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Intermittent fasting and reduction of cardiovascular disease risk

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Table of Contents

Intermittent fasting and reduction of cardiovascular disease risk

Abstract

Background: Cardiovascular disease remains one of the leading causes of death worldwide. Intermittent fasting is a unique intervention that is beginning to be studied more extensively for weight loss, positive alterations in serum lipid profile, and improvement of insulin resistance which are all modifiable risk factors for the development of cardiovascular disease.

Purpose: The research question at the center of this literature review is: does the addition of intermittent fasting reduce the risk of developing cardiovascular disease? The reduction of cardiovascular disease was studied through alterations in weight, cholesterol, and diabetic labs.

Methods: A comprehensive literature review was conducted using academic search premier ultimate and pubmed using the search terms intermittent fasting, time restricted feeding, weight loss, lipid profile, diabetes, and insulin resistance. Inclusion criteria were primary studies that were published within the last 5 years. Exclusion criteria were review articles and primary studies published prior to 2017.

Conclusions: Intermittent fasting may aid in reductions of modifiable risk factors for developing cardiovascular disease including body weight, dyslipidemia, and insulin resistance. More research consisting of large, randomized controlled trials is necessary to reproduce the results to incorporate intermittent fasting into medical guidelines.

Key Words: intermittent fasting, time-restricted feeding, obesity, BMI, lipid, insulin, diabetes.

Introduction:

Cardiovascular diseases (CVD) are the leading cause of death worldwide and include disorders like coronary heart disease, cerebrovascular disease, and rheumatic heart disease among others. 17.9 million people die each year from cardiovascular disease.[1] Many risk factors in the development of cardiovascular disease are modifiable, meaning they can be consciously manipulated by the patient. Important modifiable risk factors for the development of cardiovascular diseases include elevated blood glucose, elevated blood lipids, overweight, or obesity.[1] All of those risk factors can be primarily controlled through a healthy lifestyle such as a balanced diet, frequent exercise, and low intake of tobacco products and alcohol. These modifiable risk factors are interdependent of each other and patients who suffer from cardiovascular disease often have multiple at once.

Considering that CVD accounts for 32% of deaths worldwide,[1] it is important to investigate whether other interventions may lead to reductions in modifiable risk factors. Well-studied strategies to prevent or decrease the development of CVD include exercise, a balanced diet, and portion control, which are all considered to be within the control of the patient. By improving the modifiable risk factors of weight, dyslipidemia, and insulin resistance, there is a possibility for reduction of cardiovascular disease downstream. One potential intervention for the reduction of the aforementioned risk factors is intermittent fasting.

Essentially, intermittent fasting (IF) is strategically withholding normal caloric intake for a period of time and eating ad libitum during the time that isn't restricted. Ad libitum is a term referring to eating as much or as often as one would desire. IF is broken up into time-restricted feeding, alternate-day fasting, and the 5:2 diet. Time-restricted feeding (TRF) is a period of fasting, or abstaining from caloric intake, for 14-20 hours each day and eating all of your caloric

intake within the remaining time in a 24-hour period. A very common time-restricted feeding interval is fasting for 16 hours and eating ad libitum for 8 hours (16:8).[2] Alternate day fasting (ADF) is alternating between fasting days, where you consume anywhere from 0 to a few hundred calories in 24 hours, and feast days where you eat ad libitum according to your normal caloric intake.[2] Finally, the 5:2 method of IF is fasting 2 non-consecutive days per week according to the same parameters of ADF and eating ad libitum the remaining 5 days within a 7-day period.[3] IF has increased in popularity over the last decade or more as a novel intervention to improve overall health and combat the obesity epidemic as compared to continuous energy restriction (CER). "For many people, it is considered to be less restrictive compared to traditional methods of caloric restriction…IF diet presents a useful substitute to obese/overweight patients who find the CER diet difficult to maintain."[4] The research question at the center of this literature review is: does intermittent fasting reduce the risk for the development of cardiovascular disease?

To answer the research question this literature review will provide a review of the quantitative values that put an individual into the high-risk CVD categories of obese, dyslipidemic, or insulin resistant. Following the categorical review, the effects of IF on weight loss and body mass index, lipid panels, and insulin resistance will be presented in detail. The writing will conclude with a comprehensive discussion analyzing the entirety of the literature presented and conclusions that can be drawn from the research.

Methods:

A comprehensive literature review was conducted using academic search premier ultimate and pubmed using the search terms intermittent fasting, time-restricted feeding, weight loss, lipid profile, diabetes, and insulin resistance. Inclusion criteria for this literature review

were primary studies from 2017 to the present. Exclusion criteria were primary studies published prior to 2017 as well as review articles. The literature was placed into an annotated bibliography within categories of the improvement that intermittent fasting showed on cardiovascular risk factors (weight loss, lipid profile, insulin resistance). From the annotated bibliography came the foundation of the literature review, which was synthesized based upon AMA format in the following paper for completion of master's degree requirements.

Literature Review:

To understand those who are at high risk of cardiovascular disease due to their weight, cholesterol, and insulin resistance, it is important to know what their goal levels are in terms of BMI, lipid profile, and diabetic labs. To determine the criteria for those at risk for the development of CVD there are measured values that are assessed for each category. Obesity is defined as a body mass index greater than or equal to 30 kg/m^2, while overweight is defined as a body mass index between 25 and 29.9 kg/m^2. The goal for a healthy weight is between 18.5 and 24.9 kg/m^2. In patients with dyslipidemia, the goal levels for total cholesterol are below 200, with borderline risk between 200-239 and a high risk 240 and above.[5] Triglycerides are desired to be below 200 with borderline risk between 200-400, high risk 400-1000, and extremely high risk over 1000.[5] HDL-C, otherwise known as good cholesterol has goal levels between 35-39. HDL levels are considered low if they are below 35. The goals for patients with type 2 diabetes are to have a hemoglobin A1c of less than 7.0%, fasting plasma glucose between 72 and 126 mg/dL, and post-prandial glucose levels between 90 and 100 mg/dL.[6] Keeping these numbers within desired ranges can lead to a decrease in macrovascular complications of diabetes that lead to CVD. The effects of IF on obesity, lipid profile, and diabetes labs will be evaluated based on the current literature.

Obesity increases the risk of CVD through means of high blood pressure, atherosclerosis, acute myocardial infarction, and heart failure.[7] This paper will first discuss the effects of intermittent fasting on obesity in adults, adults with chronic disease, and adolescent patients. "It is widely accepted that obesity is associated with all-cause mortality and the development of cardiovascular events in mid-age adults."[7] In a 2021 study by Schroder, et al[7] obese women with a BMI greater than or equal to 30 kg/m^2 that were active were placed in either a 16:8 TRF group (n=20) or a control group (=12) for 3 months. Using the Framingham Heart study, an estimation of the 30-year CVD risk for each person in the study was calculated before and after the initiation of the fasting.[7] In the TRF group, there was around a 12% reduction in CVDRisk30y after the three months. The TRF group also exhibited a statistically significant decrease in body weight, BMI, fat mass, percent body fat, and fat mass index.[7]

In another study by Gabel, et al[3] with different TRF parameters, obese patients (n=23) ate ad libitum from 10 am to 6 pm and then water only fasted from 6 pm to 10 am for 12 weeks. Another 23 obese patients were a control group. The goal was to have weight loss without calorie counting. Participants were between 25 and 65 years old with a BMI between 30-45 kg/m^2, non-diabetic, with no history of CVD. After 12 weeks, the TRF group had a statistically significant decrease in BMI and body weight relative to the control group, though there was no significant difference between the groups for fat mass, lean mass, or visceral fat mass.[3] It was found through this pilot study that 12 weeks of a 16:8 diet for the obese population decreased body weight by around 3% relative to a no intervention group and also decreased daily caloric intake by around 300kcal/day without intentional caloric counts. A limitation of this study is that it is not a randomized controlled trial. The intervention group was compared to a control group from a previous study.[3]

Intermittent fasting may also assist in weight loss for those with chronic diseases. Polycystic ovarian syndrome (PCOS) is a reproductive endocrine and metabolic disorder that often leads to metabolic syndrome, type 2 diabetes mellitus, and cardiovascular diseases.[8] In Li et al,[8] fifteen overweight women (BMI greater than or equal to 24 kg/m^2) between the ages of 18-31 with anovulatory polycystic ovary syndrome were enrolled in an observational trial to undergo 5 weeks of TRF after a 1 week weight stabilization period. Fasting took place between 8 am and 4 pm daily and patients were asked to maintain their normal eating patterns within the shortened time period. Patients lost an average of 1.3 kg of weight, corresponding to a 1.7% reduction in body weight from baseline.[8] This was accompanied by significant decreases in BMI, body fat mass, and body fat percentage. In addition, 11 of the 15 patients had an improvement in their previous menstrual cycle irregularities.[8] This study is valuable because it suggests that weight loss from intermittent fasting can also lead to improvements in comorbid conditions to further improve risk factors for cardiovascular events.

In addition to being studied in adult populations, intermittent fasting is beginning to become studied more extensively in adolescents. A case series in southern California by Vidmar, et al[9] followed 4 patients between the ages of 5 and 15 with obesity and various underlying comorbid conditions over 4 months as they practiced time-limited eating, which is synonymous with intermittent fasting. This is a novel concept because most trials of intermittent fasting have been done on obese populations of adults. The time-limited eating consisted of 3-5 days a week of 16:8 fasting with the goal of helping lower BMI without developing unhealthy eating habits. At the end of the four months, the patients exhibited decreases in the z-score of their BMIs between -0.08 and -0.39.[9] Since obesity in younger populations is associated with increased risk for cardiovascular disease later on in life, the results of this case series indicate that time-limited

eating is a feasible and flexible alternative to traditional pediatric obesity treatments like bariatric surgery or continuous caloric restriction.[9]

In another study in pediatric populations by Jebeile, et al[10] twenty-one obese adolescents between the ages of 12 and 17 with a BMI >30 kg/m^2 completed a 26-week program in three phases that incorporated a very low energy diet (VLED). VLED is a form of intermittent fasting where the subjects would eat a dietary plan consistent with national guidelines 4 days a week and fast 3 days a week, keeping their kcal intake between 500-600kcal daily.[10] Patients with diabetes requiring insulin were excluded from the study. After the three phases, there was a BMI z-score reduction of -0.12 units, which is greater than the literature with other weight loss interventions at the time. Perhaps more importantly, subjects within the study reported an increase in quality of life and a decrease in emotional eating patterns.[10] Considering many of the patients had a family history of cardiovascular disease, this study suggests that intermittent fasting may be effective in weight loss for adolescents before they reach the age of potential adverse cardiovascular events. Intermittent fasting doesn't just improve cardiovascular risk through weight loss, recent literature indicates that it may also positively impact components of serum lipid profile.

The next component of this paper will discuss the effects of IF and lipid profile in adults with dyslipidemia, Ramadan fasting, and healthy adults, and explore some of the nuances between fasting types. A randomized controlled trial by Chair, et al[2] took place in 2022 where adults with prediabetes (glucose 100-125 mg/dL) and BMI categories of overweight or obese (BMI greater than or equal to 23 kg/m^2) were randomized into 3 separate interventions: alternate-day fasting, 16:8 time-restricted feeding, or usual care group. The study took place for 3 weeks in China. Patients taking insulin or anti-obesity drugs were excluded from the trial due to the possibility of confounding variables. ADF parameters were 600kcal per day on fasting days and

ad libitum on non-fasting days. The lipid profile was measured via blood testing as a secondary outcome. No serious side effects were reported, only mild feelings of hunger during the fasted hours.[2] After 3 weeks, the ADF group reported a statistically significant reduction of LDL-C, improvement of HDL-C, and a significant reduction in total cholesterol. The 16:8 TRF group reported a significant reduction in LDL-C and improvement of HDL-C, 3 months after the end of the intervention. ADF had a more significant reduction in triglycerides than 16:8 TRF.[2] Although there was no significant difference between ADF and 16:8 for LDL-C reduction, this study is an important starting point because it demonstrates that they both work in the improvement of lipid profile.

Fasting is a part of religious traditions across the world. For example, Ramadan is a month-long Islamic practice where adults fast from sunrise to sunset. In a 2020 study by Akrat, et al[5] the fasting lipid panels of 100 healthy male subjects (aged 20-74) were taken the week before the start of Ramadan and again in the final week of Ramadan. A particular emphasis was placed on changes in the measurements of total cholesterol, triglycerides, and HDL-C.[5] This study excluded obese subjects or those with a known history of dyslipidemia, hypertension, and diabetes. Changes in all three lipid measurements following Ramadan were highly statistically significant, with a corresponding p-value of 0.000 for all three.[5] Average fasting time for this study was around 11 hours daily, which is even less than traditional time-restricted feeding parameters.[5]

Fasting is not only beneficial for those with a sedentary lifestyle, IF can also prove beneficial for those with active lifestyles to decrease cardiovascular risk. A randomized pilot study from 2020 by McAllister, et al[11] took twenty-two healthy young, physically active men and randomly assigned them to eat ad libitum or 16:8 time-restricted feeding for 28 days to evaluate

if TRF can lead to improvements in cardiometabolic risk factors. All participants engaged in an average of 150 min/week of regular exercise.[11] At the end of the 28 days of the trial, both groups experienced a significant increase in HDL-C and reductions in body fat and blood pressure. This study suggests that time-restricted feeding can improve HDL cholesterol in physically active young men. "With that being said, the 28-day TRF resulted in significant increases in HDL-c which is a negative risk factor for coronary heart disease."[11]

Few studies of intermittent fasting exceed a duration of 3 months, however, a randomized trial from 2018 by Sundfor, et al[12] examined 112 subjects aged 21-70 years old with a BMI between 30 kg/m^2 and 45 kg/m^2 and randomly assigned them to either continuous energy restriction (n=58) or intermittent fasting (n=54) for the duration of 12 months. The fasting intervention was designed for a 5:2 method where females would consume 400 kcal on two non-consecutive days throughout 7 days and males would consume 600 kcal.[12] No serious adverse effects were reported. At the end of the study, there were favorable improvements in triglycerides and HCL-C, however, there was no significant difference between the IER and CER groups.[12]

A randomized controlled trial from 2019 by Cai, et al[13] set out with the goal to determine if alternate-day fasting was better than other types of fasting or non-fasting interventions for reduction of body weight and improvement of dyslipidemia. Patients with non-alcoholic fatty liver disease (n=271) were randomized into either an alternate-day fasting group, time-restricted feeding group, or control group that ate ad libitum for 12 weeks, with measurements taken at 4 weeks and 12 weeks.[13] In the alternate-day fasting group, total cholesterol levels decreased significantly at 4 weeks and 12 weeks in comparison to the control group and TRF groups. In addition, serum triglyceride levels decreased significantly in the ADF and TRF groups in

comparison to the control group.[13] Important exclusion criteria of note were cardiovascular disease, uncontrolled hypertension, and patients on lipid or glucose-lowering medications.[13]

Similar to dyslipidemia, additional prominent risk factors for the development of cardiovascular disease include elevated blood glucose and insulin resistance. The final component of this paper will explore the effects of IF and insulin resistance in patients with prediabetes, confirmed type 2 diabetes, and metabolic syndrome. Intermittent fasting is beginning to become studied as an intervention to improve insulin sensitivity and diabetic labs such as beta-cell responsiveness, AUC ratio, hemoglobin A1c, fasting blood glucose, and HOMA-IR.

In a 2018 study by Sutton, et al[14] men with prediabetes were randomized to either eTRF (6 hours of eating with dinner before 3 pm) or a 12-hour feeding window for 5 weeks and then switched to the other intervention for another 5 weeks.[14] eTRF aims to follow the circadian rhythm of humans by eating earlier in the day. “For instance, in humans, insulin sensitivity, B-cell responsiveness, and the thermic effect of food are all higher in the morning than in the afternoon or evening, suggesting that human metabolism is optimized for food intake in the morning.”[14] Eight men completed the trial and no serious adverse events were reported. After 5 weeks of eTRF, there was a statistically significant reduction in fasting insulin levels, a statistically significant increase in the insulinogenic index (a marker of B-cell responsiveness), and a statistically significant decrease in insulin resistance measured by a 3-hour incremental AUC ratio. There was no improvement in glucose levels after 5 weeks of eTRF.[14]

In addition to Sutton, et al[14] a 2018 case study published by Furmli, et al[15] followed 3 patients with type 2 DM that underwent intermittent fasting. Parameters for fasting were as such: patient 1fasted three days/week for 7 months, patient 2 fasted three days/week for 11 months,

and patient 3 practiced alternate-day fasting for 11 months. On fasting days, the patients only ate dinner. Blood sugars were measured four times daily.[15] Patients were monitored closely and told to stop fasting immediately if they felt unwell. All three patients no longer needed insulin after between 5-18 days.[15] Fasting was well tolerated for all three patients and all three patients experienced weight loss of 10% or more. "The present case series showed that 24-hour fasting regimens can significantly reverse or eliminate the need for diabetic medication."[15]

In another randomized controlled trial from 2021 by Che, et al,[16] 120 patients who were overweight with type 2 diabetes were randomly assigned to either TRF or ad libitum for 12 weeks with 2 weeks of baseline weight stabilization prior to starting the interventions. The fasting parameters were 10-hour intervals of ad libitum and 14 hours of fasting. Whichever patients had diabetes requiring insulin had their blood glucose levels closely monitored by endocrinologists throughout the trial.[16] Primary outcome measures were hemoglobin A1c, fasting plasma glucose, and body weight. Fasting diabetes labs were performed at the end of the 2 week baseline period and the end of the study. The TRF group when compared to the control group had a statistically significant reduction in HbA1c, body weight, and fasting plasma glucose with weight change having a direct correlation to the change in HbA1c.[16] Throughout the study, the TRF intervention decreased fasting plasma glucose by 15% and HbA1c by 18%, which was "approximately twice the effect of medicine."[16] A longer duration of study is necessary to determine if these results are sustainable. Another important correlation from this study was that the improvement in blood glucose was associated with a positive change in lipid profile.[16]

In a 2020 study conducted in Turkey by Kundaraci and Ozbek,[17] 70 adult patients with metabolic syndrome were randomized into either an intermittent energy restriction intervention group or a continuous energy restriction control group for 12 weeks. Metabolic syndrome is a

constellation of symptoms including obesity, hypertension, dyslipidemia, and type 2 diabetes and is a well-known risk factor for future cardiovascular disease.[17] Subjects were instructed to follow a 16:8 fasting schedule with an anticipated 25% decrease in daily normal caloric intake or to eat ad libitum with a 25% decrease in daily normal caloric intake. Measures of insulin resistance included homeostasis model assessment (HOMA-IR). The intermittent energy restriction group had a significant decrease in HOMA-IR and HbA1c while the continuous energy restriction group also experienced a significant decrease in HbA1c.[17] This study may suggest that IER with reduction of normal caloric intake is feasible and could be used as an alternative to continuous energy restriction in decreasing insulin resistance in adults with metabolic syndrome.[17]

Lastly, a three-phase observational study by Arnason, et al[6] monitored 10 participants with a confirmed diagnosis of type 2 diabetes that were all taking metformin and had a mean BMI of 36.90 kg/m^2. The study was designed in 3, two-week phases. In phase 1, subjects were within their normal dietary patterns. In phase 2 the goal was to fast for 18-20 hours per day and eat ad libitum the remainder of the time. In phase 3 the patients returned to eating within their normal dietary patterns.[6] Insulin resistance was measured using HOMA-IR. "A decrease in insulin resistance can improve glucose control, and exercise and weight loss both favorably decrease disease states."[6] The results of this study showed non-significant improvements in HOMA-IR, but the phase 2 results where the subjects intermittent fasted showed a significant increase in fasting plasma glucose and significant decreases in postprandial hyperglycemia.[6] In addition, there was a spontaneous decrease in how much the patients ate in terms of caloric intake, coinciding with a significant decrease in weight. Overall this observational study indicates that intermittent fasting may improve insulin resistance.[6]

In summary, recent literature from the last five years indicates that different forms of IF can reduce the risk of adverse cardiovascular events through avenues like weight loss, positive changes in lipid profile, and improvement in insulin resistance. Intermittent fasting led to positive changes in body weight and BMI in adults who were overweight and obese. It also was feasible in adolescent populations in those who were overweight and obese as well as patients with comorbid conditions like polycystic ovarian syndrome.[8] In terms of lipid profile, intermittent fasting demonstrated reductions in LDL-C, total cholesterol, and triglycerides and positive increases in HDL-C. This was demonstrated in patients who were overweight and obese over the short term, long term,[12] fasting during the month of Ramadan,[5] and fasting in healthy college-aged males.[11] Lastly, intermittent fasting suggested improvements in those with prediabetes[14] and type 2 diabetes mellitus. This improvement was demonstrated through decreases in insulin resistance, fasting insulin levels, hemoglobin A1c, and HOMA-IR.

Discussion:

With the current research, intermittent fasting demonstrates positive reductions in risk factors for cardiovascular disease in terms of weight loss, improvement of dyslipidemia, and insulin resistance. However, the results of the current literature aren't always consistently reproducible. "Research suggests that there are major healthy benefits to caloric restriction which include reduced risk of cancer, cardiovascular disease, diabetes, insulin resistance…"[5] In terms of obese patients, time-restricted feeding provided a potential avenue for consistent results in weight loss and reduction of BMI, two large risk factors for the development of cardiovascular disease in the future. "Obesity greatly increases the risk of metabolic diseases, such as coronary heart disease and type 2 diabetes."[3] However, there needs to be more research conducted on whether or not intermittent fasting with a VLED is better than IF with normal caloric intake since

such positive results have been seen in VLED intervention in adolescents.[10] The parameters must be more fine-tuned before altering guidelines for this intervention.

Intermittent fasting literature consistently demonstrates an impact on lipid profile in a positive way, though it is often non-specific. This means that some studies show statistically significant reduction of LDL-C, HDL-C, and total cholesterol,[2] while others showed a significant reduction in triglyceride levels and total cholesterol only.[13] Further research is needed to pinpoint specific improvements in lipid profile based on individual needs. Additionally, Sundfor, et al[12] reported favorable improvements in HDL-C and triglycerides, but there was no significant difference between the two interventions of intermittent energy restriction and continuous energy restriction at the end of one year of intervention. This suggests that perhaps the intervention of intermittent fasting was not the sole reason for positive improvements in dyslipidemia and it may be the broader intervention of non-specific caloric deficit that leads to improvements.

In terms of reduction of insulin resistance, intermittent fasting provided an avenue to slow the progression of prediabetes to type 2 diabetes mellitus by significantly decreasing the 3-hour incremental AUC ratio.[14] It also increased insulin sensitivity to the point where patients no longer needed to use supplemental insulin.[15] Both of these studies have tremendous implications for future research and provide staggering potential interventions in the future. Considering type 2 diabetes mellitus is so hard to manage with insulin, the potential to treat patients on diet alone is intriguing. Additionally, intermittent fasting has the potential to improve insulin resistance through the suggested reduction of hemoglobin A1c. Che, et al[16] presented a decrease in HbA1c by 18% which was around double the effect of diabetes medications in lowering HbA1c. However, this randomized controlled trial needs further replication to shape diabetes guidelines in the future. Similar to the results of the lipid profile literature, Kundaraci and Ozbek[17]

demonstrated a significant decrease in HbA1c in both the intermittent energy restriction group and the continuous energy restriction group. Future research is necessary to determine whether the reductions in HbA1c were due to intermittent fasting or other confounding variables. Intermittent fasting results in the reduction of insulin resistance through the measurement of HOMA-IR were not consistent in the studies collected for this literature review. Type 2 diabetes results in increased risk for the development of microvascular and macrovascular cardiac complications. The multifactorial issues of rising costs for insulin and bariatric surgery suggest the need for less invasive maneuvers to improve insulin sensitivity, such as intermittent fasting.[15]

Conclusion:

Cardiovascular diseases are the leading causes of death worldwide, accounting for 17.9 million annual deaths.[1] Current strategies to control the risk for developing cardiovascular disease include balanced, healthy diet, frequent exercise, and limited intake of tobacco and alcohol. Despite the existing strategies for controlling modifiable risk factors, cardiovascular disease remains responsible for 32% of deaths worldwide.[1] Since the prevalence of cardiovascular disease is so high, it is important to investigate other interventions that may lead to reductions in modifiable risk factors such as obesity, hyperlipidemia, and insulin resistance. A potential intervention for decreased risk for developing cardiovascular disease that has become extensively studied in the past 10 years is intermittent fasting. Intermittent fasting is strategically withholding normal caloric intake for a period of time and eating as you normally would during unrestricted times.

The research question at the initiation of the research process was: does intermittent fasting reduce the risk for the development of cardiovascular disease? The current research is abundant and can suggest that intermittent fasting in its various forms can lead to reductions in

modifiable risk factors of obesity, hyperlipidemia, and insulin resistance. For intermittent fasting to be put into guidelines for the reduction of modifiable risk factors, more randomized controlled clinical trials need to be done to reproduce the results that have been suggested by the current literature. Reproduction is necessary to determine whether the positive alterations seen were due to intermittent fasting or other confounding variables. Additionally, reproduction is necessary to fine tune parameters of studied populations and fasting interventions.

However, with that being said, there is a plethora of literature that suggests at the very least that intermittent fasting is a feasible option for weight loss, improvements in blood lipids, and diabetic labs without serious adverse reactions. This is important because IF can potentially provide an avenue for the reduction of cardiovascular disease without the need to administer extensive medications or undergo surgery that both have the potential for serious side effects. If intermittent fasting were to be incorporated into treatment guidelines for weight loss, dyslipidemia, and insulin resistance, there is theoretical potential for decreased healthcare costs for the patient due to decreased need for insulin as medication and decreased need for uncertain interventions like bariatric surgery.[15] Intermittent fasting is a non-invasive intervention that can lead to a healthier life and decreased probability of undergoing adverse cardiovascular events resulting in early death, and therefore ought to be studied in order to be incorporated into medical guidelines.

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Depositor's Name (Please Print): _____

Author's Signature: Ethan M. DeKam Date: 08–9-2022

If the Deposit Agreement is executed by the Author's Representative, the Representative shall separately execute the Following representation.

I represent that I am authorized by the Author to execute this Deposit Agreement on the behalf of the Author.

Author's Representative Signature: _____ Date: _____