting involves a period of fasting followed by a period of eating freely. While the word "fasting" may sound a bit scary, it's important to remember that fasting is really just a short period of "not eating". Fasting doesn't equate to starvation, and with all intermittent fasting diets, you get to eat every day. Fasting is really more about "when to eat" rather than not eating.

There are two major types of intermittent fasting: fasting daily for short periods of time (also called 16:8 or time restricted feeding) or fasting on certain days of the week (like 5:2 or alternate day fasting).

The great thing about intermittent fasting is that it doesn't require you to eliminate any food groups, count carbs, or avoid alcohol, so it's very convenient and easy to follow. In fact, the majority of scientific studies demonstrate super high adherence rates with all fasting diets. Most studies show that people stick to the plan on 90% of days [17, 18], and because of this high level of adherence, people lose substantial amounts of weight. Recent research shows that 10% of study participants lose 15 kg and above, 15% lose 10 kg and above, and 40% lose 5 kg and above. [18-30]. On top of that, these diets are also very sustainable. Results from long-term studies show that people can stick to these diets for extended periods of time and maintain their weight loss by incorporating fasting into their lifestyles. [24, 29].

Where did the concept of intermittent fasting come from? Fasting is not new. Humans have fasted throughout history for a variety of reasons including food scarcity or religious reasons. In the early 1900s, scientists started to examine the effects of fasting in mice. They noticed that the fasted animals lived longer and were less likely to develop all sorts of diseases, like heart disease, diabetes and cancer [31, 32]. It wasn't until recently that the concept of intermittent fasting was tested in humans. And as you'll see below, the results from these human studies speak for themselves

3. BEYOND 5:2

Intermittent fasting is a phenomenon that is sweeping the world, but a lot of people are still uneducated about it. It's not just one diet or one book. There are loads of different methods of intermittent fasting. Although 5:2 is the most popular method, it's definitely not the only way to fast. It's important to remember that 5:2 is part of intermittent fasting, but it's a bigger phenomenon than that. Think of intermittent fasting as an umbrella term used to described several different diets like 4:3, alternate Day Fasting, 16:8/Leangains, and even more extreme methods like The Warrior Diet (aka 20:4).

4. ALL THE DIFFERENT METHODS:

5:2: The 5:2 diet involves 2 days of fasting per week, where you lower to your calorie intake to 500 calories per day. On the other 5 days of the week, you can eat normally, without having to count calories or monitor food intake. You can choose any two days of the week to fast. However, most people find it easier to fast during the week (when their schedule is more routine), rather than on the weekend. The fast day meal can be consumed as one meal or as several small 100-200 calorie meals throughout the day [25].There are no strict diet prescriptions for the fast day, but it is important to consume at least 50 grams of protein to keep feeling full [33]. High protein shakes (lots of Greek yogurt combined with milk, fruits and veggies) or high protein salads (kale plus chicken, tuna, tofu, or legumes) are great options for the fast day meal.

4:3 / ALTERNATE DAY FASTING: Alternate day fasting is similar to 5:2, but instead of fasting only 2 days per week, you fast every other day. More specifically, with alternate day fasting, you alternate between a 500-calorie fast day and a normal eating day, every other day. If fasting every other day seems overwhelming, you can also do 4:3, which involves 3 fast days per week (generally Monday, Wednesday, and Friday). Similar to 5:2, it's important to eat at least 50 grams of protein on the fast day to keep hunger at bay [33]. The fast day meal can be consumed all in one go, or as mini meals throughout the day [25].

16:8 / LEANGAINS: The 16:8 diet, also known scientifically as "time restricted feeding", is a little different from 5:2 and alternate day fasting in that you fast a little every day. With 16:8, you are free to eat during an 8-hour window (let's say 10am-6pm) then you would water fast the rest of the day (6pm-10am). You can choose whatever 8-hour window works for you. If you can't go without breakfast, placing your eating window earlier in the day (8am-4pm) might be best. If you can't survive without dinner, placing the window later in the day (12pm-8pm) is a good idea. During the 8-hour eating window, you don't need to count calories or monitor food intake in anyway. Recent research shows that people following 16:8 decrease their calorie intake by about 300 calories/day, without calorie counting [23, 34] By simply limiting the period of eating to 8 hours, natural calorie restriction occurs without all the fuss of constantly recording calories. Leangains is another form of 16:8 that is popular with the bodybuilding community. Leangains differs from regular 16:8 in that it has specific diet composition recommendations for workout days versus non-workout days. For instance, on workout days, carbs are prioritized over fat, while on non-workout days, fat is prioritized over carbs.

20:4 / The Warrior Diet: The 20:4 diet is a more extreme version of 16:8. Instead of eating within an 8-hour window each day, the 20:4 diet requires you to consume all of your calories within a 4-hour window. During the other 20 hours of the day, only water is consumed. Similar to 16:8, you can place the 4-hour eating window at any time in the day that works best for you and you don't need to count calories. The Warrior Diet is a form of 20:4 that recommends skipping breakfast and lunch and consuming one large meal per day in the evening. Counting calories during the evening meal is not necessary with The Warrior Diet, but it's recommended that you stop eating when you feel full.

5. KEY SCIENTIFIC FINDINGS:

INTERMITTENT FASTING IS EFFECTIVE FOR WEIGHT LOSS, BELLY FAT LOSS, AND MUSCLE RETENTION:

BODY WEIGHT: Recent scientific evidence shows that intermittent fasting is very effective for weight loss. In the longest most comprehensive study of intermittent fasting to date, 12-months of alternate day fasting reduced body weight by 6% (6 kg) in adults with obesity [29]. This study also showed that alternate day fasting helped participants keep the weight off during a 6-month weight maintenance period. Interestingly, **postmenopausal women** lost twice as much weight (11%) with alternate day fasting when compared to premenopausal women (5%) [19], suggesting that fasting is particularly beneficial for postmenopausal women.

Intermittent fasting is also effective for weight loss when applied for shorter periods of time. In a 6-month study, the 5:2 diet produced 7% (6 kg) weight loss in young overweight women [24]. 5:2 has also been shown to help **people with type 2 diabetes** lower body weight by 6% (8 kg) after 3 months [21]. Multiple studies of alternate day fasting reveal 4-7% (4-8 kg) reductions in body weight after 2-3 months of diet [18, 20, 22, 25-27]. Fasting can also help **normal weight individuals** shed those last few pounds. For example, after 3 months of alternate day fasting, normal weight subjects lost 2-5 kg and became much leaner [30, 35]. 16:8 also called "time restricted feeding" is another great way to lose weight. After 4-months of time restricted feeding, overweight men and women lost 3% (3 kg) of body weight [34]. Similarly, after 3 months of 16:8, individuals with obesity decreased their body weight by 3% (3 kg) [23]. In both of these time restricted feeding studies, participants naturally reduced their calorie intake by about 20% (about 300 calories/day) without calorie counting [23, 34].

BELLY FAT: Intermittent fasting is also a great way to lose belly fat. After 6 months of 5:2, overweight women

lost 4 cm from their waistline [24]. In type 2 diabetics, 5:2 was shown to lower belly fat by 0.6 kg after 3 months [21]. Other forms of fasting, like alternate day fasting, are also extremely effective for belly fat loss. Short-term studies of alternate day fasting show that waist circumference decreases by 5-7 cm after 2-3 months [18, 20, 22, 25-27, 30]. Longer-term studies of alternate day fasting demonstrate 0.4 kg (7 cm) reductions in belly fat after 12 months [29]. 16:8 is also effective for trimming waistlines. After 3 months, adult subjects with obesity reduced belly fat by 0.2 kg by simply limiting their eating window to 8 hours per day [23].

MUSCLE MASS: One of the most fascinating things about intermittent fasting is that it helps maintain muscle mass during weight loss. In general, when someone is losing weight, about 75% of the weight lost is fat, and 25% is muscle. With intermittent fasting, only 10% of the weight lost is muscle, leaving the other 90% to be lost as fat. Both short-term (2-3 month) [18, 20, 27, 30] and long-term studies (12 month) [29] of alternate day fasting show that muscle mass is almost completely retained during periods of weight loss. In line with these findings, 5:2 and 16:8 also have no negative impact on muscle mass after 3 months of diet [23, 24].

It's also important to point out that muscle mass is a key determinant of metabolic rate or "metabolism" [36]. Holding on to muscle helps keep metabolism revved up, even while dropping pounds. Since intermittent fasting does not result in muscle loss, metabolism remains high [18, 20, 27, 30], which can help keep weight loss on track.

INTERMITTENT FASTING REDUCES HEART DISEASE RISK:

CHOLESTEROL LEVELS: Intermittent fasting is a powerful way to improve cholesterol levels. An increasing number of studies suggests that 5:2, alternate day fasting, and 16:8 are effective diet strategies for reducing "bad" LDL cholesterol by 10-20%, increasing "good" HDL cholesterol by 10-15%, and lowering triglycerides by 20-30%. For instance, in a 12-month study of alternate day fasting, HDL cholesterol increased by ~10% and triglycerides decreased by ~25% after the weight loss phase [29]. This study also showed that alternate day fasting may be more effective than daily calorie restriction to improve HDL cholesterol levels [29]. Short-term studies of alternate day fasting demonstrate impressive decreases in LDL cholesterol, triglycerides and striking increases in HDL cholesterol [18, 20, 22, 26, 27, 30, 35]. After 6 months of 5:2, young overweight women experienced 15% decreases in triglyceride levels and 10% decreases in LDL cholesterol levels [24]. In a recent 3-month study of 16:8, triglyceride levels decreased by 15% after 3 months in adults with obesity [23]. Similarly, 2 months of 16:8 lowered triglycerides by ~10% and increased HDL cholesterol by ~10% in young men [28]. These studies show that intermittent fasting is an amazing way to improve cholesterol profiles and protect against heart disease.

BLOOD PRESSURE: Intermittent fasting can also produce dramatic improvements in blood pressure. Alternate day fasting has been shown to lower systolic blood pressure by 5-10 mm Hg in adults with obesity [18, 20, 22] as well as normal weight individuals [30]. 5:2 is also effective for decreasing blood pressure. After 6 months of fasting 2 days per week, young overweight women decreased systolic and diastolic blood pressure by 4 mm Hg [24]. As for 16:8, men and women with obesity experienced 7 mm Hg reductions in systolic blood pressure after 3 months of fasting for 16 hours per day [23]. In sum, blood pressure is improved with 5:2, alternate day fasting, and 16:8 after relatively short periods of fasting (2-3 months).

INFLAMMATION: Certain inflammatory markers, such as TNF-alpha and IL-6, have been linked to the development of heart disease [37, 38]. Research shows that reducing blood levels of TNF-alpha and IL-6 may help lower the risk of heart attacks and strokes [37, 38]. The effects of intermittent fasting on these inflammatory mediators has been examined in one human study. After 2 months of 16:8, young men experienced 8% and 19% decreases in TNF-alpha and IL-6, respectively [28]. Studies examining the effects of 5:2 and alternate day fasting on these inflammatory parameters are currently underway, and the results should be published soon.

INTERMITTENT FASTING REDUCES DIABETES RISK:

INSULIN AND GLUCOSE: In addition to lowering heart disease risk, intermittent fasting is also an effective strategy to prevent type 2 diabetes. Both short-term and long-term studies of 5:2 and alternate day fasting show potent 20% reductions in insulin levels in adults with obesity [20, 24, 29]. Prediabetic subjects experience even greater decreases in insulin levels (30%), as demonstrated by a recent 12-month study of alternate day fasting [39]. Although only a handful of studies have examined how 16:8 impacts these diabetes risk parameters, preliminary findings show impressive 30% reductions in insulin and glucose by this daily fasting regimen [28].

INSULIN RESISTANCE: Insulin resistance is a serious condition where insulin becomes ineffective at clearing glucose from the blood stream [40]. As a result, circulating

glucose levels rise substantially , putting people at high risk for developing diabetes [40]. Intermittent fasting produces remarkable improvements in insulin resistance in healthy and prediabetic individuals. For instance, both 5:2 and alternate day fasting have been shown to lower insulin resistance by 20-25% in healthy men and women with obesity [24, 29]. More recently, it was shown alternate day fasting lowered insulin to even greater extent (45%) in people with prediabetes [39]. 16:8 is another effective strategy for improving insulin resistance. After 2 months of fasting 16 hours per day, insulin resistance decreased by 40% in young men [28]. These findings suggest that intermittent fasting may slow, and possibly even reverse, the progression of prediabetes to type 2 diabetes, by improving glucose control.

REVERSING TYPE 2 DIABETES: Dr. Jason Fung is a specialist physician at the Scarborough Hospital, Canada, and is in the process of publishing human data examining how intermittent fasting can reverse type 2 diabetes. His Intensive Dietary Management Program, established in 2013, has treated thousands of patients with low carbohydrate diets and fasting protocols. Preliminary findings from his clinic suggest that water fasting 2-3 days per week may help control glucose, lower insulin levels, and potentially eliminate the need for diabetes medications. These exciting findings offer promise for the use of intermittent fasting as a way to manage or reverse type 2 diabetes. [64, 65, 66]

INTERMITTENT FASTING MAY HELP PREVENT CANCER:

Preliminary research also suggests that intermittent fasting may be effective for preventing cancer. Animal studies have shown that fasting slows the growth of tumors located in prostate and breast tissue [41-43]. These studies also show that fasting is effective for reducing IGF-1 (insulin-like growth factor 1) by up to 50% [44]. IGF-1 promotes the growth of cancer cells, so decreasing IGF-1 can help reduce cancer risk [45]. In addition, fasting can induce autophagy in cells. Autophagy, or "self-eating", is an important process by which our bodies eliminate damaged cellular components [46]. In a ground-breaking (and Nobel Prize winning) experiment by Dr. Yoshiri Ohsumi, it was shown that fasting induces autophagy [47], which can prevent the development of tumors in malfunctioning cells [48]. These fascinating findings help explain what mechanisms are involved in the anti-cancer effects of fasting.

As for human trials, it was recently shown that prolonged overnight fasting may be effective for reducing breast cancer recurrence [49]. This study followed 2400 women with early stage breast cancer. The researchers found that women who fasted more than 13 hours per night had a much lower risk of disease recurrence when compared to women who fasted less than 13 hours per night. The effects of 5:2 on cancer risk has also been examined. After 6 months of fasting 2 days per week, young overweight women experienced improvements in a number of cancer markers, including leptin, insulin, insulin resistance, and inflammatory markers [24].

Periodic fasting is another type of fasting that may lower cancer risk. Periodic fasting involves lowering food intake to 700-1000 calories/day for the first 5 days of every month, and eating freely throughout the rest of the month. In a recent animal study, it was shown that periodic fasting slowed the growth of breast tumors in mice [50, 51]. In addition, the study demonstrated that fasting increased levels of certain immune cells, such as T-cells, B-cells, and "natural killer" cells, which infiltrate tumors and destroy them. Periodic fasting also improved the effectiveness of chemotherapy by making chemotherapy drugs more effective at attacking cancer cells [50, 51].

These exciting findings suggest that different forms of fasting (5:2, periodic fasting, and simple overnight fasting) may be effective for preventing, several different types of cancer.

INTERMITTENT FASTING BENEFITS YOUR BRAIN:

Intermittent fasting plays an important role in improving brain health and protecting the brain from neurodegenerative diseases, like Alzheimer's and Parkinson's. Dr. Mark Mattson at the National Institute on Aging in the US has been studying the effects of fasting on brain health for the past 20 years. His animal studies show that fasting 2 days per week shocks the brain (in a good way), which in turn promotes the creation of new neurons [52-54]. These new neurons are much more resistant to protein plaque accumulation, which are a major cause of Alzheimer's and Parkinson's disease.

Dr. Mattson has also shown that intermittent fasting may produce brain changes that improve memory and mood. During periods of fasting, the body produces a protein called BDNF, or brain-derived neurotrophic factor. BDNF stimulates the growth of new neurons and strengthens neural connections [52-54]. The strengthening of these brain connections boosts memory and may also have anti-depressant effects [55, 56]. In addition, Mattson's research shows that ketone bodies (produced after 12 hours of fasting) have a protective effect on neurons by helping them better cope with stress and resist disease [57]. Ketones also promote positive changes in the structure of the synapses important for learning, memory and overall brain health [57].

Taken together, this suggests intermittent fasting is a promising way of improving brain health and preventing degenerative diseases.

INTERMITTENT FASTING MAY EXTEND LIFE SPAN:

Intermittent fasting may also help you live longer. Early studies in animals show that fasted mice live longer than mice eating freely every day [31, 32]. In humans, it's been demonstrated that fasting reduces several biomarkers for aging, heart disease, cancer and diabetes, which can help to extend lifespan [55]. Until recently, researchers didn't have a good understanding of how fasting could increase life expectancy. In a very recent study, researchers at Harvard University discovered that fasting may increase longevity by manipulating the activity of mitochondrial networks in our cells [58]. Mitochondria are tiny powerhouses that regulate cellular metabolism. The study showed that intermittent fasting alters mitochondrial networks in a way that keeps mitochondria in a "youthful" state. These findings are another step forward in helping us understand how fasting can increase life span and promote healthy aging.

MYTHS OF INTERMITTENT FASTING PROVEN UNTRUE BY SCIENTIFIC FINDINGS:

- **Skipping breakfast slows metabolism and makes you put on weight:** Not true! Evidence from well controlled clinical studies [59, 60] show that there is no causal link between breakfast skipping and a sluggish metabolism or weight gain. In fact, recent findings show that skipping breakfast may actually help reduce daily calorie intake by 400 calories per day [60]. In addition, research shows that skipping breakfast actually boosts your metabolism (by about 50 calories) and also gives your body more time in fat-burning mode [61].

- **When you stop eating, you go into starvation mode:** Not true! There are no studies to date that show that intermittent fasting puts your body into starvation mode. In fact, it seems that long term calorie restriction is far likelier to induce a metabolic slow down than intermittent fasting [62].

- **Intermittent fasting slows metabolism:** Not true! Muscle is a key factor in determining metabolism or "metabolic rate" [36]. When muscle is lost, metabolic rate slows down. When muscle is gained, metabolic rate goes up. Intermittent fasting has been shown in numerous scientific studies to help preserve muscle mass during weight loss thereby preventing metabolic slowdowns [18, 20, 27, 30].

- **People will undo all their work from fast days by 'blowing' all their calories on non-fast days:** Not true! Findings from recent intermittent fasting studies show that people only consume about 10% more food (about 200 calories) more on feast days [17, 18] than they would usually eat. In order to undo all the work from the fast day, a person would need to consume 1000+ calories on the feast day. Since this doesn't happen, weight loss remains high and constant during intermittent fasting.

- **Intermittent Fasting makes you hungry all the time:** Not true! Although you may feel a bit hungry on the first 3-5 fast days, this hunger will subside very quickly. Evidence from human trials shows that hunger decreases and fullness increases on the fast day after a about a week [17, 63]. So even though the first week may be difficult, rest assured that the hunger pangs will not last for long.

6. CONCLUSION:

Intermittent fasting research is a rapidly expanding field. There have been an increasing number of studies on the different methods of intermittent fasting, and all of them boast impressive adherence, weight loss success, and sustainability long-term. More and more scientific evidence is accumulating that fasting may be an effective way to prevent multiple diseases, including heart disease, diabetes, cancer, Alzheimer's, and Parkinson's. It's also been shown that occasional fasting may help us live longer.

Scientists around the world are publishing exciting new findings every day, not just on the weight loss benefits, but also the health benefits of intermittent fasting. It's not just one scientist, it's many. And it's becoming pretty apparent that the more we research intermittent fasting, the more benefits we'll discover.

Intermittent fasting is flexible, simple, and it can be adjusted to fit into anyone's lifestyle. There are several different types of intermittent fasting to choose from. If you like the idea of being able to eat freely several times a week, then 5:2, 4:3 or alternate day fasting is probably right for you. If you would prefer eating liberally within a certain window of time each day, then 16:8 or 20:4 is your best bet. Just remember to choose the diet that works best with your lifestyle and personal preferences. At the end of the day, whichever method works for you, and is sustainable, is what's best. Intermittent fasting offers that freedom.

REFERENCES

1. Organization., W.H. Obesity Facts. 2017; Available from: http://www.who.int/mediacentre/factsheets/fs311/en/.
2. Jensen, M.D., et al., 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. Circulation, 2014. 129(25 Suppl 2): p. S102-38.
3. Obesity., E.A.f.t.S.o. Obesity Facts and Figures. 2017; Available from: http://easo.org/education-portal/obesity-facts-figures/.
4. Government., A.I.o.H.a.W.A., Impact of overweight and obesity as a risk factor for chronic conditions. 2017.
5. Lau, D.C., et al., 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children [summary]. CMAJ, 2007. 176(8): p. S1-13.
6. Yumuk, V., et al., European Guidelines for Obesity Management in Adults. Obes Facts, 2015. 8(6): p. 402-24.
7. Helble M, F.K., The imminent obesity crisis in Asia and the Pacific. 2017, Asian Development Bank Institute.
8. Gregg, E.W. and J.E. Shaw, Global Health Effects of Overweight and Obesity. N Engl J Med, 2017. 377(1): p. 80-81.
9. Institute., M.G., Overcoming obesity: An initial economic analysis. 2014.
10. Australia., G.o., Obesity in Australia. 2017.
11. Committee., H.o.C.H., Childhood obesity—brave and bold action. 2015.
12. America., B.P.f.a.H., The healthcare costs of obesity. 2017.
13. Pieper, C., et al., Development of adherence metrics for caloric restriction interventions. Clin Trials, 2011. 8(2): p. 155-64.
14. Racette, S.B., et al., One year of caloric restriction in humans: feasibility and effects on body composition and abdominal adipose tissue. J Gerontol A Biol Sci Med Sci, 2006. 61(9): p. 943-50.
15. Foster-Schubert, K.E., et al., Effect of diet and exercise, alone or combined, on weight and body composition in overweight-to-obese postmenopausal women. Obesity (Silver Spring), 2012. 20(8): p. 1628-38.
16. Pontzer, H., et al., Constrained Total Energy Expenditure and Metabolic Adaptation to Physical Activity in Adult Humans. Curr Biol, 2016. 26(3): p. 410-7.
17. Klempel, M.C., et al., Dietary and physical activity adaptations to alternate day modified fasting: implications for optimal weight loss. Nutr J, 2010. 9: p. 35.
18. Varady, K.A., et al., Short-term modified alternate-day fasting: a novel dietary strategy for weight loss and cardioprotection in obese adults. Am J Clin Nutr, 2009. 90(5): p. 1138-43.
19. Barnosky A, K.C., Trepanowski JF, Hoddy KK, Gabel K, Varady KA., Effect of alternate day fasting on markers of bone metabolism: An exploratory analysis of a 6-month randomized controlled trial. Nutrition and Healthy Aging, 2018. In press.
20. Bhutani, S., et al., Alternate day fasting and endurance exercise combine to reduce body weight and favorably alter plasma lipids in obese humans. Obesity (Silver Spring), 2013. 21(7): p. 1370-9.
21. Carter, S., P.M. Clifton, and J.B. Keogh, The effects of intermittent compared to continuous energy restriction on glycaemic control in type 2 diabetes; a pragmatic pilot trial. Diabetes Res Clin Pract, 2016. 122: p. 106-112.
22. Eshghinia, S. and F. Mohammadzadeh, The effects of modified alternate-day fasting diet on weight loss and CAD risk factors in overweight and obese women. J Diabetes Metab Disord, 2013. 12(1): p. 4.
23. Gabel K, H.K., Kroeger CM, Trepanowski JF, Varady KA., Time restricted feeding (16:8) for weight loss in adults with obesity. Nutrition and Healthy Aging, 2018. In press.
24. Harvie, M.N., et al., The effects of intermittent or continuous energy restriction on weight loss and metabolic disease risk markers: a randomized trial in young overweight women. Int J Obes (Lond), 2011. 35(5): p. 714-27.
25. Hoddy, K.K., et al., Meal timing during alternate day fasting: Impact on body weight and cardiovascular disease risk in obese adults. Obesity (Silver Spring), 2014. 22(12): p. 2524-31.
26. Johnson, J.B., et al., Alternate day calorie restriction improves clinical findings and reduces markers of oxidative stress and inflammation in overweight adults with moderate asthma. Free Radic Biol Med, 2007. 42(5): p. 665-74.
27. Klempel, M.C., C.M. Kroeger, and K.A. Varady, Alternate day fasting (ADF) with a high-fat diet produces similar weight loss and cardio-protection as ADF with a low-fat diet. Metabolism, 2013. 62(1): p. 137-43.
28. Moro, T., et al., Effects of eight weeks of time-restricted feeding (16/8) on basal metabolism, maximal strength, body composition, inflammation, and cardiovascular risk factors in resistance-trained males. J Transl Med, 2016. 14(1): p. 290.
29. Trepanowski, J.F., et al., Effect of Alternate-Day Fasting on Weight Loss, Weight Maintenance, and Cardioprotection Among Metabolically Healthy Obese Adults: A Randomized Clinical Trial. JAMA Intern Med, 2017. 177(7): p. 930-938.
30. Varady, K.A., et al., Alternate day fasting for weight loss in normal weight and overweight subjects: a randomized controlled trial. Nutr J, 2013. 12(1): p. 146.
31. Carlson, A.J. and F. Hoelzel, Apparent prolongation of the life span of rats by intermittent fasting. J Nutr, 1946. 31: p. 363-75.
32. Kendrick, D.C., The effects of infantile stimulation and intermittent fasting and feeding on life span in the black-hooded rat. Dev Psychobiol, 1973. 6(3): p. 225-34.
33. Veldhorst, M., et al., Protein-induced satiety: effects and mechanisms of different proteins. Physiol Behav, 2008. 94(2): p. 300-7.
34. Gill, S. and S. Panda, A Smartphone App Reveals Erratic Diurnal Eating Patterns in Humans that Can Be Modulated for Health Benefits. Cell Metab, 2015. 22(5): p. 789-98.
35. Heilbronn, L.K., et al., Alternate-day fasting in nonobese subjects: effects on body weight, body composition, and energy metabolism. Am J Clin Nutr, 2005. 81(1): p. 69-73.
36. Sparti, A., et al., Relationship between resting metabolic rate and the composition of the fat-free mass. Metabolism, 1997. 46(10): p. 1225-30.
37. Bacchiega, B.C., et al., Interleukin 6 Inhibition and Coronary Artery Disease in a High-Risk Population: A Prospective Community-Based Clinical Study. J Am Heart Assoc, 2017. 6(3).
38. Feldman, A.M., et al., The role of tumor necrosis factor in the pathophysiology of heart failure. J Am Coll Cardiol, 2000. 35(3): p. 537-44.
39. Varady KA, T.J., Kroeger CM., Alternate day fasting produces superior reductions versus daily calorie restriction in insulin resistance and other metabolic disease risk paramters in prediabetic adults. Submitted to Nutrition Journal, 2018.

40. Kahn, S.E., R.L. Hull, and K.M. Utzschneider, Mechanisms linking obesity to insulin resistance and type 2 diabetes. Nature, 2006. 444(7121): p. 840-6.
41. Berrigan, D., et al., Adult-onset calorie restriction and fasting delay spontaneous tumorigenesis in p53-deficient mice. Carcinogenesis, 2002. 23(5): p. 817-22.
42. Bonorden, M.J., et al., Cross-sectional analysis of intermittent versus chronic caloric restriction in the TRAMP mouse. Prostate, 2009. 69(3): p. 317-26.
43. Cleary, M.P., et al., Weight-cycling decreases incidence and increases latency of mammary tumors to a greater extent than does chronic caloric restriction in mouse mammary tumor virus-transforming growth factor-alpha female mice. Cancer Epidemiol Biomarkers Prev, 2002. 11(9): p. 836-43.
44. Lee, C. and V.D. Longo, Fasting vs dietary restriction in cellular protection and cancer treatment: from model organisms to patients. Oncogene, 2011. 30(30): p. 3305-16.
45. Renehan, A.G., et al., Insulin-like growth factor (IGF)-I, IGF binding protein-3, and cancer risk: systematic review and meta-regression analysis. Lancet, 2004. 363(9418): p. 1346-53.
46. White, E., The role for autophagy in cancer. J Clin Invest, 2015. 125(1): p. 42-6.
47. Komatsu, M., et al., Impairment of starvation-induced and constitutive autophagy in Atg7-deficient mice. J Cell Biol, 2005. 169(3): p. 425-34.
48. Choi, K.S., Autophagy and cancer. Exp Mol Med, 2012. 44(2): p. 109-20.
49. Marinac, C.R., et al., Prolonged Nightly Fasting and Breast Cancer Prognosis. JAMA Oncol, 2016. 2(8): p. 1049-55.
50. Di Biase, S., et al., Fasting-Mimicking Diet Reduces HO-1 to Promote T Cell-Mediated Tumor Cytotoxicity. Cancer Cell, 2016. 30(1): p. 136-146.
51. Wei, M., et al., Fasting-mimicking diet and markers/risk factors for aging, diabetes, cancer, and cardiovascular disease. Sci Transl Med, 2017. 9(377).
52. Anson, R.M., et al., Intermittent fasting dissociates beneficial effects of dietary restriction on glucose metabolism and neuronal resistance to injury from calorie intake. Proc Natl Acad Sci U S A, 2003. 100(10): p. 6216-20.
53. Deltheil, T., et al., Behavioral and serotonergic consequences of decreasing or increasing hippocampus brain-derived neurotrophic factor protein levels in mice. Neuropharmacology, 2008. 55(6): p. 1006-14.
54. Duan, W., Z. Guo, and M.P. Mattson, Brain-derived neurotrophic factor mediates an excitoprotective effect of dietary restriction in mice. J Neurochem, 2001. 76(2): p. 619-26.
55. Longo, V.D. and M.P. Mattson, Fasting: molecular mechanisms and clinical applications. Cell Metab, 2014. 19(2): p. 181-92.
56. Mattson, M.P., S. Maudsley, and B. Martin, BDNF and 5-HT: a dynamic duo in age-related neuronal plasticity and neurodegenerative disorders. Trends Neurosci, 2004. 27(10): p. 589-94.
57. Maalouf, M., J.M. Rho, and M.P. Mattson, The neuroprotective properties of calorie restriction, the ketogenic diet, and ketone bodies. Brain Res Rev, 2009. 59(2): p. 293-315.
58. Weir, H.J., et al., Dietary Restriction and AMPK Increase Lifespan via Mitochondrial Network and Peroxisome Remodeling. Cell Metab, 2017.
59. Dhurandhar, E.J., et al., The effectiveness of breakfast recommendations on weight loss: a randomized controlled trial. Am J Clin Nutr, 2014. 100(2): p. 507-13.
60. Levitsky, D.A. and C.R. Pacanowski, Effect of skipping breakfast on subsequent energy intake. Physiol Behav, 2013. 119: p. 9-16.
61. Nas, A., et al., Impact of breakfast skipping compared with dinner skipping on regulation of energy balance and metabolic risk. Am J Clin Nutr, 2017. 105(6): p. 1351-1361.
62. Martin, C.K., et al., Effect of calorie restriction on resting metabolic rate and spontaneous physical activity. Obesity (Silver Spring), 2007. 15(12): p. 2964-73.
63. Hoddy, K.K., et al., Changes in hunger and fullness in relation to gut peptides before and after 8 weeks of alternate day fasting. Clin Nutr, 2016. 35(6): p. 1380-1385.
64. Fung, J. The Obesity Code. Greystone Books, Canada. 2016.
65. Fung, J. The Complete Guide To Fasting. Simon & Schuster, USA. 2016.
66. Ku, M., Ramos, M.J., Fung, J., Therapeutic fasting as a potential effective treatment for type 2 diabetes: A 4-month case study. J Insul Resist, 2017. 2(1): p. 1-5.


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