ROUX-EN-Y GASTRIC BYPASS SURGERY DURING MENOPAUSE: WEIGHT LOSS OUTCOMES AND THE RESOLUTION OF METABOLIC SYNDROME

Ryan Patrick Majcher

A Thesis

Submitted to the Graduate College of Bowling Green State University in partial fulfillment of the requirements for the degree of

MASTER OF FOOD NUTRITION

August 2014

Committee:

Julian Williford Jr, Advisor
Mary Jon Ludy
Mark Earley
ABSTRACT

Julian Williford Jr, Advisor

**Background:** As obesity rates rise, new methods to provide substantial weight loss have become crucial to the healthcare industry. Bariatric surgery has proven to be the most effective treatment for obesity, and the Roux-en-Y Gastric Bypass operation has not only enabled many to lose excess weight, but also has resulted in the resolution of comorbid conditions. To date, research on the effectiveness of the RYGB surgery in postmenopausal women is minimal.

**Objective:** This study was completed to compare excess body weight lost and metabolic syndrome resolution in pre- and postmenopausal Roux-en-Y Gastric Bypass surgery patients, preoperatively to one year postoperatively.

**Methods:** A retrospective chart review was completed for 42 premenopausal and 36 postmenopausal RYGB surgery patients at Wood County Hospital in Bowling Green, Ohio. Surgeries took place between September 2008 and May 2012. Weight data was collected preoperatively, and at 2 week, 2 month, 6 month, and 1 year follow up appointments. To determine diagnosis of metabolic syndrome, preoperative, 6 month, and 1 year data was utilized.

**Results:** At 1 year, percent excess body weight lost was 68.79% for the premenopausal group and 59.44% for the postmenopausal group, which was significant, t(73)= 2.61, p=0.011. To compare the effect time on percent excess body weight lost for those with data at all follow up appointments, a repeated measures analysis of variation was done, which showed a difference between groups as time elapsed, with significance at 1 year F(3,195)=4.71, p=0.0182. Excess percent body weight lost was greater than 50% in 64 of 78 individuals at 1 year. Significance between pre- and postmenopausal groups was also found for preoperative ($X^2$ (1, n=76)
p=0.0307) and midway glucose ($\chi^2(1, n=76)$ p=0.0047), as well as midway ($\chi^2(1, n=69)$ p=0.0024) and 1 year blood pressure ($\chi^2(1, n=74)$ p=0.0089). Preoperatively, metabolic syndrome diagnosis was 54 of 78 (22 premenopausal and 32 postmenopausal), midway 37 of 78 (13 premenopausal and 24 postmenopausal), and 17 of 78 (7 premenopausal and 10 postmenopausal) at 1 year.

**Conclusion:** In this retrospective chart review, premenopausal surgery patients lost a significantly greater amount percent excess body weight at 1 year, when compared to the postmenopausal group. Metabolic syndrome incidence was also less in the premenopausal group preoperatively, midway and at 1 year. This study shows that the Roux-en-Y bariatric surgery was able to provide weight loss and resolution of metabolic syndrome in both pre- and postmenopausal women, however postmenopausal women saw less success overall. In the future, a change in bariatric surgery inclusion criteria for those women in the perimenopausal period to include those at a lower BMI may be helpful to more quickly address issues with weight allowing for greater success in the postoperative time period after bariatric surgery.
ACKNOWLEDGEMENTS

I would like to express my sincerest gratitude to my thesis advisor and mentor, Dr. Julian Williford Jr. Without his continued patience, guidance, and expertise in the field of nutrition, I would not have been able to complete the following research. From the beginning, Dr. Williford stood by my side, helping me not only to better myself in the field of nutrition, but also to better myself as a person. I would also like to acknowledge Dr. Mary Jon Ludy, who graciously provided a keen perspective on the research being performed; working along side me, throughout the process, until completion. Additionally, Dr. Mark Earley and Nancy Boudreau, and their immeasurable help in analyzing the data collected.

I am also appreciative for the opportunity to work with Dr. Peter Lalor and his outstanding associates at Wood County Hospital. Throughout the process of data collection and analysis, Dr. Lalor offered his continued expertise, making this body of research possible. It was an absolute pleasure to work such a kind, caring and compassionate physician throughout this research process.

I would also like to extend the utmost gratitude to my parents, William and Kathleen Majcher, who have provided continued support throughout the long process as I worked to complete this research composition. Finally, a special thanks is also warranted towards my family and friends. Even though it seemed that the end would never present, each and every one of them continued to provide encouragement, pushing me to completion.
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>CHAPTER I: INTRODUCTION</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study Objectives</td>
<td>1</td>
</tr>
<tr>
<td>Environmental Factors and Weight</td>
<td>3</td>
</tr>
<tr>
<td>Population of Interest</td>
<td>5</td>
</tr>
<tr>
<td>Current and Future Research Direction</td>
<td>6</td>
</tr>
<tr>
<td>Study Significance</td>
<td>7</td>
</tr>
<tr>
<td>Study Limitations</td>
<td>8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CHAPTER II: REVIEW OF LITERATURE</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>America’s Obesity Woes</td>
<td>12</td>
</tr>
<tr>
<td>Nutrition Education and Lifestyle Modification</td>
<td>14</td>
</tr>
<tr>
<td>Surgical Methods of Weight Loss</td>
<td>23</td>
</tr>
<tr>
<td>Undiagnosed Diseases and Economic Burden</td>
<td>29</td>
</tr>
<tr>
<td>Metabolic Syndrome</td>
<td>32</td>
</tr>
<tr>
<td>Pregnancy and Metabolic Syndrome</td>
<td>38</td>
</tr>
<tr>
<td>Exercise and Metabolic Syndrome</td>
<td>41</td>
</tr>
<tr>
<td>Menopause and Hormonal Alterations</td>
<td>46</td>
</tr>
<tr>
<td>Hormone Replacement Therapy</td>
<td>48</td>
</tr>
<tr>
<td>Surgical Weight Loss, Gut Hormones, and Supplementation</td>
<td>51</td>
</tr>
<tr>
<td>Menopause and Blood Pressure</td>
<td>54</td>
</tr>
<tr>
<td>Menopause and Cholesterol</td>
<td>59</td>
</tr>
<tr>
<td>Menopause and Weight</td>
<td>62</td>
</tr>
<tr>
<td>Menopause and Diabetes</td>
<td>66</td>
</tr>
<tr>
<td>Tailored Approaches</td>
<td>76</td>
</tr>
<tr>
<td>Evolutionary Context</td>
<td>78</td>
</tr>
</tbody>
</table>
# LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ATP III Criteria for Metabolic Syndrome Diagnosis</td>
<td>84</td>
</tr>
<tr>
<td>2</td>
<td>Baseline Patient Characteristics for Age, Weight, and Excess Body Weight</td>
<td>86</td>
</tr>
<tr>
<td>3</td>
<td>Percent Excess Body Weight Lost at 2 Weeks, 2 Months, 6 Months, and 1 Year</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>Percent Excess Body Weight Lost at 2 Weeks, 2 Months, 6 Months, and 1 Year For Those with Data at all Follow Up Appointments</td>
<td>91</td>
</tr>
<tr>
<td>5</td>
<td>Blood Pressure - 2 Weeks</td>
<td>93</td>
</tr>
<tr>
<td>6</td>
<td>Blood Pressure - 2 Months</td>
<td>93</td>
</tr>
<tr>
<td>7</td>
<td>Blood Pressure - 6 Months</td>
<td>94</td>
</tr>
<tr>
<td>8</td>
<td>Blood Pressure - 1 Year</td>
<td>94</td>
</tr>
<tr>
<td>9</td>
<td>Fasting Blood Glucose - Preoperative</td>
<td>96</td>
</tr>
<tr>
<td>10</td>
<td>Fasting Blood Glucose - Midway</td>
<td>96</td>
</tr>
<tr>
<td>11</td>
<td>Fasting Blood Glucose - 1 Year</td>
<td>97</td>
</tr>
<tr>
<td>12</td>
<td>Body Mass Index Classifications</td>
<td>97</td>
</tr>
<tr>
<td>13</td>
<td>Body Mass Index - Preoperative</td>
<td>99</td>
</tr>
<tr>
<td>14</td>
<td>Body Mass Index - 2 Weeks</td>
<td>100</td>
</tr>
<tr>
<td>15</td>
<td>Body Mass Index - 2 Months</td>
<td>100</td>
</tr>
<tr>
<td>16</td>
<td>Body Mass Index - 6 Months</td>
<td>101</td>
</tr>
<tr>
<td>17</td>
<td>Body Mass Index - 1 Year</td>
<td>101</td>
</tr>
<tr>
<td>18</td>
<td>Triglycerides - Preoperative</td>
<td>102</td>
</tr>
<tr>
<td>19</td>
<td>Triglycerides - Midway</td>
<td>103</td>
</tr>
<tr>
<td>20</td>
<td>Triglycerides - 1 Year</td>
<td>103</td>
</tr>
<tr>
<td>21</td>
<td>High Density Lipoprotein Cholesterol - Preoperative</td>
<td>104</td>
</tr>
<tr>
<td>22</td>
<td>High Density Lipoprotein Cholesterol - Midway</td>
<td>105</td>
</tr>
<tr>
<td>23</td>
<td>High Density Lipoprotein Cholesterol - 1 Year</td>
<td>105</td>
</tr>
</tbody>
</table>
## LIST OF FIGURES

**Figure**

1. Roux Limb Length for RYGB Surgery Patients .......................................................... 83
2. Metabolic Syndrome Incidence in Pre- and Postmenopausal Women Preoperatively, Midway, and at 1 Year ........................................................................................................ 87
3. Repeated Measures Analysis of Variation Comparing Mean Percent Excess Body Weight Lost Across Time Between Pre- and Postmenopausal Groups ........................................... 91
4. Body Mass Index Preoperatively, 2 Weeks, 2 Months, 6 Months, and 1 Year ............ 99
CHAPTER I:

INTRODUCTION

If people limit the number of calories consumed, or expend a greater number of calories per day, then weight loss can be attained, according to the laws of thermodynamics. In a personal state where calories consumed are greater than calories expended, weight gain can be predicted. On the contrary, when the energy balance shifts, so that more calories are expended through exercise, or activity, than consumed through diet, weight loss can be expected; however, varying percentages of total dietary calories from protein, carbohydrate, and fat have been shown to cause varying degrees of change in total body mass (1). The foundation behind these previous statements is that energy can neither be lost nor gained, but simply transferred between objects or entities. In summary, weight gain can be expected when any of the following scenarios or combination of scenarios are present; energy is over consumed, energy is under expended, or energy is not utilized properly within the body (2). At face value, the above concepts may seem straightforward, and therefore the ability to lose weight should be possible through exercise and diet modification (3). Unfortunately, the road to weight loss is not immediate, and the American population still continues to search out a magic pill or fad diet that will provide rapid results, when in actuality these results still hinge on the idea of calorie intake versus calorie expenditure through increased activity.

Study Objectives

This current study will be looking at weight loss in pre- and postmenopausal women, and the incidence of metabolic syndrome (MetS), in Roux-en-Y gastric bypass surgery these patients, and the effect of the weight loss procedure on these women. Preoperative weight and then
subsequent weights will be recorded at follow up appointments: 2 weeks, 2 months, 6 months, and 1 year. From the recorded weights, percent excess body weight lost will be calculated, and theses values will be compared at each follow up time point to see if there is a difference is between groups. Metabolic syndrome diagnosis, based on ATP III criteria will be recorded preoperatively, midway, and at 1 year to see whether bariatric surgery can reduce the number of diagnoses with time, and if metabolic syndrome incidence is effected by menopausal status.

Metabolic syndrome is characterized as a cluster of risk factors that are present when excess body weight is present, potentially spurred by abdominal or central obesity. Metabolic syndrome factors include high blood pressure ($\geq 130/\geq 85$mmHg), impaired fasting glucose ($\geq 110$mg/dL), abdominal obesity (men $\geq 40”, \text{women } \geq 35”$), elevated triglycerides ($\geq 150$mg/dL), and depressed HDL cholesterol values (men $<40$mg/dL, women $<50$mg/dL) (4). Under the National Cholesterol Education Program’s Adult Treatment Panel III guidelines, an individual must meet three of the previously mentioned five criteria to be diagnosed as having metabolic syndrome.

NHANES III data between 1988-1994 has revealed that the prevalence rate of metabolic syndrome in females was approximately 6% for those women between 20-29 years old. However, this number sharply jumps to 34% and 43% for those women between 50-59 years and 60-69 years of age, respectively (5). A strong predisposition in metabolic syndrome prevalence rates in women signifies that with age, it becomes harder to maintain homeostasis between calories consumed and calories expended, which can lead to weight gain along with an increase in insulin resistance, and subsequently, metabolic syndrome diagnosis. It is likely that a decrease in basal metabolic rate is owing to weight gain with age to some extent in females, in addition to numerous other changes that occur with menopause. With the gradual cessation of estrogen release in women, at the onset of menopause, a shift towards increased food consumption and
decreased physical activity can be witnessed (6). Researchers have shown that a combination of aerobic, resistance, and weight bearing exercises should be used prior to, during, and after menopause to help combat the propensity for weight gain, loss of muscle mass, and therefore a decrease in basal metabolic rate (7). This phenomenon can be attributed to multiple factors, many of which are concerned with hormones, mainly estrogen, and its profound physiologic role within the female body.

Environmental Factors and Weight

Unfortunately, there are many confounding factors that make it increasingly difficult to meet a personal weight loss goal or even to slowly lose weight. Drastic increases in obesity rates are not likely a result of genetic predispositions, seeing as the biggest growth has primarily occurred over a 20 year period, which is not a long enough span of time for natural selection to occur (8). Prior to 1980, obesity prevalence rates were <10%, and via globalization and undoubtedly easier access to unhealthy foods, these rates have tripled worldwide (9).

Recent data from 2009-2010 suggests that nearly 1/3 of the adult American population is obese, however these increases are slowing and even appear to be leveling off (10). Interestingly, between 1999-2000 and 2009-2010, an increase in obesity prevalence was observed in men, but not women (10). One factor that may have led to our current obesity epidemic deals with the possible high caloric convenience food supply that Americans must battle on a daily basis, and the hardest hit cohort of the population consuming these foods are persons of a lower socioeconomic background (11). Lake categorized our living environment into three separate groupings based on: physical design, socio-cultural rules that act as a governing body, and the overall socioeconomic status of the environment (12). Rates of physical activity are lower and
the placement of fast food establishments is more concentrated in lower socioeconomic neighborhoods, a sociological situation that has been referred to as a food desert (13).

As lifestyles in the United States have transitioned from a more leisurely, relaxing pace, to a much faster, more hectic variant, the demand for cheaper, quicker, and more convenience based food items has grown larger, and with it, personal waistlines have followed (12). Furthermore, with additional stress from work and home life, the body, through the hypothalamus-pituitary-adrenal axis, responds through the release of glucocorticoids, mainly cortisol has been shown to result in the anabolic metabolism of adipose tissue, leading to increased fat mass over time (14). Hypersecretion of cortisol also has been shown in those who consume a diet high in total calories, primarily made up of low quality dietary choices, which can lead to an elevation in blood sugar and subsequent poor glycemic control (15).

Over the course of the past several decades, weight loss modalities have broadened, and the number of diets currently being followed by persons overweight and obese is seemingly endless. Other methods of weight loss, in addition to dieting, include a variety of work out videos, pills, weight loss programs, and even exogenous hormone administration, such as human chorionic gonadotropin (hCG) (16). Weight loss programs such as Weight Watchers, Nutri-Systems, and Jenny Craig have resulted in weight loss for many obese and overweight individuals over the years, however they can become expensive over time, and weight regain is common when the program is stopped. Currently, a handful of surgical techniques are being employed to help those classified as obese, which have proven to yield the most significant results, and are being touted as the most effective means by which an individual can successfully lose a greater than 50% of excess body weight (EBW)(17).
Many of the previously mentioned weight loss modalities are, at their core, still based on the laws of thermodynamics. For example, surgical methods of weight loss can either be malabsorptive, restrictive, or a combination of both to help decrease the amount of consumed calories available to the body, at any given time. This will result in a fewer number of calories being utilized by the body, and weight loss can be observed within only weeks post-operatively, and sustained long term in many surgery patients (18). On the contrary, evidence exists that points to a marked decrease in excess weight in the first 24-months post-op, however weight regain, related to gradual stomach stretching from diet non-compliance, post-operatively, was witnessed at five years in some subjects, with their comorbid resolution rates diminishing from the original operation (19).

**Population of Interest**

A specific cohort of the population, postmenopausal women, may be at a disadvantage when it comes to their ability to lose weight. This hindrance may be due to shifts in hormone concentrations that occur with menopause along with advancing age (20, 21). For this reason, this research study will focus on the efficacy of bariatric surgery, exclusively the Roux-en-Y procedure, and its ability to provide substantial and sustained weight loss in both pre- and post-menopausal women. Park indicated that the relative risk for metabolic syndrome was elevated in postmenopausal women, when compared those who were premenopausal; where age, BMI, and socioeconomic status were adjusted (22). It is hypothesized that after the Roux-en-Y procedure, those subjects who were post-menopausal will see less weight loss, compared to those who have yet to experience menopause. Therefore, the reduction in incidence rates of metabolic syndrome should also be less in those women who are post-menopausal, and support the hypothesized poorer weight loss outcomes in the postmenopausal group. The null hypothesis would
consequently be that menopausal status will not affect weight loss observed post Roux-en-Y gastric bypass surgery, and resolution of metabolic syndrome will also remain analogous based on menopausal status.

**Current and Future Research Direction**

Knowing that the risk for weight gain and negative weight redistribution is greater in women throughout life and throughout the menopausal transition (23), warrants further study of this specific cohort to investigate whether weight loss surgery recommendations need to be altered to account for these physiological changes in women. If the removal of excess weight and resolution of metabolic syndrome incidence is less in those women that are postmenopausal, perhaps the guidelines for weight loss surgery need to be adjusted to help maximize surgery results and improve these post-menopausal women’s overall quality of life. Currently, for a patient to qualify for bariatric surgery, BMI guidelines are set at 35 kg/m² and 40 kg/m², depending on whether a co-morbid condition is diagnosed, such as; diabetes, hypertension, or hyperlipidemia or not diagnosed, respectively. Under certain circumstances, it could be beneficial to include guidelines for peri- and postmenopausal women that are set slightly lower to thereby increase the number who would be eligible for surgical weight loss techniques. This approach would address the problem at an earlier point in time, and begin to reverse the negative consequences of menopause more rapidly, improving the post-operative weight loss results. A criterion cut point between 30 and 35 kg/m², regardless of co-morbid conditions, would include a larger percentage of future bariatric patients, while still focusing on a group that is classified as obese. As it stands, the United States of America takes a stance that is far more reactive than proactive when it comes to the prevention of excessive weight gain, and its associated complications; such as, hypertension, insulin resistance, and cardiovascular disease, and this
reactive ideal is partially responsible for the body weight crisis we are currently facing. In 1993, a study by Horm and Anderson was done to see who in America was trying to lose weight, in which they found nearly 1/3 of American’s viewed themselves as overweight, but fewer than 2/3 of this group was actively trying to lose weight through physical activity and diet (24). Duncan utilized 2003-2006 NHANES data to study weight perception and classification. He found that approximately 23% of sampled participants misperceived their weight (25). Additionally, 71% of males and 65% of females who misperceived their current weight classification, based on BMI, were less likely to want to lose weight (25). In comparison, those that correctly identified themselves as overweight or obese were more likely to want to lose weight, or currently be participating in a weight loss program (25). This represents a potential key component to any weight loss program. Targeted efforts to first outline what constitutes overweight and obese should be at the forefront of any program, so the appropriate individuals can be recruited.

**Study Significance**

Weight gain and its associated co-morbid conditions are continuing to rise around the world, especially in the United States of America. As an individual’s weight continues to climb upward, quality of life tends to trend downward, which can lead to feelings of depression and social anxiety, preventing the individual from going out in public and actively participating in society. When this previously mentioned scenario presents, the individual may refrain from physical activity related to fear of negative occurrences during a physical activity session (26). Out of those that are classified as being obese, a mere 1 out of 5 routinely participate in physical activity, perpetuating the cycle of weight gain over time (26).
Benotti et al looked at 30-day post-surgery mortality rates for those who had the Roux-en-Y procedure completed and found mortality rates of 0.15% (n=81,751)(27). They found that factors such as increasing BMI and age, maleness, pulmonary hypertension, congestive heart failure, and liver disease all increased 30-day mortality rates (27). In comparison, odds ratios for all cause mortality for non-smokers with a BMI of 30 kg/m² is 1.44 and jumps sharply to 2.93 at a BMI of approximately 42 kg/m² (28).

By focusing on the underlying diagnosis of obesity and its related issues at an earlier point in time, as would be the case when performing the Roux-en-Y procedure on lower weight menopausal women, many of these potentially exacerbated problems might be avoided, therefore reducing end mortality rates while increasing the individuals quality of life. Attacking the weight problem early, and performing surgery at a lower BMI surgery cut approval score in perimenopausal women, could help reverse weight gain more quickly, and possibly prevent many of the quality of life and health issues in such operation candidates earlier, rather than waiting to intervene, when it may be too late to make a significant difference.

**Study Limitations**

This research will be a retrospective chart review that is specifically looking at pre- and naturally occurring postmenopausal women who have had the laparoscopic Roux-en-Y gastric bypass procedure. As a result of the study being retrospective in design, there is the question of how accurately the data used was collected and recorded in the assigned patient’s chart. Furthermore, the data being used has already been collected; therefore it is not possible to specifically choose what variables are to be measured. For this study, all data is present on each patient to diagnose metabolic syndrome as part of the routine workup by the facility, except for
waist circumference. Body mass index, or BMI will be used in place of waist circumference with values \( \geq 30 \text{kg/m}^2 \) equating to a waist circumference of \( \geq 35 \text{cm} \).

Other studies have used BMI as a criterion in place of waist circumference, with good results (29). On the contrary, other researchers have claimed that BMI is not accurate due to the fact that it does not directly ascertain where the extra body mass is centered (30). Burkhauser and Cawley compared BMI and percent body fat in accurately classifying obese individuals and found a instances of 23.7\% and 70.4\%, in females, respectively (31). This depicts a notable discrepancy between classifications of obesity, potentially leaving out individuals who are overweight and obese. Furthermore, while it may not play a role in this particular research, it should be mentioned that BMI does not account for excessive muscle added via exercise, which takes up less space per unit weight when compared to adipose tissue. Therefore, in those individuals with well-developed musculature, from prolonged physical activity, BMI will not be an accurate marker of body composition (32).

Menopause diagnosis is being made by age, not circulating hormone levels, since this information is not collected routinely when performing pre and postoperative lab draws. One study by McKinlay used data from the Massachusetts Women’s Health Study and found that average age when last menstrual period occurred was between 50 and 52 years (33). Several additional studies, using lab values to diagnose menopause found a median age of 51 years with less than 1\% having gone through the transition prior to age 40 and approximately 90\% by age 55 (33-35). In the future, using specific lab values such as follicle stimulating hormone, luteinizing hormone, or estrogen would provide a more accurate classification of menopausal status. It should be noted that menstrual cycles and onset of menopause can be altered in the obese, therefore if resources allow, lab values to confirm status would be helpful. For this study,
chosen age ranges paired with extensive chart review to exclude anyone with surgical menopause or early menopause was a good indicator of overall status. Individuals studied were younger than 41 years for the premenopausal group and older than 55 years in the postmenopausal group.

Another possible limitation is that follow up data was only recorded for 1 year postoperatively. Other studies have shown that as time has elapsed after surgery, a slowing of weight lost, or even weight regain is common. This phenomenon could be caused by diet non-compliance, which with time will gradually stretch out the gastric pouch, allowing more food to be consumed at one time, leading to increased caloric intake and poorer outcomes. In the future, it would be interesting to continue following patients in both the pre- and postmenopausal cohorts to see how weight fluctuates beyond the 1-year time point.

Finally, gastric bypass surgery patients were requested to have lab work completed before surgery, and after at 2 weeks, 2 months, 6 months, and 1 year. Follow up response rates were good, however there are occasions were surgery participants did not return for all follow up visits, which is typical fair in the medical profession. Available lab data for each patient was collected, regardless of whether labs for all time periods were available.
CHAPTER II:

REVIEW OF LITERATURE

When taking a stroll through the local super market, even the most oblivious individual will have a tough time escaping the obvious reality that we as a nation are overweight, and we are becoming seemingly more overweight with each passing year. Wing classifies three time periods, throughout a woman’s life, where weight gain is more pronounced: years 25 to 35, perimenopausal, and post weight loss (36). Furthermore, Davis states that obesity rates have increased in the United States because of a total decrease in physical activity, and an increase in the consumption of inexpensive, energy dense foods, collectively termed a Western lifestyle or diet. With our rapidly increasing waistline comes an elevated risk for certain health abnormalities such as cardiovascular disease, type II diabetes, and high blood pressure or hypertension (37). Individuals with increased waist circumference are also more likely to complain of lower back pain, related to herniated disks, which can affect activities of daily living, and participation in routine physical activity (37). Breathing is also negatively affected in the obese and morbidly obese individual with an increase in work of 60% and 250%, respectively (38). Jean Vague, in 1956, attributed various disease conditions; increased weight, diabetes and atherosclerosis, to an individual with a centrally located, obese [apple] body type (39). These diseases, along with a more android shaped body (increased abdominal obesity) can be collectively referred to as metabolic syndrome or Syndrome X(40). Researchers have reported that insulin resistance is the underlying factor to Syndrome X, and this resistance is what leads to the other health abnormalities seen in those with metabolic syndrome (41). American endocrinologist Gerald Reaven coined the term, Syndrome X, in 1988, while presenting at a Banting Lecture, which presents current research in diabetes and diabetes self management. Since his presentation, the
condition and related diseases have continued to grow in prevalence, and Syndrome X is now a widely used term by medical professionals in numerous specializations (41). As a result of our changing dietary habits and our expanding waistlines, new methods of weight loss are being conjectured on a rather hurried basis. In the midst of a barrage of new pills, exercise videos, self-help books, and surgical procedures, the latter has been the most effective in helping to reduce excess weight and sustain that loss over time (42).

America’s Obesity Woes

As mentioned earlier, the obesity epidemic in the United States is spiraling out of control, and the National Health and Nutrition Examination Survey (NHANES) data from 2007-2008 indicated that the overall prevalence of obesity was 32.2% among men and 35.5% among women (43). Overweight and obese individuals represent the fifth leading cause of death in adults, equating to approximately 2.8 million deaths annually (44). Current data published in the Journal of the American Medical Association showed that in 2009-2010, obesity prevalence rates were 35.5% and 35.8% in men and women, respectively (43). Regrettably, with obesity comes a two-fold increased risk of cardiovascular disease, and a five-fold increase in risk for type II diabetes (45). Obesity also affects individuals on a psychosocial level, related to negative feelings of self esteem, self worth, appearance, and social functioning, in both genders and all ethnicities (46). While these numbers are dismal, it does appear that obesity prevalence rates are starting to decrease, or level off, when compared to NHANES data previously reported. Between 2005-2006 and 2007-2008, obesity rates fell from 35.1% to 34.3% for those with a BMI ≥35 kg/m², and from 6.2% to 6.0% in those with a BMI of ≥40 kg/m² (47). Significantly larger increases in obesity rates, both in the ≥35 kg/m² and ≥40kg/m² BMI classifications was witnessed from 1976-1980, and again between 1988-1994, with rates jumping from 15% to
23.2% for the $\geq 35 \text{ kg/m}^2$, and 1.4% to 3.0% for the $\geq 40 \text{ kg/m}^2$, respectively (48). Over the same period of time, the rates of those in the overweight, 25-30kg/m², category was not significantly greater. More recently, the increase between 1999-2000 and 2007-2008 saw a lessened rise of 4.7% in men, and an insignificantly lower 2.1% jump in overweight and obese women (43).

To some, the slowing in obesity prevalence rates might seem promising, negating the need for further aggressive intervention to help alleviate the body weight problem in the United States, across all cohorts. Unfortunately, those that have emigrated from another country have also shown marked increases in weight with acculturation (49). However, to consider that more than one third of the American population currently is classified as obese presents those within the medical field the daunting task of helping to treat the problem, and lessen the burden on our medical and financial systems (50). In 2008, it was estimated that medical costs related to obesity were 147 billion dollars, or approximately 10% of the country’s total medical expenditure (51). Furthermore, individuals that currently fall into the upper echelons of the BMI classifications, with the exception of body builders, still are likely to be at a higher body weight than what is recommended for good health. Therefore, something must be done as an intervention to treat these high BMI individuals, before it is truly too late from a health perspective.

This study will review scientific literature of not only metabolic syndrome, but also the health idiosyncrasies of a specific cohort of pre- and post-menopausal women, and potential negative weight change in this group. It is widely accepted that with menopause, numerous physiologic changes occur. These can lead to a propensity for weight gain and other associated metabolic conditions, similar to those mentioned above. Additionally, focused research on the Roux-en-Y gastric bypass procedure, specifically on this particular cohort of the population, will
be reviewed. The question, “Are there differences in the efficacy and resolution of metabolic syndrome in those women who are pre- and postmenopausal?” will be addressed. If data analysis shows significant differences, a more tailored approach to bariatric surgery and specialized recommendations for this particular population will be formulated to help maximize the results of bariatric surgery, postoperatively.

**Nutrition Education and Lifestyle Modification**

Weight gain has been snowballing upwards by leaps and bounds over the past several decades in the United States, which can generally be attributed to our transition to a more convenience based diet and more sedentary lifestyle. Wing believes that by initiating a more targeted, individual approach will yield the most lasting results. By asking 3 questions, new weight loss methods can be formulated and initiated to target and help these specific cohorts of the population: 1) Can those at risk who are more prone to obesity be identified early? 2) How should we intervene to prevent weight changes in these groups? 3) What behaviors should we focus on to cause the greatest change (36)?

Recent studies related to an individual’s weight have focused on those individuals who are at a normal, healthy weight, as opposed to those who specifically need to lose excess body weight. Current research completed on those who are overweight has not produced long-term results through diet and exercise, and one current ideology revolves around educating those at a healthy weight on nutrition and diet, to prevent gains later in life (52). Forester et al designed a community-based program for normal weight individuals that consisted of a monthly newsletter on nutrition, group weight loss sessions, and a contingency system to help increase participation (53). After 1 year, 82% of the group remained at or below their entry weight versus 56% percent of the controls that received no intervention. The researchers question whether this trend would
continue into the future. As one may expect, it would be difficult to recruit individuals for this
type of study, since they are not currently classified as overweight or obese.

Kim and colleagues looked at obesity patterns cross and prospectively in South Korean
adults using the Korean National Health Examination Survey. Data results showed that diets
highest in grains, vegetables, and fish were associated with a decreased risk of metabolic
syndrome, while those higher in meat and alcohol put one at an increased risk (53). Registered
dietitians generally agree that diets high in fruits, vegetables, whole grains, and low-fat dairy,
such as those stressed in the Dietary Approaches to Stop Hypertension (DASH) diet produce
desirable results over time, and have even been shown to lower blood pressure and improve
weight in the obese population (54). This is why associations such as the Academy of Nutrition
and Dietetics, American Heart Association, and United States Department of Agriculture,
disseminate these dietary ideas to the public in hopes of making a positive change.

Esmailzadeh researched Iranian women who had been shown to have the highest
incidence rates (35% of Iranians) of metabolic syndrome when compared to other groups around
the world. Dietary energy density (kcal/gram of food) was researched through the use of a 168-
question food frequency questionnaire, with food intake data being analyzed by trained
registered dietitians. A seemingly obvious flaw to this methodology was that calories from
beverages were not calculated, which could potentially represent a large proportion of calories
consumed in this population’s diet. Similar to the United States, sugar sweetened beverage
consumption is on the rise in many countries, including those in the Eastern Mediterranean
region, which encompasses all Arab countries, Afghanistan, Iran, and Pakistan (55). Children in
the Eastern Mediterranean region rate sugar sweetened, carbonated beverages as their favorite
with 60.7% and 54.8% response rates based on male or female gender, respectively (55). This
may pose a major threat to the validity of the results, since these beverages have been linked to an increase in body weight and incidence of disease such as diabetes (56, 57). If the study were being done in the United States, beverages would most certainly need to be included in the questionnaire because they do represent a significant proportion of daily caloric consumption. Not surprisingly, Esmaillzadeh found that diets that were more energy dense resulted in an increased risk for metabolic syndrome in this population (58). This is in agreement with Kim et al, who reported further proof of the importance of consuming a healthy, well balanced diet that is more nutrient dense, as opposed to more energy dense (53, 58).

Further supporting a Mediterranean style diet, research reported that the incidence rates of metabolic syndrome were found to be 14% lower, and hypertriglyceridemia incidence was reduced by 20% in the group that consumed greater amounts of grains, vegetables, and fish. Kim also found that in men who consumed the most fish, and therefore omega-3 essential fatty acids, metabolic syndrome risk was halved compared to those who consumed the least. Unfortunately this result was not seen in women in this particular study. Conversely, the risk of metabolic syndrome and hypertriglyceridemia were 19% greater in the group that consumed more red meat and alcohol (53).

Preventing these fat deposition changes and the bleak path towards metabolic syndrome from occurring are possible through diet and exercise as described. Recent research using the National Weight Control Registry depicts a brighter overall picture, illustrating that a weight loss of thirty pounds, and maintenance of this loss for greater than one year is attainable (59). Of these participants studied, 77% were female and those that lost the most weight reported always eating breakfast along with participating in routine physical activity(59). Unfortunately, while
promising, even a loss of thirty pounds takes much time, planning, dedication, and hard work, all of which are not commonplace in our society.

Unfortunately, weight loss big or small is difficult for some cohorts of the population to achieve, especially when hormones are working in the opposite direction. Research over the years has supported this difficulty with sustained weight loss and maintenance, which has only added to an individual’s frustration on the subject (60, 61). Popularized diets, such as the Dietary Approach to Stop Hypertension (DASH), appear to be the most successful in reducing nearly all components of the metabolic syndrome as mentioned previously (62). While the DASH diet is effective, new diets are introduced monthly, and often each new diet is more absurd than the prior, only confusing the public and causing undue frustration.

Dhaliwal et al, using data from the Framingham Heart Study found that those with an increased waist to hip ratio (WHR), and waist circumference (WC) were more likely to suffer from CHD or CVD, and subsequently, death at an earlier age than someone with a normal WHR and WC (63). However, menopausal status was not factored into the previous study, and therefore, additional studies need to be conducted that specifically differentiate between those women peri- and postmenopausal women who are using estrogen replacement therapy, and those that refrain from estrogen replacement therapy.

Nahas found that abdominal obesity was the most prevalent diagnostic factor for metabolic syndrome in his group of postmenopausal women at 62.5%, while Chedraui had similar results with 54.2%, second to hypertriglyceridemia at 56.9% (64, 65). Both studies used ATP III guidelines to diagnosis metabolic syndrome, and participants were removed from the study if they were in the perimenopausal period, which was defined as a three-year period that
includes two years before the last menstrual cycle to one year past. While identifying the perimenopausal time frame is not exact, self reported data reporting when menses becomes irregular, in both timing and flow, along with the onset of common menopausal symptoms such as hot flashes and increased perspiration were used to identify this particular period in a woman’s life (66). Included individuals will be those who have experienced a year’s time since their last menstrual cycle, indicating that menopause has occurred and the perimenopausal period has ended. Nahas looked at a primarily low SES population of women between the ages of 40 and 75 years who attended a public health outpatient center in southern Brazil (64), while Hidalgo looked at a similar population in Ecuador (67). Again, when looking at a population of lower SES, it is easy, but not always accurate; to assume that diet quality is poor and the proportion of nutrient dense foods is outweighed by a calorically dense variety, and that is what ultimately leads to the metabolic syndrome incidence noted.

Okamura looked at 4939 Japanese participants in the Suita Study who predominantly resided in an urban environment. Central obesity was defined as \( \geq 90 \text{cm} \) in men and \( \geq 80 \text{cm} \) in women, which is smaller than what is normally used when following the ATP III guidelines. However, these values more accurately represent this specific Japanese population, and are a better indicator of obesity in this population since, as a whole their frame size is much smaller than those of persons in other parts of the world. Researchers found that once sex specific analysis was performed, women with elevated blood pressure and fasting blood glucose were at an increased risk for coronary artery disease and ischemic stroke (68). This study supports Kokubo’s research, which also looked at metabolic syndrome components and the risk of cardiovascular disease in those living in Japan. He found that each metabolic syndrome component synergistically increases the risk for CVD in both men and women, regardless of
whether or not abdominal obesity was one of the included factors (69). This study further supported that while there are many negative consequences of an android body shape, it does not solely place one at an increased risk for cardiovascular disease later in life. These data also reinforce the importance of regular medical exams and screening of everyone, not just those who are overweight or obese as defined by BMI.

Unfortunately, for an individual that is morbidly obese, such noticeable improvements in blood pressure, insulin resistance, and total weight loss may not be as prominent when only implementing a dietary intervention, such as the DASH diet. Furthermore, for a morbidly obese female who has gone through menopause, the DASH diet would likely yield positive results, however in total they may be inadequate, therefore requiring a different plan of weight loss attack.

Azadbakht found that when the Dietary Approach to Stop Hypertension (DASH) diet was implemented on 116 patients who had a mean BMI of 28.9 kg/m² the incidence of metabolic syndrome was reduced. Lower triglycerides and blood pressure and higher HDL-C levels with better controlled blood sugars were also observed, most of which can be attributed to the loss of weight experienced and the positive manipulation of the diet to include more wholesome components and healthy fat choices (62). A disadvantage to this particular study, and many similar studies, was that they focused on a country outside of the United States. While the information provided and results will provide benefit in a multitude of countries, the availability and sustainability of such a diet may not fare as well in the United States.

Cicero, using data from the Brisighella Heart Study, set out to investigate whether cardiovascular risk and metabolic syndrome could be attenuated or eliminated through nutrition
education and lifestyle modification (70). This longitudinal epidemiological study looked at post-menopausal women (301 before and 262 after a nutrition intervention program) to see if lab values and anthropometric measurements were altered in either a positive or negative direction at the study’s conclusion. Dietary intervention included general recommendations that stressed the importance of low-fat dairy, limiting of cheeses, the substitution of fish and chicken for red meat, total sugar consumption of <300g/day, and limiting egg intake, while concomitantly consuming more vegetables, whole grains, and extra virgin olive oil (70). The research data showed that women who were within 4 years of going through menopause had the greatest increase in BMI, systolic blood pressure, total cholesterol, LDL-C, and triglycerides, while HDL-C values fell. After the dietary intervention, the only value that improved was triglycerides, with a mean decrease of 12.6 mg/dL. When comparing baseline values to those at the study’s conclusion, BMI was slightly elevated at 25.6 kg/m² versus 26.1 kg/m², respectively (70). One could postulate that a greater increase in BMI may have taken place if the nutritional intervention was not implemented. The authors postulated that perhaps a low cholesterol diet may be more preventative of metabolic syndrome in females, and also may improve nutrition related values; however, they did caution that such a diet may increase the incidence of osteoporosis, since a low cholesterol diet may exclude dairy products (70). With proper knowledge and access to reputable information, a person can construct a diet that is low in cholesterol, while still including dairy sources. This study by Cicero included only a dietary component, which could be why the results were not shown to be as beneficial (70).

Additionally, Stampfer found that those women, regardless of menopausal status, who followed a strict lifestyle intervention of diet, exercise, and abstinence from smoking, were significantly less likely to suffer from coronary heart disease (71). Data was compiled using the
Nurses’ Health Study, in which registered nurses from across the country were recruited randomly and were asked to provide health data via a detailed questionnaire. Follow up information was collected in the same manner every two years following the original assessment. Potential risk factors and other health information were collected and compiled into a single, central database. A healthy diet was defined as one low in trans-fat and glycemic load, while stressing increased consumption of omega-3 fatty acids, cereal fiber, and folate. These dietary modifications, in addition to physical activity and the refraining from smoking, likely contributed to the decreased risk of coronary heart disease shown in the results (89). It should be noted that the Nurses’ Health Study also relied on food frequency questionnaires to compile intake data, which have their pros and cons within their own right.

More specifically, food frequency questionnaires, or FFQ’s, are commonly used to formulate and further study an individual, or population’s usual food habits over an extended period of time (72). A set of questions is presented to the individual with the FFQ. These questions relate to a particular food or food group, and the participant is required to answer appropriately, as to whether they consume, or do not consume the particular item (91). Possible responses, for all questions outlined on the FFQ, will typically provide the participant with a frequency, which they will have to choose, based on how often the particular food or beverage is consumed. Once the questionnaire has been completed, the research team, or group that compiled the FFQ can analyze all questions together, and formulate trends based on analysis of the information provided. While the FFQ can be beneficial, it does come with several limitations.

For some, specifically older individuals, the FFQ is too lengthy, and personal interest to complete the questionnaire is lost, therefore compromising the results. Furthermore, much variation can be present between diets, based on an individual’s background or ethnicity (73).
Regularly consumed foods for one ethnic group may not be congruent with another ethnic group and therefore certain vitamins or minerals being studied could potentially be overlooked (73). A tailored FFQ, similar to the one used by Fadhilah, was shown to be accurate when studying the dietary intakes of Malaysian adolescents, in Malaysia (74). Additionally, Sullivan formulated a tailored FFQ, when she studied long-chain \( n \)-3 polyunsaturated fatty acid consumption in Australia, in which the FFQ was found to be reproducible of intakes for that specific population (75). As with other methods of dietary recall and food habit investigation, there are likely to be certain aspects, related to the data collection method that are advantageous, and others that have flaw(s). Utilizing a combination of data collection methods, and individualizing these methods on the cohort being studied, can help ensure that the most accurate data is collected.

Unfortunately, diet is only one component of a healthy lifestyle. For many, dietary compliance is very hard to control, especially when hectic lifestyles and stressful jobs predominate. Levine et al found that when comparing two groups of dieters and non-dieters, those women not on a diet gained only 0.2kg while those on a diet gained 1.5kg over a three year period (52). Unfortunately, diets that are restrictive, or that remove specific items or food groups can lead to cravings, and an increase in consumption of the prohibited food, causing total intakes to rise, with subsequent weight gain, which may have lead to Levine’s study results mentioned above (52).

Access to processed foods may be far less in countries outside of the United States simply because they have not been “Westernized” to as great an extent, thus far, in their food choices. Other countries, especially those in Europe and Asia, were once the anomaly in this epidemic of obesity and disease; however, they are quickly joining the ranks of the United States on a much grander scale with diets being comprised mostly of high fat and refined carbohydrate
items (76). Kimokoti agreed when he reported that by 2030, China will have the largest proportion of overweight and obese individuals in the world, which is a alarming thought since China’s population is an astounding 1.6 billion (45). As the introduction of a more carnivorous, convenient, over-processed diet ensues globally, countries that were once slender and fit will quickly follow in the footsteps of the United States, and transform into more plump and sedentary group of people. With these anthropometric alterations, comorbid condition prevalence will surge and with it medical premiums will follow.

**Surgical Methods of Weight Loss**

Weight loss surgery has evolved over the past several decades, and is now considered the most successful and effective weight reduction option for those persons who are morbidly obese, and who have not had luck with other, more conventional weight loss modalities; such as diet, exercise, or a combination of both. It is estimated that the number of surgical weight loss procedures worldwide have increased 761% from 40,000 in 1998 to 344,221 in 2008 (77). This substantial growth in bariatric operations is due in part to an overall increase in BMI, but also because of an upsurge in bariatric surgeons worldwide, along with safer surgical techniques; open versus laparoscopic (78). Buchwald illustrates that while there has been substantial growth in bariatric surgeries between the years 1998 and 2008, trends have begun to stabilize worldwide, with the Roux-en-Y procedure being done most frequently, comprising nearly 50% of all bariatric surgeries worldwide (78).

Varieties of bariatric surgery include gastric banding, vertical banded gastroplasty (stomach stapling), gastric bypass, biliopancreatic diversion with duodenal switch, and more recently, the gastric sleeve, which can be a two-part operation to help maximize patient safety and deliver more effective results for those with a BMI greater than 50 kg/m². BMI
classifications using the 1991 National Institutes of Health criteria segregate obesity into grades I, II, and III, based on whether one's BMI is greater than 30 kg/m², 35 kg/m², or 40 kg/m², respectively (79). More recently, the classification of super obese has been utilized, which indicates a BMI that is greater than 60 kg/m² (80).

By prefacing a select number of Roux-en-Y gastric bypass [RYGB] and biliopancreatic diversion with duodenal switch [BPDDS] operations in the super obese population with the gastric sleeve, many post-op complications can potentially be avoided (81). Some patients may not need the malabsorptive RYGB or BPDDS procedure, if enough weight can be lost via the gastric sleeve, which may also help to improve overall mortality rates (81).

The weight loss surgeries briefly mentioned above result in either a restriction in the stomach’s physical size, or a bypass of a section of the gastrointestinal tract to promote nutrient malabsorption (82). Currently, the gold standard for weight loss is the laparoscopic Roux-en-Y procedure, which includes both a restrictive and malabsorptive component (83). More specifically, the RYGB surgery restricts gastric volume through the creation of a small gastric pouch along the lesser curvature of the original stomach, with the subsequent rerouting of intestines, pulling nutrients from the stomach, directly to the mid/distal jejunum (84). For an individual to be eligible for bariatric surgery, certain criteria must be met; and the subject must go through a multistep, preoperative set of tests and exams, so that the physician and bariatric team can be certain surgery is the best and safest option for the participant (85). First, the individual must have a BMI of ≥40 kg/m² or ≥35 kg/m² if a co-morbid condition is present, such as diabetes or hypertension (86). Additionally, encounters with other medical specialties are mandatory, in addition to the primary surgeon, which will include psychiatry, cardiology, and
also an extensive set of appointments with a registered dietitian, which is commonplace for any bariatric surgery center.

Some researchers have questioned the need for pre-surgery meetings with a registered dietitian, postulating that weight loss outcomes are not improved for those participating in a medically supervised weight loss program before surgery. Parikh, Jamal, and Ochner have analyzed pre and post surgery outcomes, between those who completed a mandated medically supervised weight loss program versus those individuals that had no such encounters. All three found that pre surgery medically supervised weight loss participants did not lose more weight when compared to the non-intervention group (87-89). Furthermore, drop out rates were higher in the medically supervised weight loss cohort, potentially due to frustration with results at each preoperative meeting.

Again, the Roux-en-Y gastric bypass procedure works by having not only a malabsorptive component, but also a restrictive component, which is why resulting weight loss is typically greater with this surgery, as opposed to other methods (90). The lesser curvature of the stomach is partitioned to 30mL in size and the jejunum is anastomosed to the new stomach pouch, bypassing a large section of the normal digestive tract (91). This newly created, alimentary or roux limb can be of varying lengths, depending on the preoperative BMI of the surgery patient (91). Brolin compared the efficacy of varied roux limb lengths, in the super obese, and found that using a 150 centimeter versus a 75 centimeter length, produced greater excess weight loss at two years post-operatively, 64% versus 50%, respectively (92). A longer roux limb, creates a lengthened section where malabsorption occurs, which is why weight loss is more pronounced, however the risk for nutrient deficiency is also increased and must be supplemented appropriately, which is typically accomplished through additional vitamins that
persons must take for the remainder of his/her life (92). Not surprisingly those who opt for weight loss surgery with a malabsorptive component are at highest risk for vitamin and mineral deficiencies post operatively (93).

As mentioned previously, the Roux-en-Y procedure has been improved, and is now conducted in such a way to minimize health risks and maximize both weight loss efficacy and overall outcome. Researchers studied 27 morbidly obese individuals who had a combined 101 co-morbid conditions going into surgery, such as hypercholesterolemia, hyperlipidemia, diabetes, gastro esophageal reflux disease, and sleep apnea, prior to having the Roux-en-Y operation (18). In 18 months, 98 of the original 101 co-morbid conditions were resolved, which was a direct result of the excess weight lost over the specified time period (18).

It is not surprising that weight loss can be achieved due to the restrictive and nutrient malabsorptive components of the Roux-en-Y procedure. However, additional alterations in hormones occur that help improve insulin resistance and decrease an individual’s resting energy expenditure (REE), which also help to yield a reduction in weight. A study of 31 morbidly obese individuals, who underwent the Roux-en-Y gastric bypass procedure, reported a mean decrease in REE of 396 kilocalories plus/minus 157 kcal/day (94). Additionally, all patients that had diabetes preoperatively resolved this issue, and surgery patients resumed normoglycemia 6 months postoperatively (94). Furthermore, all cases of dyslipidemia were resolved 6 months postoperatively, with values for total cholesterol, LDL-C, and triglycerides returning to within normal limits. Contrary to the belief that hormones cause a change in REE, Redman et al found that caloric restriction lead to weight loss and a decreased REE, independent of hormones (3). Instead, these researchers believed that the body incurs a “metabolic adaptation” and the reduction in REE is directly proportional to the decrease in metabolically active tissue, both fat
and muscle, from lost weight (3). Additionally, Pereira et al researched REE and weight loss on those following a low glycemic or a low fat diet. Participants assigned to the low glycemic diet had an REE 80 kcal/day higher and experienced less hunger when compared to those on the low fat diet (95). Furthermore, those on the low glycemic diet also had improved insulin resistance, lipid profile, blood pressure, and lessened inflammation, when compared to those that followed the low fat diet (95). Diet composition, as well as total caloric intake level can affect an individual’s REE, as evidenced by the studies outlined above.

Suter et al. followed 379 Roux-en-Y gastric bypass weight loss surgery patients. The average preoperative BMI in this particular cohort was 46.3 kg/m². After five years, 74.9% had lost >50% of excess weight and, on average 64.9% had a BMI of <35 kg/m². Some weight regain was noticed in the super obese patients between the five and seven year mark, with 24.4% showing weight regain at five years and 35.5% in those patients at the seven year mark (96). Even with weight regain in those super obese and super super-obese patients, gastric bypass surgery was still effective in helping to reduce total body weight, and aided in the resolution of co morbid conditions present in the beginning (96).

Christou et al followed 1035 bariatric surgery patients for a mean period of 16.4 (72% patient follow up at study conclusion) years to investigate long-term morbidity, mortality, and health care costs for those morbidly obese individuals opting for bariatric surgery. Researchers found that those individuals who had either open or laparoscopic RYGB surgery showed significantly greater weight loss, when compared to those who had the vertical band gastroplasty procedure, 68.7kg versus 57.3kg, respectively (97). Christou states that a larger increase in the gut hormone PYY postprandially, in addition the subsequent suppression of ghrelin, increased satiety, promoting earlier meal termination, which explains why the RYGB is more successful
surgery, in terms of excess body weight lost, when compared to gastric banding. Health care visits for all conditions was lessened in those who had bariatric surgery in the 5-year follow up period, indicating that while the surgery is costly, this money can be recouped over the long run with overall 5-year mortality reduced by 89% (97).

Papasavas et al. followed 71 bariatric surgery patients who were all over the age of 55, with a mean age of 59 years. They reported that morbidity and mortality between individuals over 50 and those of a younger age were the same. However, those over 50 who experienced a perioperative complication, such as a small bowel obstruction, anastomotic ulceration or bleeding, or deep vein thrombosis, had a slower recovery, which can be attributed to their older age and less resilient physiology. Efficacy and resolution of obesity related co-morbidities were similar to those mentioned above, with decreases in medications used to treat diabetes, hypertension, and sleep apnea by 87%, 70%, and 86%, respectively, regardless of age (98).

Even with lengthier recovery times, significant weight loss can be attained with similar mortality rates when comparing older versus younger surgery participants. This makes the research done by Papasavas especially important because it outlines the effectiveness, and thereby, the importance of bariatric surgery on an older cohort of the population that encompasses the majority of postmenopausal women (98). This allows practitioners to make such a recommendation for postmenopausal women, over the age of 50, who require surgical intervention to allow for weight loss and comorbid condition resolution.

A paucity of research has been reported relating menopause to weight loss surgery. However, it is known that with menopause comes the propensity for weight gain and its associated health conditions (99). Therefore it would seem reasonable to assume that a surgery
that can result in sustainable, significant weight loss would be highly beneficial to this particular
cohort of the population. Teitelman looked at 195 women at the University of Pennsylvania who
had menstrual pattern irregularities, and who were also clinically obese, to see if bariatric surgery
and subsequent weight loss would resolve these conditions (100). The data showed that of the 98
anovulatory individuals pre-op, 70 (71.4%) resumed normal menstrual patterns after surgery as a
result of weight loss. Those who lost the most weight as a result of the bariatric surgery were
more likely to regain regular menses post-op (100). A similar study by Escobar-Morreale et al
looked at 12 pre-menopausal women, with polycystic ovary syndrome (PCOS), who underwent
bariatric surgery. They found that all 12 had improved PCOS related lab values, and normal
menstruation resumed with weight loss (101). These studies indicate that with weight loss, major
physiologic changes occur, such as the resumption of menses in those women who experienced a
cessation due to obesity.

Undiagnosed Diseases and Economic Burden

Obesity and its related co morbid conditions, mainly diabetes, hypertension, and
hyperlipidemia, are putting an enormous strain on the health care system, with estimated costs of
$174 billion in 2007, according to the American Diabetes Association; and, $403.1 billion in
2006 according to the American Heart Association in relation to both diabetes and
cardiovascular disease, respectively (102). Bariatric surgery, primarily the laparoscopic Roux-en-
Y procedure results in the greatest reduction in excess weight, as mentioned (103). Costs for this
surgery are approximately $17,000, and this has decreased recently due to improvements in
technology, surgical experience, and dedicated surgical weight loss centers scattered across the
country (104). It is estimated that through a reduction in prescription drugs, hospital visits, and
physician appointments, the initial investment for the bariatric surgery can be recouped in only 25 months, making it a cost effective option for the treatment of obesity, in the long run (104).

In lieu of these stated benefits, focusing specifically on menopausal women who fall into the categories of either overweight or obese, and lowering their surgery criteria inclusion points could help to alleviate a portion of the burden associated with obesity and its treatment that is currently placed on the healthcare system (105). Lowering the surgery criteria would greatly help this cohort of the population because of their known propensity for the hormone driven weight gain and weight redistribution following the menopausal change. Furthermore, with a reduction in weight, the incidence rates of metabolic syndrome could potentially be decreased which, would immensely improve an individual’s quality of life after surgery. The risk factors associated with metabolic syndrome are insulin resistance, dyslipidemia, hypertension, and an increased waist circumference, according to the National Cholesterol Education Programs ATP III guidelines (4). A reduction in weight via surgical intervention can help alleviate many, if not all of the previously stated ailments, and as a consequence, reduce total healthcare costs through decreases in prescription drug use, physical therapy, occupational therapy, and related physician visits (104).

A rather startling component to the study completed by Hidalgo et al. was that approximately 40% of those studied with diabetes and hypertension were not aware that they possessed either of these conditions (67). Unfortunately, this is not uncommon in those of lower socioeconomic status, primarily due to the fact that access to adequate health care is lacking, and therefore, the diagnoses are not always made in timely manner. While this may not be surprising in other countries outside of the United States, Palaniappan found similar results in Asians living in Northern California, as mentioned earlier (106). This was not as heavily attributable towards
low socioeconomic status, but rather a result of differences in body size and diagnostic criteria used for the target population. In either instance, it is imperative that these potential differences be recognized in order to more accurately, and efficiently diagnose those women with metabolic syndrome or any of its components early on, so that a proper intervention can be initiated, saving money through appropriate care for the specific medical condition.

Along the same lines, Hadaegh studied BMI and diabetes risk to ascertain whether a correlational relationship could be drawn between the two (107). It was found that 2.3% of women who were of a normal weight had metabolic syndrome, while 41.7% of obese women did not have metabolic syndrome. Hadaegh does point out that the highest incidence (62%) of diabetes in their study population was in those who were obese and had metabolic syndrome, as one would expect (107). This illustrates why it is important to look at contributing factors of the metabolic syndrome condition, such as abdominal obesity or lab values, and not just one single component. As mentioned earlier, a large proportion of inhabitants around the world are dealing with diseases that have not even been diagnosed because of lack of health care, knowledge deficit. Using the NHANES 2005-2006 data set, Cowie et al found that approximately 40% of the U.S. population meets the diagnostic criteria for diabetes, but have not been formally diagnosed (108). Furthermore, undiagnosed pre-diabetes, based on impaired fasting glucose or impaired glucose tolerance was similar and showed a much sharper increase with age, possibly due to increasing weight and gradual pancreatic dysfunction (108). Similarly, Zhang found in 2007 that there were approximately 6.3 million cases of undiagnosed diabetes mellitus in the U.S., which is responsible for an 18 billion dollar economic burden, mostly related to the treatment of other diseases, in place of diabetes, since an accurate diagnosis was not made (109). Screening the entire population routinely is a fundamental step in attacking the problem of
overweight, obesity, and disease at an earlier point in time. Many local governments and non-profit organizations hold health fairs/screenings periodically, which help provide access and awareness to health conditions for the masses that help with diagnosing health conditions in a timelier manner. The authors suggest that everyone, regardless of weight be screened for diabetes since there are so many undiagnosed cases are present (107).

**Metabolic Syndrome**

In the year 2000, metabolic syndrome prevalence was reported as 47 million, which is equal to approximately 40% of the adult population, encompassing both males and females (110). Since then, the numbers have only risen, especially as our diets continue to become less healthy, and the population becomes more ethnically diverse and sedentary, making over nutrition the cause of a greater number of deaths worldwide, in place of under nutrition (111). Other factors such as smoking, family history of coronary heart disease, and aging contribute to an increased risk for metabolic syndrome diagnosis (112). The two age groups that have the highest number of diagnosed metabolic syndrome cases are those between 20-29 years and those over 60 years of age (110), indicating an increase in prevalence for the age cohort that encompasses postmenopausal women (112). Both of these age groups have their own sets of negative health related consequences, and both will be further elaborated upon in this literature review. While it is not the largest proportion currently, adolescence represents 3.5% of the total metabolic syndrome cases in America (113). This group is one to monitor closely, since many people who develop the condition early will carry it on into adulthood, which again stresses the importance of early intervention. While there is no magic bullet to erase the effects of metabolic syndrome, there are numerous lifestyle modifications that can be introduced that can significantly blunt its effects, and over time, potentially erase it altogether.
Metabolic syndrome is characterized as abdominal obesity, elevated blood pressure, impaired fasting glucose, depressed high density lipoprotein cholesterol levels, and elevated triglycerides (45). Some postulate that it is the adipose tissue itself that leads to metabolic syndrome via the action of adipokines from the tissues paracrine and endocrine activity (114). Guidelines put forth by the National Cholesterol Education Program (NCEP) under the Adult Treatment Panel III state that an individual must have 3 of the 5 following characteristics to be diagnosed with metabolic syndrome: abdominal obesity (waist circumference >88cm in women and >102cm in men), triglycerides ≥150 mg/dL, depressed HDL-C (<40mg/dL in men and <50mg/dL in women), blood pressure ≥130 or ≥85 mmHg, and fasting glucose ≥110mg/dL (4).

Stefanska et al. looked at long-term weight gain and metabolic syndrome with additional data collected on C-reactive protein [CRP] and adiponectin, a protein similar to leptin that may play a role in weight regulation and satiety (115). This study used women recruited randomly between the ages of 50-60 years who were from a larger cohort of 40-60 year old women chosen from the Department of Laboratory Medicine at the Medical University in Bydgoszcz, Poland. These women provided researchers with their weight from age 20 through self-reported questionnaires that allowed researchers to measure weight gain over a period of 30 to 40 years. Not surprisingly, it was found that those that gained the most weight had the greatest insulin resistance and most elevated triglycerides, blood pressure, and fasting blood glucose. Levels of adiponectin and HDL-C values were the lowest in the group that gained greater than 30 kilograms, both which can have a protective effect against insulin resistance and the circulatory system. It was also established that CRP mimicked weight gain most closely, and it acted as an accurate indicator in those studied (115). The more weight gained, the more elevated CRP levels appeared, and vice versa. Unfortunately, one major flaw with this particular study was that
weight from age 20 was self-reported; therefore we cannot be certain that these values were accurate, related to the inconsistencies that are inherent among self-reported data. Furthermore, it is not evident when weight gain occurred, and the researchers cannot assume that it was in the time surrounding pregnancy or later on in life during menopause, or anywhere in between.

Tchernof researched 61 obese, postmenopausal women, who were prescribed to follow a medically supervised weight loss program that consisted of a 1200 calorie per day, American Heart Association Step II Diet (116). This calorie-controlled diet was followed for just over one year (13.9 months). Women lost on average 14.5 pounds (6.2kg), and it was found that CRP levels were directly proportional to weight lost, since those who had larger weight decreases, had subsequently larger decreases in plasma CRP (116). Research has shown that when CRP levels are continually elevated, creating a state of constant, low-level inflammation, cardiovascular disease risk is increased (117). Obese/overweight women should, therefore, find it advantageous to strive for weight loss, regardless of amount, which can potentially help reduce the total risk of cardiovascular disease, a known risk for women who have gone through menopause.

Along the same lines, several researchers have begun using low-level markers of inflammation to help delineate those with future potential risk for CVD and metabolic syndrome. Adipose tissue has recently been discovered as an active endocrine organ that secretes a wide variety of molecules, such as tumor necrosis factor alpha [TNF-α], interleukin-6 [IL-6], leptin, adiponectin, and resistin (114, 118). The secretion of these compounds differs as the adipocyte, or fat cell is enlarged, which is one of the underlying causes of several abnormalities present in metabolic syndrome, such as insulin resistance. As concentrations of TNF-α and IL-6 become elevated, a signal is sent to the liver to produce more CRP, which puts the body in a constant
state of low-level inflammation. Furthermore, as adipocytes grow, circulating levels of leptin and adiponectin decrease, both of which help to regulate appetite through the inhibition of neuropeptide-Y, which acts as an appetite stimulant. Once this hormonal balance is thrown awry, hunger and weight may increase, and with this negative weight change comes an increase in insulin resistance, thereby starting the vicious cycle of weight mismanagement.

Chedraui set out to investigate whether these pro-inflammatory cytokine levels differed between postmenopausal women that have metabolic syndrome and those that do not have the condition (118). Chedraui hypothesized that with menopause comes an increase in body weight, and therefore the odds of low-level inflammation via the previously mentioned mechanism could exist. In his study, the data indicated that cytokine levels did not differ between those subjects with or without metabolic syndrome. However, levels of IL-6 were significantly elevated in those with marked abdominal obesity, and both IL-6 and TNF-α were elevated in those with hypertension (118). Nahas found that CRP levels of >1mg/dL were found in 3.9%, 7.8%, 16.9%, 17.8%, and 21.4% of his study group that were positive for 1, 2, 3, 4, and 5 components of metabolic syndrome, respectively (64). From these data, there is a distinct, positive, linear relationship between an elevated CRP and an incidence of metabolic syndrome components. Perez-Lopez also found that when CRP levels were >3.0mg/dL, incidence rates of future cardiovascular events were increased, even when adjustment was made for age. Elevated levels were shown to increase the risk of stroke 2-fold, and myocardial infarction 3-fold in men (119). This study found no difference in CRP and risk between men and women, which supported the importance of this inflammatory marker in future disease diagnosis for all genders (119).

Additionally, Cintra et al. looked at CRP levels in those women who had undergone both bariatric surgery, and abdominoplasty at a later time to remove excess skin from the abdominal
area. Researchers wanted to see whether or not levels of CRP would change once a large proportion of subcutaneous fat was surgically removed, as would be the case after abdominoplasty surgery. Data indicated that CRP levels were immediately lessened post-op, and that HDL levels simultaneously increased (120). Because visceral fat is more metabolically active, it was hypothesized that removing a large quantity of subcutaneous fat would not have a large effect on circulating CRP levels. This study pointed to the contrary, and it showed an additional way to help decrease rates of low level inflammation, of which CRP is an accurate, and widely used marker (120). As stated above, CRP has a positive relationship with weight gain; therefore we want levels to remain on a downward trend, which is the case when weight is lost, regardless of amount or weight loss method.

Bray discovered added factors that could be related to various inflammatory markers secreted by the fat cell as it expands (5). Compounds such as interleukin-6 and C-reactive protein, as mentioned previously, and other various cytokines move through portal circulation, where they cause for the release of additional “procoagulatory” factors, which increase the likelihood of vascular damage and cardiovascular disease (5). The interaction of numerous hormones and cytokines can have a profound impact on a person’s physiology and his/her ability to gain or lose weight. Adipose tissue has been shown to be metabolically active and is capable of secreting numerous proteins that can affect metabolism, bodily functions, and unfortunately weight (121). Again, specific proteins, or adipokines; TNF-\(\alpha\), resistin, IL-6, IL-8, angiotensinogen, and plasminogen activator inhibitor-1 are capable of modulating an individual’s metabolism, feeding behavior, muscle tone, energy balance, and insulin sensitivity, all of which can negatively affect an individual when homeostasis is not present (121).
Pandey looked at 498 (274 pre-menopausal and 224 post-menopausal) urban women living in India to investigate the relationship between menopause and metabolic syndrome in this country, and found similar results to those reported above (122). Women were between 35 and 66 years old, and were only included in the study if it had been 1 year since their last menstrual cycle, which was a common cut off point in other studies, such as those by Nahas and Hidalgo. Steiner stated that women who have gone through menopause would have had one year pass since their final menstrual period, which can be confirmed via hormonal testing where levels of follicle stimulating hormone and luteinizing hormone will be elevated to levels beyond what was present during the early reproductive stages (123). These fluctuations, in addition to the year elapsed, since last menstruation, are diagnostic of the menopausal change.

The reviewed studies indicated that there was a significant correlation between a woman’s age and her incidence of metabolic syndrome. However, menopausal status did not seem to cause an increase in prevalence when adjusted for age, which translates to an increased risk for metabolic syndrome as a woman ages, without regard to menopausal status (122). Women who were 35 years old or greater were at the highest risk for having metabolic syndrome, which was significantly earlier than when natural menopause would naturally occur. The authors mention that there are a variety of extemporaneous factors that could affect the prevalence of metabolic syndrome, such as socioeconomic status, genetics, lifestyle, and also criteria for defining the condition (122). Nearly all studies reviewed use the guidelines published by the National Cholesterol Education Program under the Adult Treatment Panel III (4). However, there are minor diagnostic modifications made to certain criteria under the ATP III Panel, which better suit the population studied. Varying lifestyle differences seem to play a significant role in incidence rates, therefore, maintaining a healthy weight and consuming a
healthy diet throughout the life cycle puts one at a decreased risk for numerous diseases. In summary, there are a paucity of studies that specifically focus on menopause and metabolic syndrome, which shows that more research into the topic should be conducted to better determine if risks are higher for postmenopausal women, and if so, what can health professionals do to help correct the growing incidence of metabolic syndrome among these women in the United States.

Many of the above metabolic syndrome factors begin to play a significant role in women once they go through menopause, and endogenous estrogen is no longer released. A great deal of research is being conducted in this area to help delineate what compounds control what factors of the syndrome, and if these factors can be modulated through interventions, such as physical activity or dietary alterations. Additional research into the effects that bariatric surgery plays on these metabolism-altering compounds is also important, and could explain why some procedures are more effective than others.

**Pregnancy and Metabolic Syndrome**

Alterations in hormone concentrations occur not only through the perimenopausal period, but also during pregnancy. Cuadros et al. designed a study that looked at the connection between menopause and metabolic syndrome in Spanish women. This 10-year retrospective study looked at 574 women and found that hypertension was more common in postmenopausal women, but this diagnosis was attributed to an increase in BMI and advancing age, not specifically menopause (124). In his study, Cuadros used a different cut point for BMI, classifying those with a BMI $\geq 28.8$ kg/m$^2$ as being obese, which was based on reports that this value was better suited for females in this cohort of the Spanish female population. The authors of this paper posed the idea that those women who have reported more pregnancies would be more prone to excess
weight gain with age, and therefore they would have a higher probability of being diagnosed with metabolic syndrome following menopause (124). With pregnancy comes a barrage of hormonal changes that in some can lead to insulin resistance and gestational diabetes, as well as subsequent gains in total weight with each pregnancy.

Furthermore, the ability to lose excess weight gained becomes more difficult in multiple pregnancy scenarios. For example, a woman who was a normal weight at the time of conception of her first child may continually gain in excess with each additional pregnancy, failing to lose this extra weight in between pregnancies. Often, after her third or fourth pregnancy, the woman is now classified as obese, now having to face menopause, which only worsens the situation. Many researchers have reported that in women who have gestational diabetes for one pregnancy will be significantly more likely to be diagnosed as a type II diabetic later in life. One study by Hone on diabetes and pregnancy estimate that up to 50% of women diagnosed with gestational diabetes were diabetic prior to conception (125). As previously mentioned, undiagnosed diabetes is common, therefore making frequent screening imperative, especially in relation to pregnant women, facilitating a healthy, term pregnancy. Jarvela et al found that women who were gestational diabetics for their first pregnancy, had a 4.6% and 5.3% risk of being diagnosed with type I diabetes or type II diabetes later on in life, respectively. It was also found that women were at an increased risk for the development of diabetes, post pregnancy, if they were over the age of 30 years, and had a BMI that classified them in the obese category, or were prescribed insulin to manage blood sugars throughout the pregnancy, when diet and lifestyle changes were not enough to maintain normoglycemia (126). Additionally, Lauenborg followed 481 gestational diabetics, who were able to manage blood sugars through diet intervention with no added insulin, and found that diagnosis of diabetes mellitus was twice as likely to occur, over a 10-year period
after pregnancy(127). Increased incidence rates of type II diabetes is linearly consistent with increases in BMI, and both Jarvela and Lauenborg found that women who were overweight or obese prior to conception were more likely to be diagnosed with diabetes, type II diabetes later in life (126, 127).

Cohen et al found similar results when he looked at NHANES III data on 4699 non-pregnant women over the age of 20 years to see if there was an increase in risk for metabolic syndrome with each follow up session. Women included had prior live births that ranged from 0 to 22, with an average of 2.1 per woman. He found that a total of 22.6% of the women were found to have metabolic syndrome, and that each additional birth was equal to a 13% increase in risk, once age, race, income, education, SES, and behavioral risk factors were controlled. It was also found that women who breastfed for >1 month were at a 22% lower risk for having metabolic syndrome (128). However, this decreased risk was not evident when BMI was included in the analysis, illustrating that weight does play a significant role in the prevalence of metabolic syndrome (128). More research should be completed on breastfeeding, parity, and metabolic syndrome, because the possibility of a link existing is likely, and if it could be established, this information could be used to help further promote the practice of breastfeeding.

Ramos and Olden looked at metabolic syndrome in women living in the United States between the ages of 18 and 44 years who were surveyed in the NHANES III data set (129). The purpose of the study was to estimate the prevalence of metabolic syndrome in this population group, and to postulate whether fetal exposure to metabolic syndrome, and its related health conditions at conception, would put the fetus at risk for disease later in life. To investigate this relationship, data was compiled to account for NHANES participants who reported their mother to have had diabetes, hypertension, or myocardial infarction. If there was a positive correlation,
taking a strong, proactive stance towards prevention could be implemented, and the vertical
transmission of metabolic syndrome from parent to child could potentially be broken. Ramos and
Olden used normal criteria for diagnosing metabolic syndrome and added a sixth criterion, C-
reactive protein. Once the data was analyzed, those who had a mother with diabetes were nearly
twice as likely to be diagnosed with the diabetes prone phenotype later in life, and were also
more likely to be classified as obese, have a low HDL-C, and have an elevated CRP. Garn et al
also examined the relationship between parents and children, and found that those born to lean
parents were the leanest later in life, and those with even one obese parent were more likely to be
obese throughout adolescence and adulthood (130). At age 17, children born to obese parents
were three times as heavy as those born to lean parents (130). These researchers even
recommend that in the physician’s office and school clinics, siblings of obese children should
also be screened, since there is a 40% chance that other siblings are obese, based on a two sibling
family (130).

When looking at these data, it may be more environment than genetics that is causing
these values to surface. The debate on whether nurture versus nature plays a more pivotal role in
development could be brought up here; however, both probably play a role. Attacking the nurture
side of the debate is more easily accessible, and again researchers are brought back to the idea of
prevention, rather than backtracking once the damage has been done, frantically trying to reverse
each metabolic syndrome components.

**Exercise and Metabolic Syndrome**

Another contributing factor to metabolic syndrome is lack of routine physical activity.
Exercise has also been touted as a successful method in maintaining a healthy weight, but could
it possibly play an integral role in the fight against metabolic syndrome incidence, in conjunction
with menopause? With age and a sedentary lifestyle, physical function decreases along with total muscle mass, while the risk of arthritis and joint dysfunction is increased (131). Benefits of exercise include improvements in lipid values, lowering of blood pressure, reductions in lower back pain, improvements in mood, increased bone mass, and most importantly a deficit in calories, which can lead to weight loss over time (132). Unfortunately, many adults are not meeting the required, minimum recommendations for physical activity, resulting in a reduction in expended calories, which can lead to weight gain over time (49). Blanck et al found that normal weight, postmenopausal women who were more sedentary, reporting minimal physical activity weekly were at a 50% greater odds of gaining 10 pounds over the 7 year period, following the cessation of menses, compared with those who reported little sedentary activity (132).

Furthermore, data from the Healthy Women’s Study followed 541 healthy, premenopausal women throughout menopause, and found that 20% gained >4.5kg over the three years, while only 3% lost 4.5kg (36). Kuller and colleagues collected data from both men and women at age 17, and then interviewed participants again at age 34 and 47 to see if changes in weight had occurred. They found that women gained an average of 7.3 kilograms, primarily between ages 17 and 35, with minimal gains between 35 and the final data collection point at 47 years (133). Furthermore, Wing found that weight was not related to baseline BMI values; rather physical activity was found to be the main determinant in weight lost or gained over the three-year study period (36). Joseph et al, in a prospective controlled study, researched 115 women in Baltimore, Maryland, who were all postmenopausal, and who had both metabolic syndrome, as well as those that were postmenopausal and did not have metabolic syndrome. Those who had a diagnosis of uncontrolled diabetes (>198mg/dL 2 hours post 75g oral glucose tolerance test),
poorly controlled blood pressure (>160/90 mmHg), or very high triglycerides (>400mg/dL) were not included in this study. It seems unusual to exclude these individuals because the excluding criteria was directly related to their diagnosed metabolic syndrome. However, the researchers wanted to eliminate outliers that could possibly skew the results, since the elevated values mentioned above were well beyond normal limits.

Bariatric surgery has been a proven means to help remedy obesity related health abnormalities, even in their severest forms, which cannot always be said about exercise and diet modifications in those persons who are morbidly obese. Muscle is the most insulin-sensitive body tissue; therefore, decreasing this insulin resistance, through an increase in muscle mass via exercise, can substantially aid in the normalization of blood sugars levels (134). Patterson et al researched the benefits of diet and exercise, compared to the RYGB operation and found that weight loss was more pronounced with the bariatric surgery group and life expectancy was increased by 2.4 years (135). In addition, they stated that as a person’s BMI becomes more elevated, the benefits of surgery become more pronounced, and the years of additional life are increased (135). Joseph, however, reported that those individuals who were placed on the 6-month lifestyle and low-intensity exercise intervention had a 45% reduction in metabolic syndrome prevalence, when compared to the control that received neither intervention (136). Mitrakou also mention that something as simple as walking 2.5 hours per week can help to reduce the risk of coronary events by 30% (137). This proves that when exercise is recommended, a low-intensity variant over time can yield significant weight loss, and help prevent the occurrence of metabolic syndrome, or revert it in those who already had metabolic syndrome.
Votruba also looked at weight loss for the morbidly obese and found that if recommendations of 3 to 5 hours of moderate to vigorous activity are completed weekly, minimal weight loss will result; however disease risk can be lessened (138). Starting slowly and moving forward via small, incremental steps could, over time, yield promising results, and potentially may increase the odds of compliance through behavior modification. However, this still may not be enough to help those persons with significantly elevated BMI’s, making weight loss surgery the only alternative.

Esposito et al. also confirmed the benefit of both diet and exercise when she looked at 180 patients with metabolic syndrome (99 men and 81 women) in an Italian hospital. Half (n=90) of the randomly selected study group was assigned information on following a Mediterranean Diet, which stressed the consumption of whole grains, fruits, vegetables, nuts, and olive oil, while those in the control group followed a diet containing 50-60% calories from carbohydrate, 15-20% protein, and <30% from fat (139). Physical activity levels were recorded and were shown to increase by 60% during the study, but they were not an integrated part of the study design. After the two-year study period was completed, it was found that insulin resistance and C-reactive protein levels were significantly decreased in the intervention group, and that only 40 of the original 90 individuals still had signs of metabolic syndrome, compared to 78 of 90 in the control group. This lessening from 90 to 78 in the control could have been due to the increase in exercise, which shows the benefits of each dietary regimen separately and also together with exercise (139).

Finley et al looked to examine the relationship of not only cardio-respiratory fitness such as walking, running, cycling, or swimming, but also diet and macronutrient intake distribution in the subjects to see if a relationship between these variables and metabolic syndrome could be
found (140). Previous research by Brunner et al showed that there was no relationship between the percentage amounts of macronutrients consumed on metabolic syndrome prevalence, but exercise was not included in this study (141). Finley found comparable results in his study, also uncovering a strong inverse relationship in those that exercised the most, consequently having a lessened incidence of metabolic syndrome (140). Even though there was a difference in the macronutrient distribution between the various exercise groups, once all variables were analyzed, this relationship with a lessened incidence of metabolic syndrome was still clear, therefore showing how powerful exercise can be in lessening the chance of being diagnosed with this multi component condition (140).

A major flaw, with Finley’s research was that the study population was made up of >95% non-Hispanic white men and women of the middle and upper classes. This cohort of the population is generally more health conscious, and has easier access to adequate health care and more nutrient dense foods, which could have been why the baseline metabolic syndrome prevalence was only 15%; while the general population figures are significantly higher at 34%, according to NHANES 2003-2006 data (29). Stewart et al. looked at older adults, who were hypertensive and frequently had metabolic syndrome, to see if exercise positively influenced incidence rates. He found that after six months of moderate exercise, 45 minutes, three times per week, lean muscle mass and HDL-C were increased, while total and abdominal fat were decreased (142). These improvements resulted in a decrease in metabolic syndrome incidence by 17.7%, in the study population, and further reductions could be possible if the study duration was lengthened (142). In any case, the evidence is rather clear that frequent exercise, of all intensities can be beneficial in helping to reduce the prevalence of metabolic syndrome;
especially before weight and comorbidity conditions become so severe that bariatric surgery is the only intervention left that can result in a positive change.

**Menopause and Hormonal Alterations**

Menopause brings many changes to the female body, many of which are orchestrated by the gradual decrease or cessation of estrogen production and its subsequent release. Other changes that occur involve androgen production, with a gradual, unavoidable decrease with age and a more pronounced reduction, once menopause has occurred. Androgen compounds such as dehydroepiandosterone (DHEA) are produced by the action of luteinizing hormone (LH) and adrenocorticotropic hormone (ACTH), which involves both the ovaries and adrenal glands (143). With age, the body’s ability to synthesize hormones is attenuated, and therefore circulating levels are depressed, when compared to levels found throughout the earlier decades of life. These reductions in hormone concentrations can negatively affect a variety of bodily functions.

While testosterone is primarily thought of as a hormone proprietary towards males, it is present in females, and it is also negatively affected as women grow older, and the effect or decrease in testosterone is again more pronounced throughout menopause. Testosterone in the female body is either free in circulation (1-2%), albumin bound (31%), or tightly bound to sex hormone binding globulin (SHBG). The free and SHBG variants are available to cells (144). Depressed testosterone levels in both men and women have been thought to cause depression, decreased energy, decreased muscle mass and strength, along with changes in memory or cognition (144). Researchers have not elucidated whether it is this reduction in testosterone that causes women to experience these symptoms once menopause has occurred, or if there are other factors yet to be identified that are playing a role. It has been proposed that testosterone
replacement should be added to traditional hormone replacement therapy to help ameliorate these consequences that are associated with depressed testosterone levels (145).

Additionally, and perhaps of a more important health implication, a shift in body fat distribution has been observed in women as they age, becoming more pronounced throughout the menopausal transition (146). Using magnetic resonance imaging techniques, researchers have found that there is in fact the propensity for a redistribution of fat from peripheral stores to a more central or android location, as a woman ages (21). Increases of between 22% and 35% android redistribution of fat were observed in women not on estrogen replacement therapy, while there was only 13% greater fat deposition on women receiving estrogen replacement therapy (21). This accumulation of fat at the midsection can increase the risk for numerous co-morbidities; such as, insulin resistance and heart disease. Davis et al conducted a literature review to further glean what changes occur to weight, as a woman moves through the various stages of menopause, and they also found that with changing hormone concentrations, body fat shifts towards a woman’s midsection, and poses an increased risk of cardiovascular disease, as previously thought (46). Furthermore, Davis et al relate weight gain, at the time of menopause to age, not a change in hormone status, stressing the importance of maintaining a healthy weight throughout all life stages.

Estrogen also increases cholesterol removal by the liver, potentially slowing the progression of atherosclerosis in premenopausal women, as a result of continued endogenous estrogen production (147). Additionally, research has indicated that estrogen plays a protective role in the unwanted redistribution of fat. Women on estrogen replacement therapy (ERT) were shown to have less of a shift to central obesity than those not on ERT (148). Estrogen plays a role in adipose tissue metabolism, and when its concentration declines, lipoprotein lipase (LPL)
shifts from femoral adipocytes to those found in abdominal adipocytes (148). Increased LPL in the abdominal area leads to more fat storage and unwanted fat accumulation in the abdominal region, rather than the periphery (148-150).

**Hormone Replacement Therapy**

While it is thought that the administration of exogenous estrogen, in postmenopausal women can help reduce a shift towards abdominal obesity and blunt total weight gain, caution must be exercised. Many women look towards hormone replacement therapy to help alleviate associated menopausal symptoms such as hot flashes and night sweats (151). Unfortunately, an increased risk of CHD and breast cancer has been shown with prolonged use of estrogen replacement therapy (ERT) in some studies, which is why the therapy is not used long term (152-154). Researchers believed that progestin, when added in with the estrogen therapy would act as a protective factor against breast cancer in those women that had an intact uterus, but this was also disproven by Ross et al, who reported that in fact breast cancer rates were ~10% greater each year, in those women who received both the estrogen and progestin replacement therapy (155). Other research by Simon found that the risk of stroke in women was not elevated when combined estrogen and progestin therapy was initiated, with a mean follow up of 4.1 years (156). Researchers have predicted that women who use estrogen replacement therapy lead healthier lives, eliminating many related risk factors for heart disease and stroke, such as cigarette smoking, limited physical activity, and unhealthy dietary habits (156). Simon also found that those women with atrial fibrillation at baseline, regardless of warfarin, or other anticoagulation therapy, were found to have a 6.5 increased risk of stroke overall when using hormone replacement hormone therapy (156).
Estrogen replacement therapy and continuous combined estrogen plus progestin replacement therapy (CCRT) has also been shown to cause an increase in breast cancer risk, when used long term. Ross found that postmenopausal women using ERT had 10% greater risk in breast cancer over the course of 5 years of use [OR= 1.10, CI= 95%], and those using CCRT were at a significantly higher risk for breast cancer overall [OR= 1.24, CI= 95%] (155), as mentioned previously. Chlebowski, using data from the Women’s Health Initiative, also looked at CCRT and breast cancer risk, and found that fewer diagnosis of breast cancer were made in the first two years, however the number of diagnosis increased between two years, until the 5.6 year intervention period ended (157). Furthermore, the risk for breast cancer significantly decreased when the hormone therapy was discontinued, suggesting that the therapy was contributing to the increase in observed breast cancer incidence rates (157). Because the risk of continuing with the Women’s Health Initiative study outweighed any benefits, the study was discontinued. While the information obtained from this study was monumental in relation to the effects of hormone replacement therapy in women, it must be noted that average age of women who participated was 63 years old, significantly beyond when menopause would have naturally occurred. It is normally recommended to start replacement therapy soon after the transition has taken place, which would not have been the case with these individuals.

Gramling, also using the Women’s Health Initiative data, looked at breast cancer risk and family history, to see if this external factor would affect a women’s risk (158). The researchers reported that women using hormone therapy, who also had a family history of breast cancer, were not at an increased risk for being diagnosed with breast cancer, when compared to women on HRT who did not have a familial history of breast cancer (158). Additionally, Sellers et al followed 35,919 women between the ages of 55-69 years, and found that those women with a
history of breast cancer were no more likely to be diagnosed when using HRT, when compared to those women that did not have a family history (159).

While the relationship is not clear, incidence rates of lung cancer have also been shown to increase, with prolonged use of estrogen and progestin replacement therapy, when confounding variables such as smoking were taken into account (160). Using data from the Vitamins and Lifestyle Study (VITAL), Slatore found that incident rates were shown to be 50% greater in those women who used the combined hormone therapy for greater than 10 years, however there was no increase in lung cancer risk in women only using supplemental estrogen (160). Differences noted when combined therapy was used were dose dependent, therefore if therapy is going to be initiated, it should not be carried out over long periods of time, minimizing cancer diagnosis risk. On the contrary, Schabath found that lung cancer incidence rates were reduced in women on either estrogen or combined estrogen progestin replacement therapy by 35% and 39%, respectively (161). Interestingly, it also was found that women who smoked cigarettes had further reductions in lung cancer rates. The researchers attributed this reduction in lung cancer rates to estrogen receptors binding to carcinogenic polycyclic aromatic hydrocarbons, preventing them from damaging lung tissue (161). This benefit was not as prominent in those who had been smoking for longer durations or in those women who had BMI values that fell into the overweight and obese categories, either ≥25 kg/m² or ≥30 kg/m², respectively (161).

Other research suggests that instead of relying on exogenous estrogen compounds, phytoestrogens can be used with varying degrees of success. Phytoestrogens are not estrogen, but bind to estrogen receptors, tricking the body, causing a reaction as if estrogen was present (154). At present, the American College of Obstetricians and Gynecologists recommend three plant based phytoestrogen supplements in the management of menopausal symptoms: black cohosh,
soy isoflavones, and St. John’s Wort (154). Due to the fact that HRT is controversial in some cases, many are seeking alternatives, making phytoestrogens increasingly appealing to women. As with any herbal supplement, more research needs to be completed and full disclosure of administration should be provided at physician appointments.

As shown, hormone replacement therapy has been used as a treatment modality for postmenopausal women for many years, and treatment results have varied from negative, to positive, to indifferent, depending on the particular study. One important factor that has determined the effectiveness of hormone replacement therapy and subsequent cardiovascular risk lies in the population studied and duration of treatment. Women who have a history of atherosclerosis, previous myocardial infarction (MI), diabetes mellitus, metabolic syndrome, and who are current long-term smokers, are not recommended for hormone replacement therapy, because it can lead to an increased chance of a cardiac related event (162).

Surgical Weight Loss, Gut Hormones, and Supplementation

A few of the key hormones that are thought to play a role in energy balance and weight loss, as well as take part in the resolution of various comorbid conditions, are glucagon like peptide-1 (GLP-1), leptin, ghrelin, and peptide tyrosine-tyrosine (PYY) (163). Both GLP-1 and PYY slow gastric emptying, promote insulin release, and cause a feeling of satiety more quickly, which prevents over eating and an unbalanced energy intake (164). Leptin is secreted by adipocytes and acts on the hypothalamus, where it causes a decrease in energy intake, release of insulin, and a subsequent increase in energy expenditure. Ghrelin has the opposite effect, and it is thought to increase hunger cues, and therefore increase energy intake, subsequently decreasing insulin secretion from the pancreas, preventing hypoglycemia (164). After the RYGB procedure,
circulating levels of GLP-1, peptide tyrosine-tyrosine, and leptin are elevated postprandially, which helps to impart a feeling of satiety, increase energy expenditure, and decrease energy consumption, all of which can lead to weight loss. Ghrelin levels are depressed in RYGB individuals and found to be much higher after both fed and fasting states in those that did not undergo the surgery. Higher levels of ghrelin, after food is ingested, would cause the individual to continue eating, which over time can lead to increased total caloric intake and weight gain. The way in which the RYGB procedure alters the functionality of the gastrointestinal tract is what makes it so successful, and why many surgeons refer to it as the gold standard in surgical methods for weight loss.

Because nutrient absorption is lessened with the RYGB procedure, a multivitamin, along with calcium and vitamin D are required to supplement the diet, preventing deficiency (165). Rossi conducted a cross-sectional study of 44 women after RYGB surgery (38 healthy control subjects), to compare nutrient intakes between the two groups, three years postoperatively (166). It was found that iron, zinc, thiamin, and B12 were less than the recommended daily allowance for the surgery group and not the controls. Furthermore, total caloric intake from protein was found to be 35% and 10% for the non-operated versus operated group, respectively (166). Other studies have found caloric intake from protein to range between 14.9 and 22%, which is less than what was observed by Rossi. It is not surprising that protein consumption witnessed here was greater than the 15% average consumption typically seen in most studies concerning macronutrient distribution. In any case, dietary protein levels that consist of 10% of an individual’s total caloric intake is low for any cohort of the population, let alone bariatric surgery patients, who are not absorbing essential nutrients as efficiently. Suboptimal protein intakes may
cause a loss of muscle mass postoperatively, which may hinder attaining normoglycemia postoperatively, due to the fact that muscle is the most sensitive tissue to insulin in the body.

Bone loss and metabolic bone disease has also been researched, in regards to bariatric surgery, and it is thought that those who have had surgery are at higher risk, when compared to those who have not had surgery, however much research still needs to be completed formulate a causative mechanism. Metabolic bone disease, and bone loss is thought to present in bariatric surgery patients as a result of decreased dietary intake of calcium and vitamin D, as well as the impaired absorption of these two nutrients needed for bone health (167). Brzozowska reports that an early incidence of bone remodeling is witnessed within the first three months after surgery, when compared to circulating urinary concentrations of bone turnover makers, even when adequate vitamin and mineral supplementation was utilized (168). Further studies by Bruno illustrated that serum osteocalcin and N-terminal telopeptide were elevated compared to baseline values, indicating a prolonged increase in bone turnover (169) Bano reports on bone mineral density after bariatric surgery and found that both men and postmenopausal women, not on hormone replacement therapy, had the lowest bone mineral density scores, when compared to controls (170).

For those with preoperative malabsorption, as a result of diagnosed Celiac Disease, it has been shown that a gluten free diet may protect against bone loss and help to increase bone mineral density during the beginning stages of bone loss (170, 171). With diet non-compliance in Celiac Disease, malabsorption occurs, and key nutrients, including those for bone health pass rapidly through the GI tract, providing minimal benefit. When gluten is removed from the diet, gastric transit time is reduced and absorption can occur, delivering nutrients throughout the body. Mora found that adults with Celiac disease were more likely to have decreased bone mineral
density as a result of poor diet adherence and subsequent malabsorption (172). Unfortunately, a gluten free diet is difficult to follow, and it may be too restrictive and cause surgery patients to restrict too much from the diet, and cause deficiencies in other nutrients, specifically those needed to maintain healthy bones. However, for surgery patients who have diagnosed Celiac Disease, diet adherence is imperative to yield a healthy outcome postoperatively. To prevent these nutrient deficiencies, the use of vitamins and a healthy, balanced diet is imperative after bariatric surgery, especially the RYGB procedure. It is also recommended that perimenopausal and postmenopausal women status post bariatric surgery have frequent bone density scans, especially as weight is lost, to attribute bone loss to either menopause or weight loss (77).

**Menopause and Blood Pressure**

High blood pressure, or hypertension, is a health condition that is characterized by an increase in pressure against the artery wall, depending on whether the heart is contracting or relaxing in between beats (173). Blood pressure readings are written with the systolic pressure over the diastolic pressure in millimeters of Mercury (173). Diagnosis of hypertension occurs when blood pressure readings are greater than 140/90 mm Hg (173). Typically, women have a lower blood pressure when compared to men throughout the first four decades of life; however, a shift occurs between 45 and 64 years, when blood pressure levels are comparable, and then at 65 years and beyond, more women than men are diagnosed as being hypertensive. In 2003, life expectancies for males and females in the U.S. climbed to 74.8 and 80.1 years, respectively (174). As a result, a greater proportion of the population will be faced with medical comorbidities like hypertension, therefore making diagnosis and prevention of the utmost importance (174). One reason for increases in blood pressure for all populations is related to our increased consumption of convenience based, high salt food items. Unfortunately, those of a
lower socioeconomic status consume these foods more often due to lack of access to healthier alternatives.

Gustafsson, in his 27-year prospective cohort study on Northern Swedes, encountered similar results when he found that systolic blood pressure was greatly elevated in those women who were of a low socioeconomic status (SES) at both 16 and 21 years of age (175). Baseline data included blood pressure, BMI, and socioeconomic status at 16 and 21 years old. These data were recorded, and it was postulated whether or not this would correlate with metabolic syndrome risk at follow up when participants were 43 years old. The researchers found that there was in fact a strong correlation between SES during adolescence and prevalence of metabolic syndrome later on in life for women, but not men. It was not hypothesized why this might be the case.

However, if one thinks about how a low SES individual lives, it becomes somewhat clear that no matter in what part of the world you reside, low cost food is typically those foods highest in fat, calories, and sodium. This trifecta, which outlines a typical Westernized diet, especially the latter, can lead to an elevation in blood pressure among individuals that are salt sensitive, which might be the root cause of what was observed in these two studies. It is therefore important to consider all factors synergistically, instead of one objective value, such as BMI. This study by Gustafsson, in particular, is of increasing importance, since it potentially acts as a predictor for metabolic disease occurrence later in life.

Data compiled from the National Health and Nutrition Examination Survey indicated that prevalence rates of hypertension between 1988-1994 were 23.9% (176). Between 1999-2000, prevalence rates of hypertension were slightly increased to 28.5%. However, there was no noted
increase between 1999-2000, or 2007-2008 (176). One specific cohort of the U.S. population, males and females over the age of 65 years, has been shown to be at an increased risk for being diagnosed with hypertension, along with several other related health co-morbidities, such as hyperlipidemia and diabetes (177). Women over the age of 65 have increased prevalence rates of hypertension when compared to men, according to NHANES data, and these same women are less likely to control their blood pressure with pharmacotherapy (177). Resorting to blood pressure control methods that include various lifestyle and diet modifications is more likely to be employed by women, since this cohort of the population is more health conscious and able to make these stated changes, as opposed to solely relying on pharmacotherapy.

Postmenopausal women appear to be at an increased risk for being diagnosed with hypertension, which could be related to a multitude of factors; however, not one mechanism is responsible for this increased risk (178). Amundson states that hyperinsulinemia activates the sympathetic nervous system, therefore causing sodium and water retention, increasing whole body pressure, leading to hypertension (179). Next, Staessen researched 278 premenopausal and 184 postmenopausal women and found hypertension rates of 10 and 40%, respectively (180). When the population was stratified by age and body mass index, the odds of being diagnosed with hypertension was 2.2 in postmenopausal women, when compared to those who were premenopausal (180). A similar, prospective cohort study looked at 315 men, who were age and BMI matched, with 315 premenopausal, perimenopausal, or postmenopausal women. When analyzed, researchers found that postmenopausal women had a 4-5 mm Hg increase in systolic blood pressure when compared to all other groups studied (181). It can be assumed that with menopause, some physiologic change occurs that makes a woman more apt to have abnormal, elevated blood pressure readings, when compared to the rest of the population. Several potential
mechanisms for this increased risk in hypertension will be detailed below; however, no single hypothesis has been conjectured to explain this blood pressure phenomenon.

Not all, but many women experience weight gain following menopause (182). Weight gain and subsequent insulin resistance can increase sympathetic nervous system activity, which causes an increase in the secretion of renin from the kidneys (178). An increase in sympathetic nervous system stimulation has also been shown to cause a shift in body composition, more towards the abdominal region, which can lead to greater amounts of oxidative stress and inflammation. Estrogen exhibits an increase in the production of superoxide dismutase, which inhibits nicotinamide adenine dinucleotide phosphate (NADPH) and thereby reduces oxidative stress, protecting the vessel walls (183); however, this protection is lost following menopause. Renin is a component of the renin-angiotensin-aldosterone axis (RAS), and has a profound effect on extracellular fluid volumes, and therefore can cause fluctuations in blood pressure (184). Renin concentrations can be elevated under three circumstances; a drop in blood pressure is encountered, sodium chloride concentrations are depressed, or the sympathetic nervous system is stimulated (184). Any one of these previously mentioned physiologic scenarios could result in a shift in fluid concentrations in and around the cells, as well as vasoconstriction, which lead to an increase in blood pressure.

Estrogen dilates the endothelium of the vessel wall, which is one reason hormone replacement therapy is employed in postmenopausal women, since endogenous estrogen production is slowly diminished (162). A reduction in vasodilation and vascular tone has been shown to be similar in both men and postmenopausal women, which is a reversal of what is typically seen, with men typically having an increased risk of heart disease and hypertension when compared to women during the first four to give decades of life (182). In order to receive
this cardio protection through vessel dilation, it is important that women who receive supplemental estrogen are good candidates, and do not have heart disease risk factors, as previously mentioned (185). If the vessel wall is atherosclerotic prior to endogenous estrogen administration, greater stress can be put on the vessel wall when dilation occurs, resulting in damage (185). Inflammation and inflammatory markers accompany this damage, and research has found levels of both C-reactive protein and blood triglycerides to be elevated, both of which can lead to a narrower vessel opening and therefore, an elevation in pressure against the vessel wall(186).

Furthermore, with age, regardless of gender, salt sensitivity is increased, which may be a result of impaired vasodilation at the level of the kidney (182). In postmenopausal women, this increase in salt sensitivity is more pronounced, which leads researchers to believe that sex hormones have a potential protective effect against this occurrence (187). Salt sensitivity can be increased in those who are diabetic, obese, and greater than 60 years of age (188), which is why diet and lifestyle modifications can be beneficial to overall health with advancing age. Research by Weinberger found that 26 and 51% of his study population could be classified as salt sensitive, based on whether they had normal or high blood pressure, respectively (188). Furthermore, it was found that individuals who were sensitive to salt, and who were not currently diagnosed as being hypertensive, had a much greater incidence of being hypertensive with age (188). The underlying mechanism behind this increase in salt sensitivity is not fully known; however, in those that are salt sensitive, renal pressure must be elevated beyond what is normal to successfully excrete excess sodium in the urine (187). Additionally, as dietary sodium intake increases, the renin-angiotensin system (RAS) should be suppressed to modulate blood pressure. However, with menopause, RAS function has been altered, and therefore, blood pressure
becomes a function of sodium intake (187). For this particular study by Schulman, a total of forty women participated with nine being salt sensitive prior to surgical menopause. At their four month follow up, an additional twelve women were salt sensitive, while still having normal overall blood pressure, indicating a significant increase salt sensitivity incidence shortly after surgical menopause (187). For these salt sensitive women, the more dietary sodium consumed, the more likely blood pressure will become elevated, which poses an emerging dilemma, given our current, salt-laden, over-processed food supply. It would be prudent to follow these women as time elapsed since surgical menopause to see if diagnosis of hypertension is also increased.

**Menopause and Cholesterol**

An abnormal lipid profile is one of the possible criteria that must be met in order for a diagnosis of metabolic syndrome, using the National Cholesterol Education Program, ATP III guidelines. In a situation where values for total cholesterol are elevated beyond the recommended 200 mg/dL, there is an increase in the risk of heart disease and other heart related diseases. Unfortunately, an abnormal lipid profile becomes more commonplace with age, as bad habits build. Unfortunately, these bad habits can increase an individual’s risk for certain diseases of the cardiovascular system. Kannel, in 1976 stated that in affluent societies, women were much less likely to suffer from atherosclerotic and coronary heart disease when compared to men, which is likely the opposite of what is found today, as our environments have shifted to more convenience based, high calorie, and high fat food items (189). In general, abnormal lipids are defined when any of the following are present: total cholesterol ≥200 mg/dL, LDL-C ≥130 mg/dL, triglycerides ≥150 mg/dL, and HDL-C <40 mg/dL in men and <50mg/dL in women, according to the ATP III guidelines, published by the National Cholesterol Education Program (NIH). Many of these values become negatively skewed with age, which can be the result of
numerous factors, some of which are part of the natural aging process (53). Decreased total physical activity and increased weight are the two major contributors to an abnormal lipid profile, specifically a decrease in total HDL cholesterol (190).

Concurrently with the aging process and menopause, the proportion of abdominal fat can increase, as well as an individual’s overall body mass index. This can increase the risk for a variety of health abnormalities, such as cardiovascular disease and coronary heart disease (191). Ito found when total fat mass is increased, as indicated by an elevated waist circumference and increased waist to hip ratio, dyslipidemia was more prevalent, even when BMI was normal (20-23.5 kg/m²) (191). The cohort of the population studied was a mix of Japanese males and females, which could potentially skew the results, since their diets are not typically similar to that of a western diet, in addition to their overall smaller body size. Even as a result of this difference in populations studied, it still is indicative of a propensity for a dyslipidemia to occur when waist circumference and waist to hip ratio are increased, making these two measurements a beneficial, inexpensive screening tool.

It is difficult to attribute a change in these lipid values with the menopausal transition, since they have a higher propensity to occur as one ages; however, research has been completed to attempt to differentiate the roles age, menopause, and a change in ones lipid profile play. Kim et al looked at 1,679 women who were stratified into three groups: premenopausal, perimenopausal, and postmenopausal, based on menstrual patterns and follicle stimulating hormone levels (53). It was found that with menopause, an increase in both HDL and LDL cholesterol was observed during the transition from pre- to postmenopausal (53). Other research, using data from the Atherosclerosis Risk in Communities (ARIC) study, found that at fixed age intervals, no difference in HDL-C was noted between those women who were pre- and
postmenopausal (192). It was also found that women receiving estrogen replacement therapy had decreased values for LDL-C and slightly increased values for HDL-C, signifying an additional protection from exogenous estrogen (192). Furthermore, data analyzed from the Framingham Heart Study also found no change in HDL-C levels throughout the transition of menopause (189). In summary, LDL-C levels appear to be inversely associated with exogenous estrogen administration and chronological age and positively associated with BMI and waist circumference (193).

Other research by Williams et al looked at HDL-C in women, both pre- and postmenopausal, and further differentiated between various subclasses of HDL-C particle size, each of which has differing effects on the body (194). Specifically, HDL₂ particles are larger and more buoyant, therefore providing a cardioprotective effect, when compared to HDL₃ particles, which are smaller, and fail to provide the same benefit (195). Particle size of LDL-C also varies, with smaller, denser particles causing greater damage to the heart and cardiovascular system (195). Smaller, dense, LDL-C particles are less prevalent in premenopausal women, making up only 10-13% of total LDL-C, whereas postmenopausal women have between 30-49% small, dense LDL-C particles (196).

Woodard et al also found that with menopause there was an increase in LDL-C, and either a slight increase or no change noted in HDL-C, similar to those studies outlined above. Researchers in this study further examined HDL-C composition and found that HDL-C particle size is larger in postmenopausal women, which could provide for a more pronounced protective effect against CVD for this particular cohort of the population (197).
Aloysio researched 9309 women, who were classified as either pre-, peri-, or postmenopausal, as part of the Italian Climacteric Research Group Study (ICARUS), and found that total cholesterol, triglycerides, LDL-C, and HDL₃ levels were increased by 14%, 12%, 27%, and 7%, respectively, between pre- and postmenopausal women (198). It was also reported that those women classified as being postmenopausal were less educated than similar women classified as being premenopausal, which could signify an overall change in beliefs on healthcare (198).

On the contrary, Stevenson et al found that with menopause came a profound negative influence on total cholesterol, triglycerides, LDL-C, and HDL-C, after potential confounding variables such as BMI and age were accounted (199). The authors attribute this change to the gradual decrease in endogenous estrogen that occurs with menopause, which is in agreement with research by Brown, who found those women receiving exogenous estrogen had a more desirable lipid panel, when compared to those not receiving such therapy (192). Furthermore, both total cholesterol and LDL-C were found to be elevated in those individuals with greater body mass indices, further showing that weight loss can yield improvements in lipid values (199).

**Menopause and Weight**

As an individual grows older, there is an increased incidence of weight gain and elevated body mass indices, which can be partially attributed to a decreased metabolic rate, because of a lessening of total body muscle mass (32). With natural menopause a decrease in fat free muscle mass has been noted while total fat mass tends to trend upward, a scenario that is not desirable in most circumstances (200). Maintaining a weight that is not too low or too high is a difficult
balance to attain, and previous research showed that those who were too lean also had higher rates of mortality; however, Calle found that this was related to smoking status and concurrent illness, not leanness in and of itself (201). In women, a body mass index of between 22.0 to 23.4 and 23.5 to 24.9 in men was associated with the lowest rates of all cause mortality (201). Weiss reported that 50% of women try and lose weight after the menopausal transition, which signifies a potential gain at this life stage (16). In comparison, Serdula utilized data from the 1996 Behavior Risk Factor Surveillance System, and found that approximately 43.7% of women between 18-29 years old were actively trying to lose weight compared to 49.1% of those between 50 and 59 years (202). On the contrary, Yaemsiri analyzed 2003-2008 NHANES data and found that women trying to lose weight was 60.5% and 50.1% based on whether they were less than or greater than 55 years of age, respectively (203). From these studies, it is evident that a significant proportion of the female population is attempting to lose weight at or near the fifth decade of life, indicating a pronounced weight gain and subsequent opportunity for intervention.

Generally, weight gain and peak body weight occur in women at approximately 50 years of age, indicating a greater need for an intervention directed specifically at this cohort of the population (204). A reduction of total weight by 10% will reduce the number of years that a woman has to live with hypertension, hypercholesterolemia, or diabetes, which is why an emphasis on prevention is imperative (205). Weight gain, even when weight remains in the healthy BMI range, can still put one at increased odds for certain diseases, stressing the importance of healthy weight maintenance (8). A shift in body composition to a more centralized concentration of adipose tissue, or android body shape, is noticed in women, especially throughout the menopausal transition (206). Taylor used dual emission x-ray absorptiometry (DEXA) to measure body composition in 96 healthy, white women between the ages of 16 and
80 years, and found that total body fat as a percentage of weight was higher in older aged individuals (206). Waist to hip ratio and trunk to leg fat ratio were both increased in older participants, indicating a shift to a more centralized fat deposition (206).

Increased weight, specifically during menopause in women, has been linked to increased risk for breast cancer, as well as cancer of the endometrium, kidney, colon, and esophagus (207). It is estimated that between 11,000 and 18,000 deaths per year, in women, as a result of breast cancer could be avoided if women maintained a BMI of <25 kg/m² (208). Franceschi et al found that for every eight-unit increase in a woman’s BMI, an odds ratio of 0.8 and 1.2 is present for premenopausal and postmenopausal women in regards to breast cancer diagnosis, respectively (209). Overall breast cancer risk was less in those women who were at a healthy weight prior to and throughout the menopausal transition. Theoretically, breast cancer burden could be lowered by 12% if women reduced their weight to the lowest, healthy BMI quintile, with up to 40% reduction in those women over 70 years of age, related to their increased risk as a cohort (209).

Ley et al looked at 234 non-obese male and female subjects to see if there was a difference in body composition with age, specifically in women during the menopausal transition (210). Dual emission x-ray absorptiometry was used to measure body composition, and the data showed that BMI was slightly greater in men than in women, and also greater in postmenopausal women when compared to those that were premenopausal. Postmenopausal women also had a greater proportion of total fat mass, with increased amounts of trunk and centrally located fat stores, indicating a shift throughout the menopausal transition, as indicated in various other studies (210). Another interesting finding from this particular study showed that in men, a higher BMI was indicative of more lean tissue, while in females a higher BMI was
associated with increased fat mass. This is why BMI values must be carefully considered and also why more precise XRAY scanning methods such as DEXA should be used, when available, because of its clearer depiction of overall body composition.

Another study by Guo et al also used DEXA imaging techniques, and found similar results when looking at 102 men and 108 women, who took part in the Fels Longitudinal Study, at Wright State University (211). By utilizing DEXA imaging, it was possible to delineate between body fat, lean tissue, bone, and other body structures, so that a clearer picture can be drawn as to what changes occur with age (211). Researchers also focused on the women in this study to see if a relationship between the menopausal transition and body composition could be specifically noted. It was hypothesized that women, who began the transition through menopause at a healthy weight and body composition, would be less likely to have negative health outcomes when the transition was complete. Guo found a marked decrease in fat free mass, with increased amounts of total body fat, weight, and BMI, throughout the menopausal transition (211).

Reinforcing these findings, Blumel found that BMI prior to the menopausal transition had a profound effect on BMI at the five-year follow up (205). Specifically, only 1.6% of women studied who started with a BMI of <25 kg/m² were obese at follow up, compared to 28.6% of women who started out with a BMI between 25 and 30 kg/m² (205). Interestingly, it was found that women with lower BMI values at the start of the study had larger increases in weight, when compared to the heavier subset of the cohort. However, even with greater gains, they still remained in the normal BMI classification at the five-year follow up (205).

Both studies mentioned above reiterate the importance of taking a proactive stance in regards to weight, one of which is centered on women and the menopausal transition. By focusing specifically on overweight and obese premenopausal women, there is the potential that
several health concerns, related to increased weight, can be alleviated throughout the peri- and postmenopausal time period. Adjustments to bariatric surgery BMI cut points may be adjusted to include those women who are premenopausal and overweight, or class I obese (BMI values between 25 and 35 kg/m²). These adjustments may help more women attain a normal weight prior to menopause via surgical techniques, and allow them to maintain this new normal weight throughout the postmenopausal years, a time when weight gain can be more pronounced.

If this research reveals that there is a lessened effect of bariatric surgery on postmenopausal women, criteria can be adjusted accordingly, to include more women before the menopausal transition. As these studies have shown, women beginning menopause at a healthy BMI have a decreased odds of gaining weight throughout the transition, even with alterations in their hormonal milieu. Those women who are overweight or obese early in life would, therefore, benefit from surgery or some other intervention that can help decrease their weight to a healthy level, or to a body mass index between 18.5 and 24.9 kg/m². Throughout the latter decades of a woman’s life, there is an increased incidence of a variety of diseases, as stated above, with many relating to an increased body weight. Maintaining a healthy weight throughout all stages of life is therefore imperative, when aiming to minimize the modifiable risks and subsequent incidence of these comorbid conditions.

**Menopause and Diabetes**

Diabetes is a crisis that has reached epidemic proportions on a global scale, and its reversal is not likely, unless changes to our food supply and our lifestyles occur (212). As a result of improvements in available healthcare and medicine in general, life expectancies have continued to increase, and with this increase has come a greater chance of being diagnosed with
a number of diseases, including diabetes mellitus. For women specifically, assuming menopause occurs at approximately 50 years of age, they can expect 30 to 40% of their entire life to be comprised of the postmenopausal years, which is why this cohort is of specific interest to the medical community (213).

Diabetes is found primarily in two forms, which are dependent on whether or not the pancreatic beta cells are actively producing insulin. The less common variant is commonly referred to as Type I diabetes, and is evidenced by the loss of pancreatic beta cell function and the inability to produce insulin, requiring the individual to administer exogenous insulin via injections. Type I diabetes accounts for approximately 5% of total diagnosed cases, and typically is diagnosed at a younger age, which is why it is sometimes referred to as juvenile onset diabetes. On the contrary, Type II diabetes makes up the majority of diagnosed cases at approximately 95%, and is a result of increased insulin resistance, typically from an excess of total body fat (214). The pancreas is still able to produce insulin; however, because of increased insulin resistance at the level of the cell, hypersecretion of insulin must occur to overcome the resistance, eventually causing the pancreas to fail. As mentioned previously, hyperinsulinemia can negatively affect blood pressure through the action of the sympathetic nervous system. It is therefore common for diagnosed Type II diabetics to slowly make the transition to a Type I classification with time, as resistance increases, and the pancreas loses its ability to produce sufficient insulin to maintain blood sugar homeostasis.

As indicated previously, Type II diabetes is thought to be very much dependent on a person’s weight, and therefore many of the associated symptoms and risks can be alleviated or significantly improved with weight loss. Routine physical activity and a diet that is balanced in macronutrient composition are ways to help maintain a healthy weight and body mass index
between 18.5 and 24.9 kg/m². Colditz showed that diagnosis of diabetes in women was elevated even at BMI levels of 22.0-22.9 kg/m², 24.0-24.9 kg/m², and >31.0 kg/m² with an age adjusted relative risk of three fold, fivefold, and fortyfold, respectively, when compared to someone with a BMI of less than 22 kg/m² (215). Through this same study by Coldtiz, it was found that throughout the middle of a woman’s life, weight gain is more prominent, leading to a greater chance of diabetes diagnosis. However, this incidence can be lessened with a weight loss of even five kilograms, or 11 pounds (215). When an individual’s weight becomes grossly elevated, classifying him or her into the overweight and obese categories, diet and exercise may not be the most practical means by which to bring body weight back to within normal limits. For this specific cohort of the population, weight loss surgery has proven to be a relatively safe and viable option to both facilitate significant weight loss and lower the risk for many associated disease, including diabetes. Weight loss surgery, specifically the Roux-en-Y gastric bypass procedure, has been shown to provide drastic improvements in a Type II diabetic’s blood sugar, with evidence of normalization possible postoperatively. Blood sugar control in both diagnosed and undiagnosed diabetic women can be affected during the peri- and postmenopausal period. Certain related factors, such as the maintenance of a healthy weight, can help to blunt this change in blood sugar control, which can either be from lifestyle modifications or surgical intervention.

As alluded to in the previous paragraph, diagnosis of diabetes is more common in women throughout the menopausal transition, and can sometimes be overlooked, since many of the symptoms between the two are similar (216). Changes that occur with menopause, such as an increase in body weight, increased abdominal obesity, impaired glucose metabolism, and a decrease in lean body mass can all result in poor blood glucose control and subsequent a diagnosis of diabetes (216). To further complicate matters, in those women who have been
diagnosed with diabetes, vasomotor symptoms characteristic with menopause, such as hot flashes and abnormal sweating, can be confused with a state of hypo- or hyperglycemia, when in reality blood sugars are within a normal range (217-219). Hot flashes are typically observed during the early morning hours or at night in menopausal women, which are two common times that one may experience blood sugar abnormalities, especially if on insulin therapy or oral diabetic medications that increase endogenous insulin production, such as those from the sulfonylurea category (220). Diagnostic hypoglycemia can be traumatic for many, and treatment may be based more on convenience, rather than proper protocol. A significant proportion of daily calories can be attributed to unnecessary treatment of hypoglycemia, and when done chronically, can result in significant weight gain (221). Furthermore, with menopause many women experience increased incidence of depressive symptoms, many of which can lead to an elevation in intake, also leading to weight gain, making euglycemia more difficult to attain (222). Self-monitoring of blood sugars need to stressed through the primary care physician or endocrinologist so that true diagnostic lows can be handled appropriately.

In addition to the consumption of additional calories through the treatment of false lows, a woman’s blood sugar could on the contrary run in the hyperglycemic range, which over time can lead to increased weight and elevated triglycerides (217). These examples further reiterate the importance of tight blood glucose control and frequent blood glucose monitoring, especially throughout the peri- and postmenopausal period, when changes are more likely to occur. A routine hemoglobin A1C could be a beneficial addition to lab work for postmenopausal women, regardless of whether a diagnosis of diabetes is present, allowing practitioners to monitor blood glucose trends more closely.
Research has been completed to investigate whether the risk for diabetes is elevated during menopause when confounding variables such as weight, modifiable lifestyle behaviors, and age are taken into account. A longitudinal cohort study by Soriguer followed 475 women for 6 years as part of the Pizarra study, and it was found that there was no increase in the diagnosis of diabetes in women from the pre- to postmenopausal period, after age and physical activity level were taken into account (223). Furthermore, it was found in this study that age and a gradual increase in weight throughout the six-year study period were the primary factors that increased a woman’s odds of being diagnosed with diabetes, not the menopausal transition itself (223).

Wu and colleagues followed 5412 women as part of a community based population survey, carried out by the Yang-Ming Crusade, and found that the strongest predictor of impaired fasting glucose (IFG) was years since menopause (224). For each year following menopause, in women who were not on hormone therapy and greater than 49 years old at the time of menopause, a 6% increase in risk for IFG was found (224). Additionally, Pirimoglu, followed 30 women after surgical menopause, completing oral glucose tolerance tests before surgery, and after at 3, 6 and 12 month intervals. It was found that glucose levels and insulin response were both significantly elevated after surgery throughout the 12-month follow up period (225). An elevated insulin response likely indicates an increase in insulin resistance at the cellular level, which may wear out the pancreas prematurely and lead to a future diagnosis of diabetes. Furthermore, the strongest predictors of being diagnosed with diabetes are family history, body mass index, systolic blood pressure, and triglyceride level, which is not surprising since all of these factors can be related to increased weight, increasing the risk for insulin resistance, and poor glycemic control.
Other studies have looked into the effects of free testosterone in postmenopausal women, and its relation to impaired fasting glucose levels. Golden et al followed 1973 postmenopausal women who were between the ages of 45-84, and who were not taking any form of hormone replacement therapy as part of the Multi-Ethnic Study of Atherosclerosis. It was found that in those women with decreased testosterone levels, the likelihood of impaired fasting glucose was more prevalent, but not diagnosis of diabetes (226). Furthermore, if estradiol concentrations were elevated and sex hormone binding globulin was depressed, impaired fasting glucose and a greater incidence of diabetes was present (226). Jee-Young Oh et al found the opposite when looking at type II diabetes risks and insulin resistance, based on free testosterone levels in circulation. When levels are decreased, typical of postmenopausal women, fasting glucose was impaired and the incidence of type II diabetes was elevated (227). A finding of interest from this study showed that within the same study population, men who had low testosterone showed the same effect as women, with impaired fasting glucose and a great incidence of type II diabetes (227). The previous study illustrates how hormones can have a profound, differing effect on type II diabetes based on an individual’s gender, which is why treatment must take into account a variety of additional factors, including but not limited to life stage, gender, environment, and physical activity.

Sex hormone binding globulin has been used more recently as an indicator of insulin resistance (228). A low sex hormone binding globulin concentration was more likely to be present in an individual who was hyperinsulinemic, which could be indicative of a future diagnosis of diabetes (228). Ding et al conducted a case control study and followed 359 newly diagnosed diabetic women and another 359 non-diabetic women as controls. Both groups were postmenopausal and neither was on hormone replacement therapy. It was found that those
women with elevated levels of sex hormone binding globulin were consistently found to have a lessened risk for type II diabetes diagnosis (228). It was also found in Ding’s research that those women in the control group, who had adverse health profiles at baseline, were more likely to be diagnosed with diabetes at the study’s conclusion (228). Again this stresses the importance of a healthy lifestyle in the prevention of type II diabetes. Goodman-Gruen conducted a cross-sectional study of 657 postmenopausal women, not on hormone therapy to see if a link could be ascertained between sex hormone binding globulin and insulin resistance. Their research showed that those women who were obese and had an android body shape, consistently had lower sex hormone binding globulin levels and these levels were not affected by smoking, physical activity, or alcohol use (229). Using sex hormone binding globulin, in conjunction with other criteria can help to predict future diagnoses of diabetes, giving medical practitioners a new tool in the fight against diabetes.

Improvements in glycemic control have been found in postmenopausal women who are also on hormone replacement therapy. Ferrara et al looked at 14,435 women who were members enrolled in a health maintenance organization continuously between January 1st, 1995 and December 31st, 2006. It was found that over the study period, women who were using hormone replacement therapy had reductions in glycosylated hemoglobin (HbA1c) when compared to type II diabetics not receiving exogenous hormone replacement therapy (230). Age adjusted mean values for HbA1c were 7.9% for those on hormone therapy, and 8.5% for those not on hormone therapy, which was significant (230). Similarly, Rossi and colleagues looked at 673 non-obese, postmenopausal women in whom 144 women were taking 17-beta-estradiol, and 529 women who were receiving no form of hormone replacement therapy (231). It was found that those women using 17-beta-estradiol had a reduced overall incidence of type II diabetes over the 3.7
year follow up period of 4.16% and 10% in the hormone replacement group, and the non-users group, respectively (231). This research shows an increased risk for type II diabetes diagnosis in postmenopausal women that accompanies the cessation of endogenous estrogen production. Central obesity rates between those women receiving hormone therapy and non-users was significantly different at 49.3% versus 57.2%, respectively, which may account for the difference in type II diabetes risk, since central obesity, along with insulin resistance, is a strong predictor overall.

As previously mentioned, weight loss surgery, specifically the Roux-en-Y gastric bypass procedure, can markedly improve fasting and postprandial blood sugars immediately postoperatively. MacDonald et al followed up with 154 morbidly obese individuals who underwent the RYGB procedure for an average of nine years, and also 78 morbidly obese individuals who did not undergo surgery for 6.2 years who were used as the control group (232). It was found that mean glucose levels in the surgical group went from 187 mg/dL preoperatively to less than 140 mg/dL postoperatively, while oral hypoglycemic agent use fell from 31.8% to 8.6% postoperatively (232). On the contrary, oral hypoglycemic use jumped from 56.4% to 87.5% in the control group, and all cause mortality was 28% and 9% in the control versus surgical group, respectively (232).

Similarly, Pories et al found that in a cohort of 608 morbidly obese individuals who underwent gastric bypass surgery, most had significant reductions in issues that related to blood glucose levels, hemoglobin A1C, and insulin use, postoperatively (214). Specifically, 121 out of 146 individuals (82.9%) diagnosed with diabetes had complete resolution, and 150 out of 152 (98.7%) with glucose impairment had resolution of these issues (214). The authors owed these
improvements to weight loss. However, current data relates these benefits to not only weight loss, but also to changes in the hormonal milieu that is present after surgery.

Sugerman also saw similar results when following 1025 morbidly obese individuals who underwent gastric bypass surgery, with 83% diabetes resolution and the cessation of all oral hypoglycemic agents (233). Wittgrove et al. found similar results when looking at 500 bariatric surgery patients between 1993 and 1999, of which 85 were diagnosed as having diabetes at the time of the gastric bypass operation. Follow up included >80% of original participants and was anywhere between 3 to 60 months in length. Out of the 85 diagnosed diabetic individuals, 39 were using oral diabetic agents preoperatively, as compared to zero individuals at the 60-month follow up appointment (18). Preoperatively, 64 individuals had elevated hemoglobin A1C levels, and only 3 remained elevated postoperatively (18). Wittgrove attributed these reductions in diabetes incidence to improvements in overall dietary quality and smaller, more frequent feedings throughout the day, along with a decreased insulin resistance as excess body weight was shed. Again, while these factors will help with blood sugar control and insulin resistance, there are hormones also playing a prominent role to yield the results noted.

Schauer et al compared diabetic individuals who received either intensive medical nutrition therapy (MNT) alone, or in conjunction with either the sleeve gastrectomy or gastric bypass procedure, and found marked improvements in both surgical cohorts (234). Improvements in both hemoglobin A1C and fasting blood glucose levels were observed in both surgical groups, while those receiving only MNT noticed smaller and slower improvements, which were attenuated throughout the final 6 months of follow up, possibly indicating decreased adherence to dietary recommendations (234). Insulin use was decreased significantly in the surgical groups from 46% and 45% in the gastric bypass and sleeve groups, to 4% and 8%,
respectively. Those in the MNT group had much less successful results, with 51% needing insulin at baseline, and 38% still needing this treatment at 12 months follow up. This provides further evidence that the RYGB procedure is superior to traditional treatment when aiming to alleviate abnormal blood glucose labs and elevated hemoglobin A1C present in diabetes.

For example, le Roux et al. looked at a small sample of lean and obese controls, as well as those who underwent the Roux-en-Y gastric bypass procedure, and found that surgery patients had elevated postprandial levels of both peptide tyrosine-tyrosine and glucagon like peptide-1, which provides a sense of satiety and decreased gastric motility, promoting less intake and subsequent weight loss, when compared to controls (235). Furthermore, RYGB patients had an early and exaggerated insulin response, which they owe to better glycemic control, when compared to control subjects (235). Umeda et al. followed 10 morbidly obese individuals who underwent the RYGB procedure, and evaluated these patients at 7, 30, and 90 days postoperatively to observe any changes in hormone concentrations and glycemic control (236). It was found that the homeostasis model assessment of insulin resistance (HOMA-IR) decreased from 7.8 to 2.6 at 7 days postoperatively, which occurred without significant weight loss (236). Postprandial GLP-1 concentrations peaked earlier, and a decrease in plasma glucagon and blood glucose concentrations occurred throughout the test meal, providing improved glycemic control and earlier satiety, independent of weight loss (236). These alterations in hormone concentrations after gastric bypass and improvements in glycemic control are why the RYGB procedure is being recommended almost exclusively to those individuals who are morbidly obese, and also have diabetes. As further research is completed, recommendations pre- and postoperatively can be better tailored to various cohorts of the population, such as those women in the pre-, peri-, and postmenopausal stage of life, to provide for the best outcome.
Tailored Approaches

Current research studies completed in countries outside the United States, or on specific population subtypes within the United States have required a more tailored approach to better suit the population of interest. Recommendations through the National Cholesterol Education Program, Adult Treatment Panel III criteria concerning; blood sugar, blood pressure, lipid levels, and waist circumference can be modified to provide a more accurate depiction of the group studied. Primarily, criteria concerned with waist circumference and BMI are altered, based on the population. Certain cohorts of the population are genetically smaller framed, and therefore standard measurement criteria are not appropriate, and may leave out study worthy individuals. Both Hee Jung Lee and Palaniappan used different BMI and waist circumference values based on their target population of South Korean and Asian Americans living in Northern California, respectively, when looking at uric acid levels in postmenopausal women (106, 237). Okamura also studied those living in Japan, and used similar BMI criteria in order to be more representative of the Asian population being observed (68).

Hee Jung Lee set out to study serum levels of uric acid in both pre- and postmenopausal women to test if elevated uric acid levels could help predict metabolic syndrome incidence rates (237). The target population was women residing in Seoul, South Korea, who had an annual health exam at Anam Hospital. Because this population has a smaller frame size and overall smaller body structure, guidelines set forth by the World Health Organization specifically for those of Asian-Pacific ethnicity were used. These differ from the standard ATP III guidelines, in that to be considered obese, a woman’s waist circumference must be >80cm, as opposed to the normal criterion of >88cm (4).
Palaniappan set out to investigate why Asian Americans have a greater prevalence of metabolic syndrome, even though their BMI values are consistently lower, primarily within the current healthy range of between 18.5 and 24.9 (106). To better conform to this population’s smaller body size, the World Health Organization recommended using BMI cut points of 23 to 27.4 kg/m² to represent overweight and >27.4 kg/m² to represent obese (106). This study found that the prevalence rates for those persons with type II diabetes mellitus (T2DM) and CVD, had BMI values within in the high/normal range, using the European scale of 18.5 to 24.9 kg/m², and therefore were being overlooked as having an abnormal condition. To illustrate this point, Palaniappan found that in women with a BMI of 25 kg/m², metabolic syndrome prevalence was 12% in non-Hispanic whites and a significantly elevated 30% for Asians. In those non-Hispanic whites with a BMI of 25 kg/m², an individual of Asian background would have a similar prevalence rate for metabolic syndrome at a BMI of 19.6 kg/m². It was also noted that metabolic syndrome prevalence was higher in Asians across all BMI categories, not just the one previously illustrated. In this study group, it was also found that blood pressure readings in the Asian population were significantly higher than that of the non-Hispanic white group (106).

Cohen et al investigated a more tailored approach to bariatric surgery, when he operated on 37 class I obese individuals (BMI 30-35 kg/m²) and found that comorbid condition resolution was observed in 36 patients, and 81% excess weight was lost. Similarly, Geloneze et al looked at type II diabetics with a BMI between 25 and 29.9 kg/m², who agreed to have the duodenal-jejunal exclusion surgery completed, which left the full stomach intact, but completely bypassed the duodenum and proximal jejunum (238). Bypassing these sections of the intestinal tract results in hormonal alterations similar to that of the RYGB, and it was found that at 24 weeks postsurgical intervention, fasting glucose was reduced by 14% (control 7%), A1C from 8.78% to
7.84% (control 8.93% to 8.71%) and average daily insulin requirement by 93% (control 29%) (238). Both studies demonstrated that the benefits of performing bariatric surgery on individuals who would not typically qualify under current NIH guidelines.

Cerci followed 10 males and 15 females for one year status post either the Roux-en-Y gastric bypass or sleeve gastrectomy procedure. Mean starting BMI was 33.2 kg/m², and BMI at one year was 27.2 kg/m², indicating a significant weight reduction for these grade I obese individuals (239). At the studies start, there were 14 individuals with diagnosed type-2 diabetes mellitus, all who were taking oral diabetic medications, insulin, or a combination of both to manage blood sugars. At one year, this was reduced to two individuals, and the remaining surgery participants were able to discontinue their blood sugar lowering medications or insulin therapy (239).

Evolutionary Context

Throughout the world, our diets are becoming more and more convenience-based, which is wreaking havoc on our individual physiology, and may be exacerbated by our “thrifty” genes. The thrifty gene hypothesis states that when poor fetal growth conditions are experienced, glucose-insulin metabolism is affected later in life, and the propensity for type II diabetes is increased (240). Neel outlined the thrifty gene in the context of our evolutionary past, and predisposition to periods of both feast and famine (241). Because food supply on a daily basis was not guaranteed many years ago, our bodies were forced to store ingested nutrients to the utmost degree. Many years ago this efficient nutrient storage was necessary for survival, however, our “thrifty” genes currently are being bombarded with an excess of energy, and our bodies simply cannot process it appropriately. As a result, this excess energy is primarily being
stored as fat. As fat tissue accumulates, hormones and weight distribution are altered, and so begins the downward spiral towards a host of health abnormalities and a shortened lifespan. A change in numerous factors is needed. While the human body is forgiving and resilient it cannot adapt quickly enough to counteract the damage we are bombarding upon it, through poor diet and a sedentary lifestyle.

A different evolutionary approach to menopause postulates that women go through the menopausal transition so that they can in turn help their offspring nurture the next generation (242). If women continued to produce offspring beyond the fifty-year mark, they would direct their energy towards these boys and girls, failing to help their older offspring, potentially putting them at a disadvantage. Williams suggests that through early termination of fertility with age, or menopause, energy can now be directed towards their children’s offspring, helping to increase overall survival during this crucial stage (243). Even though no concrete explanation exists as to why women go through menopause, it is evident that maintaining a normal weight through the transition can be beneficial towards the individual and allow for more healthy years in the postmenopausal period of time (242).
CHAPTER III:
METHODS AND PROCEDURES

This retrospective chart review focused on the Roux-en-Y Gastric bypass operation in pre- and postmenopausal women. Surgical operations were completed at Wood County Hospital’s Center for Weight Loss Surgery, in Bowling Green Ohio, by a single bariatric surgeon. The multidisciplinary team at the Center for Weight Loss Surgery consisted of the primary surgeon, nurse practitioner, registered nurse, registered dietitian, and insurance coordinator. One psychologist completed the pre-surgery psychology clearance; however this individual did not work solely for the weight loss center. Lab work and pre-surgery medical clearance was granted by various practitioners, which are chosen by each surgery candidate. Techniques used throughout appointments both pre- and postoperatively followed protocol at Wood County Hospital, set forth by the Center’s for Weight Loss Surgery.

Subjects

To complete this study, approval through the Bowling Green State University Human Subjects Review Board was granted, approval #314768-3. Approval was also granted through the Wood County Hospital’s institutional review board. Data concerning patient’s date of birth, social security number or photograph was not included in this study. Data was collected for 78 patients who had the Roux-en-Y gastric bypass procedure completed at Wood County Hospital, in Bowling Green, Ohio between September 2008 and May 2012. A total of approximately 100 patient charts were reviewed, but ended up being excluded due to an abundance of missing information or an age too close to the mean onset age for menopause. Women who had surgical menopause or hysterectomy listed in their past medical history were not included in this study.
A total of 78 surgery patients were included for analysis: 42 premenopausal and 36 postmenopausal at the time of their surgery.

Mean age for premenopausal surgery participants was 29.5 years and approximately 61 years for the postmenopausal group. Preoperative excess body weight was calculated by subtracting patient’s preoperative weight from their ideal body weight, which was found by utilizing the Hamwi Method. To calculate a woman’s ideal body weight using this method, a base weight of 100 pounds was utilized for a 5-foot tall woman. For every inch over 5 feet, an additional 5 pounds was added. Therefore a woman who was 5’3” would have an ideal body weight of 115 pounds. Mean excess body weight prior to surgery was found to be 182 and 152 pounds based on pre- and postmenopausal cohorts, respectively.

Postoperative gastric bypass complications included intolerance to both food and liquid. This was potentially due to esophageal or gastrointestinal stricture, which was ameliorated with balloon dilation. Common food intolerances postoperatively were most often reported as red meats, or other tough protein foods, which are more difficult to digest, specifically after gastric bypass surgery. When protein foods are added into the diet after surgery, it is important that patients chew these foods well, otherwise intolerance may result due to the newly created stomachs decreased ability in regards to digestion. Many issues with tolerance were a direct result of the patient’s non-compliance to dietary recommendations and the introduction of new food items too quickly postoperatively, which often resulted in nausea, bloating, and emesis.

Ten patients required post-op cholecystectomy due to gallstone formation. Gallstone formation is common when a substantial amount of weight is lost in humans, in a short period of time. One patient was readmitted 2.5 months post-op for bowel obstruction and further surgery, which lead to respiratory distress, tracheostomy placement and ventilator support. At this time a
percutaneous endoscopic gastrostomy tube (PEG tube) was placed in the patient and enteral nutrition was initiated to meet nutritional needs. This patient was in the postmenopausal group at age 61. Other complications noted in patients were not a direct result of the Roux-en-Y gastric bypass procedure; but rather, a result of the patient’s non-compliance. At 1 year, mortality rates in patients who received the Roux-en-Y gastric bypass procedure were 0.

Postoperatively, the gastrointestinal tract is divided into two sections: the afferent and alimentary or roux limb. The afferent limb is primarily composed of the bypassed duodenum and its primary function is to carry digestive juices from the remnant stomach to the distal jejunum where partial absorption of ingested food occurs. The roux limb is anastomosed to the newly created gastric pouch and allows food to be carried along where it joins the afferent limb and allows for nutrient absorption. Minimal absorption occurs prior to this point due to the fact that digestive secretions have not yet been introduced. Roux limb length was determined based on the individual’s preoperative height to weight ratio, or body mass index. Again, a longer roux limb allows for greater malabsorption via additional bypassed intestine, and further downstream intestinal reconnection of the afferent limb, which allows for greater individual weight loss for those patients with preoperative BMI values greater than 50 kg/m². For this study, possible roux limb lengths were 100, 150, or 200cm, with frequencies of use as 52, 25, and 1, respectively, as shown in Figure 1.
Data Collection

Patient charts were analyzed and necessary data was collected to monitor weight loss between the pre- and postoperative time points. Necessary information to diagnose metabolic syndrome was collected to monitor incidence rates from the pre- to postoperative period. Blood pressure, weight and also weight lost was collected at follow up appointments, which occurred at 2 weeks, 2 months, 6 months, and 1 year after surgery. If available, metabolic syndrome lab data was collected at the same follow up appointments, however to diagnose metabolic syndrome, data was utilized from the preoperative, 6 month, and 1 year appointments. Several patients did not have data at 6 months, and for these individuals, data was used from the 2-month visit.

In total, collected data was comprised of basic anthropometric measurements such as height and weight. From this data, ideal body weight, body mass index, weight lost, and percent excess body weight lost was calculated. Additionally, blood pressure was recorded at 2 week, 2 month, 6 month, and 1 year visits. Diagnosis of hypertension was made per each patient’s medical history, which was completed prior to surgery as part of the Weight Loss Center’s standard medical workup.
Because waist circumference was not collected, body mass index was used in its place. A value of $\geq 30\text{kg/m}^2$ was deemed abnormal, or equivalent to a woman having a waist circumference greater than 35 inches. Additional data to diagnose metabolic syndrome was based off of the National Cholesterol Education Program’s ATP III guidelines. Criteria that must be met to signify abnormal fasting blood sugar, hypertension, hypertriglyceridemia, and depressed HDL cholesterol can be found in Table 1. Per the NCEP ATP III guidelines, 3 or more of the criteria must be met to make a formal diagnosis.

Table 1: ATP III Criteria for Metabolic Syndrome Diagnosis

<table>
<thead>
<tr>
<th>ATP III Guidelines for Metabolic Syndrome Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Waist Circumference (BMI used as substitute)</strong></td>
</tr>
<tr>
<td><strong>Fasting Glucose</strong></td>
</tr>
<tr>
<td><strong>Triglycerides</strong></td>
</tr>
<tr>
<td><strong>HDL Cholesterol</strong></td>
</tr>
<tr>
<td><strong>Blood Pressure</strong></td>
</tr>
</tbody>
</table>

*Must meet 3 of the above 5 criteria for Metabolic Syndrome Diagnosis*

Statistical Analysis

Statistical analysis was completed using SAS Statistics version 9.3 with the assistance of Nancy Boudreau, Associate Professor in Applied Statistics and Dr. Mark Earley PhD, Associate Professor in the School of Educational Foundations, Leadership, and Policy at Bowling Green State University in Bowling Green, Ohio. Frequency distributions were utilized to determine the number of surgery patients with abnormal laboratory and health related values preoperatively, and again at follow up appointments. The number of participants diagnosed with metabolic syndrome preoperatively, midway, and at one year, according to ATP III criteria was recorded.
Menopausal status was determined based on age, and those categorized as premenopausal were between the ages of 20 and 41 years, while postmenopausal surgery participants were between 55 and 70 years of age. Percent excess body fat lost was calculated for all patients, and these data were compared using t-tests where a p-value of < .05 indicated significance. A repeated measures analysis of variance (ANOVA) was also conducted, which included only those with percent excess body weight lost at all follow up appointments to compare the effect of time on the percent weight lost between groups.
CHAPTER IV:
RESULTS AND DISCUSSION

Preoperative patient weights ranged between 207 and 395 pounds, (mean of 291.18 pounds ±44.59) for all surgery patients. When further classifying weight by menopausal status, premenopausal women’s weights ranged between 207 and 395 pounds (mean 309.64 pounds ±42.64), and postmenopausal women’s weights were between 216 and 364 pounds (mean 269.64 pounds ±36.75). These baseline age and weight characteristics are summarized in Table 2.

Table 2: Baseline Patient Characteristics for Age, Weight, and Excess Body Weight

<table>
<thead>
<tr>
<th></th>
<th>Premenopausal</th>
<th>Postmenopausal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>42</td>
<td>36</td>
<td>78</td>
</tr>
<tr>
<td>Mean Age</td>
<td>29.5 years (±4.37)</td>
<td>61 years (±4.23)</td>
<td>45.33 years (±17.03)</td>
</tr>
<tr>
<td>Mean Preoperative Weight</td>
<td>309.64 pounds (±42.648)</td>
<td>269.64 pounds (±36.759)</td>
<td>289.6 pounds (±44.56)</td>
</tr>
<tr>
<td>Mean Excess Body weight</td>
<td>182 pounds (±37.75)</td>
<td>152 pounds (±34.84)</td>
<td>167 pounds (±39.08)</td>
</tr>
</tbody>
</table>

Metabolic Syndrome Diagnosis in Participants

Prior to surgery, using the National Cholesterol Education Program’s ATP III guidelines, 54 of 78 patients had metabolic syndrome (22 premenopausal and 32 postmenopausal), indicating that at least 3 of the 5 metabolic syndrome diagnostic criteria were met. At midway follow up, the number of subjects with metabolic syndrome was decreased to 37 patients (13 premenopausal and 24 postmenopausal), and at the end of 1 year metabolic syndrome decreased further to 17 (7 pre menopausal and 10 postmenopausal). These data signified an improvement in metabolic syndrome status in patients over time, status post bariatric surgery. Figure 2 illustrates
the incidence of metabolic syndrome in both pre- and postmenopausal groups preoperatively, and again at midway and 1 year.

Figure 2: Metabolic Syndrome Incidence in Pre- and Postmenopausal Women Preoperatively, Midway, and at 1 Year.

Diet

Within 24 hours postoperatively, patients had an upper gastrointestinal series completed to identify any leaks at anastomotic sites, or around the newly created gastric pouch. After patients ingested oral barium, an XRAY was completed which will show any abnormalities as the barium traveled throughout the gastrointestinal tract. If the upper gastrointestinal series is negative, surgery patients are started on sips of water. At first, it is recommended that each patient consume 1 ounce of water every 60 minutes, which was later advanced to 1 ounce of water every 30 minutes to ensure adequate hydration, and weaning of intravenous fluids. By drinking only water postoperatively, a reduction in inflammation at the anastomotic junctions between stomach and intestine is promoted, improving tolerance as additional fluids and foods are added. Water intake was recorded by each patient and given to the physician for review when
rounding. After 24 hours, a clear liquid diet is initiated, which included Crystal Light, broth, sugar free popsicles, and sugar free Jell-O. Sugar intake is limited on the clear liquid diet due to the increased likelihood of intolerance postoperatively, due to the high osmolarity of the sugared solution and rapid transit from stomach to small bowel. When on clear liquids, each patient was encouraged to pay close attention to how the newly created gastric pouch felt, refraining from further drinking if nausea, pain, bloating, or discomfort presented.

Gastric bypass patients were discharged home on a full liquid diet, which was recommended for two weeks postoperatively, further allowing the new stomach and anastomotic junctions to heal. Meeting calorie and protein requirements when on the full liquid diet was not imperative during this two-week postoperative period, which was explained prior to discharge from the hospital. After two-weeks on the full liquid diet, patients were encouraged to slowly introduce new singular foods into the diet, continuing to refrain from hard to digest meats, which could cause tolerance issues, as explained previously. It was not required to puree meats after surgery, however patients were encouraged to start with flaky fish or ground turkey and chicken to help promote tolerance. At each follow up appointment, continued stress was placed on the complete chewing of foods to reduce the stress placed on the new gastric pouch, improving food tolerability. Avoidance of high sugar foods and beverages was also discouraged due to reduced transit time in the stomach and gastrointestinal tract, potentially leading to diarrhea and further malabsorption of vitamins, minerals, protein and other essential nutrients. Raw vegetables and fruits with their skin, along with other high fiber dietary items, were also not recommended within the first several months after surgery.

The amount of food consumed at each meal was small, equal to approximately one ounce. This typically provided a feeling of fullness, mainly as a result of the newly created
stomachs smaller capacity. After several months, pending on diet tolerance, patients may be advanced to what was referred to as the maintenance diet. At this time no foods were restricted, however there were certain items that should only be consumed with caution because of possible problems related to gastrointestinal tract tolerance, specifically those high in sugar. The rationale behind smaller, more frequent, nutritionally balanced meals continued to be encouraged, which helped allow for continued weight loss while still meeting calorie, protein, vitamin, and mineral needs. If dietary recommendations were not followed postoperatively, unhealthy weight loss could occur, resulting in dumping syndrome and excess malabsorption, increasing the odds of nutrient deficiency and future hospital admission.

Vitamin and mineral supplement adherence was estimated to be near 100% based on patient self-reported follow-up data at 2 months, 6 months and 1 year. Bariatric chewable multivitamins were recommended, but if not available, any hard chewable multivitamin would suffice. Roux-en-Y gastric bypass patients were required to take two multivitamins daily for life to help prevent deficiency. Calcium supplementation was accomplished with calcium citrate, which does not require stomach acid for absorption. Other vitamin and mineral supplements typically recommended were vitamin D, B12, folic acid, and iron. Individual vitamin or mineral supplementation was only recommended if a known deficiency was present.

**Excess Body Weight Lost**

Excess body weight was calculated by subtracting ideal body weight from the preoperative weight. Percent excess body weight lost (%EBWL) was calculated at each appointment by dividing excess body weight by weight reduction measured at each appointment. This value was multiplied by 100, which provided percent weight lost. Preoperative mean excess weight in the premenopausal group was 182.02 pounds (±37.75), and 152.69 pounds (±34.84) in the
postmenopausal group. When comparing percent excess body weight lost between the four follow-up appointments, there was no significant difference between the pre- and postmenopausal groups at 2 weeks, 2 months, and 6 months. At 1 year, premenopausal percent excess body weight lost was 68.79% (±16.38) and 59.44% (±14.44) for postmenopausal women, which was significant, t(73)= 2.61, p=0.011. At 1 year, 64 individuals lost greater than 50% of their percent excess body weight. A summary of weight loss results is shown in Table 3.

Table 3: Percent Excess Body Weight Lost at 2 Weeks, 2 Months, 6 Months, and 1 Year

<table>
<thead>
<tr>
<th></th>
<th>Premenopausal</th>
<th>Postmenopausal</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 weeks</td>
<td>16.03% (±4.56)</td>
<td>15.93% (±6.56)</td>
<td>0.9362</td>
</tr>
<tr>
<td>2 months</td>
<td>30.64% (±7.79)</td>
<td>28.25% (±8.40)</td>
<td>0.1985</td>
</tr>
<tr>
<td>6 months</td>
<td>51.91% (±10.29)</td>
<td>48.16% (±11.07)</td>
<td>0.1386</td>
</tr>
<tr>
<td>1 year</td>
<td>68.79% (±16.38)</td>
<td>59.44% (±14.44)</td>
<td>0.0111</td>
</tr>
</tbody>
</table>

*p-values < .05 are considered significant

To compare percent excess body weight lost between only those patients who had data for all follow-up appointments, a repeated measures analysis of variance was conducted. Similarly, no significance in percent excess body weight lost was found between pre- and postmenopausal groups at 2 weeks, 2 months, and 6 months. However, at 1 year, percent excess body weight lost for the premenopausal group was 68.89 pounds (±17.11), and 59.71 pounds (±14.29) in the postmenopausal patients, which was significant t(65)= 2.38, p=0.0201. When comparing mean excess body weight lost across time between groups, the data showed a more pronounced variance between pre- and postmenopausal women, with significance at 1 year F(3,195)=4.71, p=0.0182, as seen in Figure 3.
Figure 3: Repeated Measures Analysis of Variation Comparing Mean Percent Excess Body Weight Lost Across Time Between Pre- and Postmenopausal Groups

Percent excess body weight lost using the repeated analysis of variation test is summarized in Table 4.

Table 4: Percent Excess Body Weight Lost at 2 Weeks, 2 Months, 6 Months, and 1 Year for Those with Data at All Follow Up Appointments

<table>
<thead>
<tr>
<th></th>
<th>Premenopausal</th>
<th>Postmenopausal</th>
<th>p-value</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 weeks</td>
<td>16.20% (±4.92)</td>
<td>15.79% (±6.61)</td>
<td>0.7782</td>
<td>0.28</td>
</tr>
<tr>
<td>2 months</td>
<td>30.39% (±7.69)</td>
<td>28.54% (±8.63)</td>
<td>0.3582</td>
<td>0.93</td>
</tr>
<tr>
<td>6 months</td>
<td>52.38% (±10.03)</td>
<td>48.04% (±11.25)</td>
<td>0.1006</td>
<td>1.67</td>
</tr>
<tr>
<td>1 year</td>
<td>68.89% (±17.11)</td>
<td>59.71% (±12.29)</td>
<td>0.0201</td>
<td>2.38</td>
</tr>
</tbody>
</table>
Hypertension was a diagnosed comorbid condition in 42 patients preoperatively, as listed in the patient’s preoperative medical history. Using criteria from the National Cholesterol Education Program ATP III guidelines, hypertension was present when either the systolic blood pressure was \( \geq 130 \) mm Hg or diastolic blood pressure was \( \geq 85 \) mm Hg.

At 2 weeks postoperatively, 31 of 73 patients had diagnosed hypertension, based on the criteria above. Of these 31 women, 14 were premenopausal and 17 were postmenopausal. At 2-month follow-up, this value increased slightly to 34 of 77 (16 premenopausal and 18 postmenopausal). At 6 months, diagnosed hypertension decreased to 28 of 69 patients (8 premenopausal and 20 postmenopausal. In the premenopausal group, 77.14% had normal blood pressure and 22.86% had readings diagnostic of hypertension. In the postmenopausal group, 41.18% had normal blood pressure, while 58.82% were abnormal, which was significant between groups, \( \chi^2(1, n=69) \) \( p=0.0024 \). Finally, at 1 year only 21 of 74 patients (6 premenopausal and 15 postmenopausal) had blood pressure readings diagnostic of hypertension. In the premenopausal group 84.62% had normal blood pressure and 15.38% were hypertensive. In the postmenopausal group 57.14% had normal blood pressure while 42.86% were hypertensive, which was significant between groups, \( \chi^2(1, n=74) \) \( p=0.0089 \). Elevated versus normal blood pressure readings, stratified by menopausal status at 2 weeks, 2 months, 6 months, and 1 year can be found in Tables 5-8.
Table 5: Blood Pressure - 2 Weeks

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>Sys &lt;130 AND Dia &lt;85</th>
<th>Sys &gt;=130 OR Dia &gt;=85</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>26 61.90%</td>
<td>14 45.16%</td>
<td>40</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>16 38.10%</td>
<td>17 54.84%</td>
<td>33</td>
</tr>
<tr>
<td>Totals</td>
<td>42</td>
<td>31</td>
<td>73</td>
</tr>
</tbody>
</table>

Frequency Missing = 5
\[ X^2 (1, n=73) p=0.1554 \]

Table 6: Blood Pressure - 2 Months

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>Sys &lt;130 AND Dia &lt;85</th>
<th>Sys &gt;=130 OR Dia &gt;=85</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>25 58.14%</td>
<td>16 47.06%</td>
<td>41</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>18 41.86%</td>
<td>18 52.94%</td>
<td>36</td>
</tr>
<tr>
<td>Totals</td>
<td>43</td>
<td>34</td>
<td>77</td>
</tr>
</tbody>
</table>

Frequency Missing = 1
\[ X^2 (1, n=77) p=0.3332 \]
Table 7: Blood Pressure - 6 Months

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>Sys&lt;130 AND Dia&lt;85</th>
<th>Sys=130 OR Dia&gt;=85</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>27 65.85%</td>
<td>8 28.57%</td>
<td>35</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>14 34.15%</td>
<td>20 71.43%</td>
<td>34</td>
</tr>
<tr>
<td>Totals</td>
<td>41 69</td>
<td>28 69</td>
<td>69</td>
</tr>
</tbody>
</table>

Frequency Missing = 9
\[ X^2 (1, n=69) p=0.0024 \]

Table 8: Blood Pressure - 1 Year

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>Sys&lt;130 AND Dia&lt;85</th>
<th>Sys=130 OR Dia&gt;=85</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>33 62.26%</td>
<td>6 28.57%</td>
<td>39</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>20 37.74%</td>
<td>15 71.43%</td>
<td>35</td>
</tr>
<tr>
<td>Totals</td>
<td>53 74</td>
<td>21 74</td>
<td>74</td>
</tr>
</tbody>
</table>

Frequency Missing = 4
\[ X^2 (1, n=74) p=0.0089 \]
Fasting Blood Glucose

Fasting blood glucose values ≥110mg/dL were considered abnormal, with normal fasting values between 70 and 110mg/dL. Preoperatively, 30 of 76 patients had values classified as abnormal. Of these 30 patients with values ≥110 mg/dL, 12 were premenopausal and 18 were postmenopausal. In the premenopausal group 71.43% had normal fasting values and 28.57% were abnormal. In the postmenopausal group 47.06% had normal fasting levels while 52.94% had impaired levels, which was also significant between groups, \( X^2 (1, n=76) p=0.0307 \). Midway impaired fasting glucose values decreased to 15 of 76 patients (3 premenopausal and 12 postmenopausal). In the premenopausal group 92.50% had normal values and only 7.5% were abnormal. In the postmenopausal group, 66.67% had normal values while 33.33% were abnormal, which was significant between groups \( X^2 (1, n=76) p=0.0047 \). At 1 year impaired fasting glucose incidence was further decreased when only 10 of 67 patients (3 premenopausal and 7 postmenopausal) had fasting blood glucose of ≥110 mg/dL, which was not significantly different between groups.

Mean blood glucose values preoperatively, midway, and at 1 year were 116.03 mg/dL (±37.99), 99.76 mg/dL (±29.68), and 96.06 mg/dL (±21.38), respectively. Preoperatively, blood sugar values for premenopausal women ranged between 81-290 mg/dL, while postmenopausal women were between 81-237 mg/dL. Midway, fasting blood glucose levels for premenopausal women ranged between 73-261 mg/dL, and postmenopausal values were between 79-136 mg/dL. Finally, fasting blood glucose values at 1 year follow up for premenopausal women ranged between 58-182 mg/dL and 75-187 mg/dL for postmenopausal women. Incidence of impaired fasting glucose in pre and postmenopausal women preoperatively, midway, and at 1 year can be seen in Tables 9-11.
Table 9: Glucose - Preoperative

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>&lt;110mg/dL</th>
<th>&gt;=110mg/dL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>30</td>
<td>12</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>65.22%</td>
<td>40.00%</td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>16</td>
<td>18</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>34.78%</td>
<td>60.00%</td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td>46</td>
<td>30</td>
<td>76</td>
</tr>
</tbody>
</table>

Frequency Missing = 2  
\( X^2 (1, n=76) p=0.0307 \)

Table 10: Glucose - Midway

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>&lt;110mg/dL</th>
<th>&gt;=110mg/dL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>37</td>
<td>3</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>60.66%</td>
<td>20.00%</td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>24</td>
<td>12</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>39.34%</td>
<td>80.00%</td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td>61</td>
<td>15</td>
<td>76</td>
</tr>
</tbody>
</table>

Frequency Missing = 2  
\( X^2 (1, n=76) p=0.0047 \)
Table 11: Glucose - 1 Year

<table>
<thead>
<tr>
<th>Glucose 1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
</tr>
<tr>
<td>Premenopausal</td>
</tr>
<tr>
<td>Postmenopausal</td>
</tr>
<tr>
<td>Totals</td>
</tr>
</tbody>
</table>

Frequency Missing = 11

$X^2 (1, n=67) p=0.1548$

Body Mass Index

For adults, both male and female, normal BMI ranges are classified between 18.5 and 24.9 kg/m². Values greater than 25kg/m² begin to classify those that are in the overweight and obese categories. Body mass index classifications for underweight, normal, overweight, and obesity are shown in Table 12.

Table 12: Body Mass Index Classifications (244)

<table>
<thead>
<tr>
<th>Classification</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>&lt; 18.5 kg/m²</td>
</tr>
<tr>
<td>Normal weight</td>
<td>18.5–24.9 kg/m²</td>
</tr>
<tr>
<td>Overweight</td>
<td>25–29.9 kg/m²</td>
</tr>
<tr>
<td>Obesity (Class 1)</td>
<td>30–34.9 kg/m²</td>
</tr>
<tr>
<td>Obesity (Class 2)</td>
<td>35–39.9 kg/m²</td>
</tr>
<tr>
<td>Extreme Obesity (Class 3)</td>
<td>≥ 40 kg/m²</td>
</tr>
</tbody>
</table>
Due to the fact that waist circumference data was not routinely collected by the Centers for Weight Loss Surgery, body mass index was utilized as a substitute to signify abdominal obesity. For this study, body mass index values that were greater than 30kg/m² were used as the equivalent to having a waist circumference greater than 35 inches.

Preoperative BMI ranged between 36.96 kg/m² and 62.17 kg/m², with a mean of 49.07 kg/m² (±6.36). BMI values all were within the inclusion criteria for surgery of 35kg/m² with a comorbid condition diagnosed, or 40 kg/m² without comorbid condition. When stratifying BMI by menopausal group, ranges for premenopausal surgery patients ranged between 41.03 kg/m² and 61.00 kg/m² (mean 50.62 kg/m²), while postmenopausal ranges were between 36.96 kg/m² and 62.17 kg/m² (mean 47.27 kg/m²). Overall, mean BMI values decreased at each follow up appointment. BMI values at 2 weeks, 2 months, 6 months, and 1 year were as follows: 44.51, 40.87, 35.06, and 31.13 kg/m², respectively. Figure 4 illustrates body mass index preoperatively, and at 2 week, 2 month, 6 month, and 1 year follow up visits. Preoperatively, all BMI values were greater than the minimum 35kg/m² requirement for bariatric surgery eligibility. At each follow up appointment, reductions in weight result in a decrease in BMI as shown. A summary of body mass indices for each time period is presented in Tables 13-17. Values for pre- and postmenopausal patients are shown and data is present preoperatively and at 2 week, 2 month, 6 month, and 1 year follow up appointments.
Figure 4: Body Mass Index Preoperatively, 2 Weeks, 2 Months, 6 Months, and 1 Year

Table 13: Body Mass Index - Preoperative

<table>
<thead>
<tr>
<th>Preoperative BMI</th>
<th>18.5-24.9 kg/m²</th>
<th>25-30 kg/m²</th>
<th>30-35 kg/m²</th>
<th>35-40 kg/m²</th>
<th>40+ kg/m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>42 (53.85%)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>36 (46.15%)</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>78</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>&lt;=30</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative BMI</td>
<td>78</td>
<td>78</td>
</tr>
</tbody>
</table>
Table 14: Body Mass Index - 2 Weeks

<table>
<thead>
<tr>
<th>Frequency Column</th>
<th>BMI - 2 Weeks</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&gt;=30</td>
<td>Total</td>
</tr>
<tr>
<td>Premenopausal</td>
<td>41</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>54.67%</td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>34</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>45.33%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Frequency Missing</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

Table 15: Body Mass Index - 2 Months

<table>
<thead>
<tr>
<th>Frequency Column</th>
<th>BMI - 2 Months</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;30</td>
<td>&gt;=30</td>
</tr>
<tr>
<td>Premenopausal</td>
<td>0</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>0.00%</td>
<td>53.95%</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>1</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>100%</td>
<td>46.05%</td>
</tr>
<tr>
<td>Total</td>
<td>1</td>
<td>76</td>
</tr>
<tr>
<td>Frequency Missing</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
\[ \chi^2 (1, n=77) p=0.2827 \]
Table 16: Body Mass Index - 6 Months

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>&lt;30</th>
<th>&gt;=30</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>6</td>
<td>31</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>37.50%</td>
<td>54.39%</td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>10</td>
<td>26</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>62.50%</td>
<td>45.61%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>57</td>
<td>73</td>
</tr>
</tbody>
</table>

Frequency Missing = 5  
\[ X^2 (1, n=73) p=0.2326 \]

Table 17: Body Mass Index - 1 Year

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>&lt;30</th>
<th>&gt;=30</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>17</td>
<td>23</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>53.13%</td>
<td>53.49%</td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>15</td>
<td>20</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>46.88%</td>
<td>46.51%</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>43</td>
<td>75</td>
</tr>
</tbody>
</table>

Frequency Missing = 3  
\[ X^2 (1, n=75) p=0.9751 \]
Triglycerides

Triglyceride values $\geq 150$ mg/dL were considered abnormal. Preoperatively, 49 of 76 (23 premenopausal and 26 postmenopausal) had abnormal levels that were $\geq 150$ mg/dL. Midway this value decreased to 21 of 75 (8 premenopausal and 13 postmenopausal), and again fell to 10 of 66 (3 premenopausal and 7 postmenopausal) at 1 year follow up. Mean triglyceride levels preoperatively, midway, and at 1 year were 183.89 mg/dL (±85.515), 127.71 mg/dL (±53.484), and 100.65 mg/dL (±50.825), respectively. Triglyceride ranges for premenopausal women preoperatively, midway, and 1 year were as follows; 58-442 mg/dL, 47-254 mg/dL, and 42-225 mg/dL, respectively. Preoperative, midway, and 1 year triglyceride lab values ranges for postmenopausal women as follows: 66-383 mg/dL, 45-277 mg/dL, and 30-252 mg/dL, respectively. No significance preoperatively, midway, or postoperatively was found when comparing pre- and postmenopausal groups. Incidence of elevated triglycerides in pre- and postmenopausal women preoperatively, midway, and at 1 year can be seen in Tables 18-20.

Table 18: Triglycerides - Preoperative

<table>
<thead>
<tr>
<th>Preoperative Triglycerides</th>
<th>Frequency Column Percent</th>
<th>$&lt;150$ mg/dL</th>
<th>$\geq 150$ mg/dL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>18</td>
<td>18</td>
<td>23</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>66.67%</td>
<td>46.94%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>9</td>
<td>26</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td></td>
<td>33.33%</td>
<td>53.06%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td>27</td>
<td>49</td>
<td>76</td>
<td></td>
</tr>
</tbody>
</table>

Frequency Missing = 2

$X^2 (1, n=76) = p = 0.0987$
Table 19: Triglycerides - Midway

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>&lt;150mg/dL</th>
<th>&gt;=150mg/dL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>31 57.41%</td>
<td>8  38.10%</td>
<td>39</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>23 42.59%</td>
<td>13 61.90%</td>
<td>36</td>
</tr>
<tr>
<td>Totals</td>
<td>54</td>
<td>21</td>
<td>75</td>
</tr>
</tbody>
</table>

Frequency Missing = 3  
$X^2 (1, n=75) p=0.1328$

Table 20: Triglycerides - 1 Year

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>&lt;150mg/dL</th>
<th>&gt;=150mg/dL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>30 53.57%</td>
<td>3  30.00%</td>
<td>33</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>26 46.43%</td>
<td>7  70.00%</td>
<td>33</td>
</tr>
<tr>
<td>Totals</td>
<td>56</td>
<td>10</td>
<td>66</td>
</tr>
</tbody>
</table>

Frequency Missing = 12  
$X^2 (1, n=66) p=0.1697$
High Density Lipoprotein Cholesterol

An HDL cholesterol level <50mg/dL was considered abnormal. Preoperatively, 56 of 76 patients (31 premenopausal and 25 postmenopausal) had an HDL cholesterol level less than 50 mg/dL, indicating abnormality. Midway this value increased to 60 of 75 patients (33 premenopausal and 27 postmenopausal), and then again decreased to 29 of 66 (18 premenopausal and 11 postmenopausal) at 1 year follow up. Mean HDL cholesterol values preoperatively, midway, and at 1 year were 42.66 mg/dL (±10.557), 42.05 mg/dL (±11.906), and 52.88 mg/dL, respectively. Premenopausal HDL cholesterol ranges preoperatively, midway, and at 1 year, was from 23-69 mg/dL, 18-89 mg/dL, and 29-119 mg/dL, respectively. Furthermore postmenopausal HDL cholesterol ranges preoperatively, midway, and at 1 year were 23-60 mg/dL, 22-68 mg/dL, and 31-138 mg/dL, respectively. No significance preoperatively, midway, or post operatively was found when comparing pre- and postmenopausal groups. Incidence of depressed HDL cholesterol levels in pre- and postmenopausal women preoperatively, midway, and at 1 year can be seen in Tables 21-23.

Table 21: High Density Lipoprotein Cholesterol - Preoperative

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>&gt;50mg/dL</th>
<th>&lt;50mg/dL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>10 50.00%</td>
<td>31 55.36%</td>
<td>41</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>10 50.00%</td>
<td>25 44.64%</td>
<td>35</td>
</tr>
<tr>
<td>Totals</td>
<td>20</td>
<td>56</td>
<td>76</td>
</tr>
</tbody>
</table>

Frequency Missing = 2
X² (1, n=76) p=0.6799
Table 22: High Density Lipoprotein Cholesterol - Midway

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>&gt;=50mg/dL</th>
<th>&lt;50mg/dL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>6</td>
<td>33</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>49.00%</td>
<td>55.00%</td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>9</td>
<td>27</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>69.00%</td>
<td>45.00%</td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td>15</td>
<td>60</td>
<td>75</td>
</tr>
</tbody>
</table>

Frequency Missing = 3
\[ X^2 (1, n=75) p=0.2983 \]

Table 23: High Density Lipoprotein Cholesterol - 1 Year

<table>
<thead>
<tr>
<th>Frequency Column Percent</th>
<th>&gt;=50mg/dL</th>
<th>&lt;50mg/dL</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premenopausal</td>
<td>15</td>
<td>18</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>40.54%</td>
<td>62.07%</td>
<td></td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>22</td>
<td>11</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>59.46%</td>
<td>37.93%</td>
<td></td>
</tr>
<tr>
<td>Totals</td>
<td>37</td>
<td>29</td>
<td>66</td>
</tr>
</tbody>
</table>

Frequency Missing = 12
\[ X^2 (1, n=66) p=0.0825 \]
Review of Hypotheses

H1: Premenopausal bariatric surgery patients will see greater percent excess body weight lost and greater reductions in metabolic syndrome incidence when compared to postmenopausal surgery patients.

When comparing percent excess body weight lost between pre- and postmenopausal surgery patients at the Center for Weight Loss Surgery at Wood County Hospital, no significant difference was found between groups at 2 weeks, 2 months, 6 months postoperatively. However, at 1 year, premenopausal women lost a significantly greater percent of their original excess body weight when compared to those in the postmenopausal group, 68.9% versus 59.7%, respectively \( t(73)= 2.61, p=0.011 \). Preoperatively, 54 of 78 surgery patients were diagnosed with metabolic syndrome (28% premenopausal and 41% post menopausal). The incidence of this condition was reduced to only 17 of 78 patients at 1 year (9% premenopausal and 13% postmenopausal). Significant differences between groups was also found for preoperative \( (X^2 (1, n=76) p=0.0307) \) and midway glucose values \( (X^2 (1, n=76) p=0.0047) \), in addition to blood pressure readings at 6-months \( (X^2(1, n=69) p=0.0024) \) and 1 year \( (X^2(1, n=74) p=0.0089) \).

H0: No difference will be witnessed in relation to percent excess body weight lost and metabolic syndrome incidence reduction between pre- and postmenopausal bariatric surgery patients.

For this research study, \( H_0 \) is rejected. Though no statistical significance was found at these three follow up time points, premenopausal women did lose a greater percentage of excess body weight at each. Premenopausal women also fared better when looking at diagnostic criteria for metabolic syndrome diagnosis.
Discussion

Rising rates of morbid obesity and the associated health abnormalities that accompany increased body weight have caused medical expenditures to rise exponentially worldwide (102). To help slow and even reverse further weight gains, numerous methods to aid in weight loss and long-term weight maintenance have been promoted (16). While lifestyle intervention and diet modification can lead to weight loss in many, those that are classified in the extreme obese category, having a BMI greater than 40kg/m², may not be able to lose enough weight via these means to provide for comorbid condition resolution and a significantly better quality of life. For this subset of the population, surgical intervention is likely the most effective means for substantial weight loss and maintenance.

With advancing age, physical activity becomes more difficult. Add to this aging a significant excess in body weight, and any amount of activity can prove to be not only challenging, but also impossible for some. For these specific situations, surgical intervention in a patient, with purposeful malabsorption and food intake reduction is the most sensical option to yield long-term body weight success. This current study has shown that the Roux-en-Y gastric bypass procedure is able to provide safe and effective weight loss in those women 55 years old and greater, as depicted in the postmenopausal group.

Again, the Roux-en-Y gastric bypass procedure allowed for significant weight loss in both pre- and postmenopausal women, and also promoted a reduction in the diagnosis of metabolic syndrome in these two specific groups. Incidence rates of metabolic syndrome were recorded preoperatively, midway, and at 1 year. The aim of this study was to see if a difference could be drawn between a woman’s ability to lose weight, based on menopausal status, and
whether or not one group had greater reductions in metabolic syndrome incidence, postoperatively.

Both pre- and postmenopausal groups saw noteworthy weight loss as a result of the Roux-en-Y gastric bypass procedure at all follow up appointments, which is supported by the majority of literature on this specific surgical weight loss modality (17, 18). Metabolic syndrome incidence reduction was also noted in both groups at follow up appointments. Alexandrides saw similar results when he followed both Roux-en-Y and duodenal switch patients postoperatively. Both surgeries lead to the normalization of blood sugar and lowering of insulin resistance, which resulted in the resolution of metabolic syndrome in nearly all patients (245). Furthermore, Vidal found the resolution of metabolic syndrome incidence was comparable between those who had the Roux-en-Y and sleeve gastrectomy procedure, indicating that with weight loss, regardless of surgery type, rates of metabolic syndrome can be lessened (246). Due to the fact that the Roux-en-Y gastric bypass procedure results in such great weight loss, it has been touted as the most effective means by which to reduce the diagnosis of metabolic syndrome, especially when it is compared to solely lifestyle and diet modifications and alternatives in the morbidly obese patient (247-250). For this particular study, premenopausal women saw a significantly greater loss of excess body weight at 1 year, and greater reductions in metabolic syndrome incidence, supporting the study’s hypothesis. This was in agreement with research by Sugerman who found that weight loss was less in those women greater than 60 years of age who had gastric bypass surgery, when compared to younger individuals (233). The fact that excess body weight lost was only statistically significant between groups at one year is somewhat surprising even though at all follow up points premenopausal women lost a greater percentage of excess body weight than
their postmenopausal counterpart. It is worth noting that both groups saw postoperative weight loss likely greater than what would have been attainable via lifestyle and diet modification.

With each decade of life the ability to lose weight via conventional means is more difficult, and many healthcare providers are hesitant to target those older than 65 years who are classified as either overweight or obese. It is thought that older individuals may lose lean muscle mass and bone mineral density when dieting, predisposing them to other health comorbidities and risks in the future (251). Furthermore, if too many healthy foods are restricted, through improper dieting, nutritional deficiencies may result, weakening the immune system and the body’s ability to heal, if insult or injury should occur (252). This study has indicated that the Roux-en-Y gastric bypass procedure can allow for weight loss in older women, potentially improving their health and overall quality of life. With improvements in an individual’s quality of life after significant weight loss, stress levels may also lessen, and those that were once confined to their homes because of weight may now interact and confidently participate in society. Previous research has shown that health related quality of life (HRQOL) scores were lower in the obese and decreased further with weight gain, which may be due to negative perceptions of body weight, increased disease risk, or physical impairments (253). Baseline BMI was 40kg/m² (±5.0kg/m²), and mean age was 50 years (±8 years). Rothberg found that obese individuals who participated in a medically supervised weight loss program had modest increases in health related quality of life scores, even with an average weight loss of 45 pounds (± 22 pounds) at the 6 month follow up visit. The most significant increases in HRQOL scores from baseline to follow up were found in those with the lowest baseline BMI values, greater reductions in BMI from baseline to follow up, or fewer baseline comorbidities (254). These studies indicate that weight is very closely related to an individual’s HRQOL score, and with
weight loss, improvement can be seen. Furthermore, if weight loss can help reduce comorbid condition diagnosis, even greater increases in HRQOL scores may result. In the future, it would be interesting to obtain HRQOL scores both pre- and postoperatively in regards to bariatric surgery outcomes. This additional data could be used to further elucidate the benefits of weight loss surgery, beyond simply the number on the scale.

While the surgical component is necessary for weight loss and subsequent comorbid condition resolution, proper diet, lifestyle modifications, along with vitamin and mineral supplementation are also needed for a healthy outcome. Dietary recommendations for postoperative success are reviewed in depth at each medically supervised weight loss appointment prior to surgery. These include, but are not limited to smaller portions, focusing on protein first at meals, not drinking fluids thirty minutes before or after eating, chewing foods thoroughly, consuming more fruits and vegetables, and choosing more nutrient dense foods. Vitamin and mineral supplementation was also reviewed during these appointments and individual supplements were recommended if a known deficiency was found per the patient’s lab work. Supplements were started after the surgery patients 2 week follow up appointment to help promote tolerability. The use of protein supplements was also encouraged postoperatively to help meet needs and prevent the loss of muscle mass as weight was lost. Protein supplements were to contain less than ten grams of sugar and greater than fifteen grams of protein, which met needs without causing gastrointestinal distress.

Food intolerances and gastrointestinal complaints were recorded at follow up appointments. Most often, foods were introduced too quickly after surgery and general discomfort, abdominal pain, nausea, and emesis resulted. Increased portions were also the cause of postoperative intolerance. Typically, when a mistake was made in regards to the diet it was
made only once due to the unpleasant symptoms that resulted. Having follow up appointments at 2 weeks, 2 months, 6 months, and 1 year helped to keep the patient on track with diet and supplementation, addressing any issues as they should present. Support was also provided if the patient was not reaching weight loss goals, and troubleshooting was done to help remedy any evident problems and allow for greater success at the patient’s next appointment. For those who followed the diet and supplementation recommendations, success was more pronounced, and these patients looked healthier than their non-compliant counterparts at each follow up appointment. Surgical weight loss can either be healthy or unhealthy, depending on how regimented the individual is in the both the pre- and postoperative stages. For some, weight loss surgery may be viewed as a quick fix, however there are numerous changes that must be orchestrated to yield the best results throughout the remainder of the patient’s life.

With weight loss, big or small, a host of health improvements can be witnessed, as mentioned previously. First, improvements in blood pressure have been shown in those who have lost weight. A meta-analysis of 25 randomized controlled trials between 1966 and 2002, concerning weight loss and blood pressure showed that for each kilogram of bodyweight lost, reductions in systolic and diastolic blood pressure of 1mm Hg could be expected (255). When combined with the substantial weight losses from bariatric surgery, it is no surprise that diagnosis of hypertension was cut in half between the preoperative and 1-year follow up appointment. Throughout follow up appointments, those on antihypertensive medications were either instructed to reduce their daily dose, or discontinue the medication to prevent issues with low blood pressure. In this study, it was likely the individual’s weight loss that provided improvements in blood pressure, however modifications to the diet should not go unnoticed. Prior to surgery, participants met with a registered dietitian to help build healthy habits to aid in
preoperative weight loss and success after surgery. One key point stressed by the dietitian was the reduction of processed foods to help reduce the total intake of sodium and unhealthy fats. It is this reduction in sodium that has been shown to yield reductions in blood pressure, which may also owe to the reductions noted in this study (255).

Fasting blood sugar values also showed improvement between preoperative and follow up appointments. Resistance at the level of the cell is lessened and blood sugar homeostasis is more easily attained for those with type II diabetes, after weight loss has been achieved. For this study, reductions in those with impaired fasting glucose was found at each follow up appointment, indicating that with reductions in weight, blood sugar control was more easily attained. Many of those patients who were on oral diabetic medications or insulin for type II diabetes were able to either cut their daily dose, or discontinue using the medication, while still keeping fasting and postprandial blood sugar levels within the normal range. It is important to keep in mind that postoperatively, a type I diabetic would still require insulin to manage blood sugar levels because of the complete lack of endogenous insulin production. As weight is lost, the total required daily dose would be less, and adjustments will be necessary to prevent issues with hypoglycemia, until weight has stabilized.

As a result of better blood sugar control and again weight loss, reductions in triglycerides was observed at follow up appointments. Preoperatively 64% had elevated triglyceride levels, compared to only 15% at 1 year. This reduction was likely due to a combination of factors, which include, but are not limited to weight loss, improved blood glucose control, and healthy diet changes. Specifically, the Academy of Nutrition and Dietetics recommends maintaining a healthy weight, consuming moderate high quality carbohydrates, choosing healthy fats, and increasing overall vegetable intake to help lower elevated triglyceride levels. These before
mentioned points were reviewed pre- and postoperatively by the registered dietitian, helping to build healthy, long term lifestyle habits in the patients.

HDL cholesterol (HDL-C) levels can be affected by various factors, which include weight, activity level, and diet. Using the National Cholesterol Education Programs ATP III guidelines, women with HDL cholesterol levels less than 50 mg/dL was classified as being abnormal. This retrospective chart review indicated that levels were frequently depressed preoperatively and at postoperative follow up appointments. This continued depression in HDL-C levels is somewhat worrisome because of HDL cholesterol's known effect to protect against coronary heart disease. Several decades ago, data obtained during the Framingham Heart Study showed an inverse relationship between elevated HDL-C lab values and coronary heart disease (256). When comparing HDL cholesterol levels between pre- and postmenopausal patients, no significance was found. Preoperatively, greater than 70 percent had HDL cholesterol levels less than the recommended 50mg/dL, indicating an abnormal lab value, and midway this number increased slightly higher to 80 percent. At 1 year, improvements were noticed in HDL cholesterol levels with only 44% having a value in the abnormal range. The increase in those with abnormal HDL levels preoperatively to midway could be a result of limited physical activity after surgery, in addition to less weight loss when compared to that at 1 year’s time.

In place of waist circumference, body mass index, or BMI was used to indicate obesity. While reductions in total weight were the primary objective of bariatric surgery, it is not realistic to expect great enough weight losses to classify all surgery participants in the normal BMI range of 18.5 to 24.9kg/m² as an end goal. The improvement in health and overall quality of life that resulted from even modest weight losses should not be dismissed, even if one’s BMI was still in the overweight or grade I obese category. It is encouraging that 9 surgery participants were able
to lose enough weight to be classified within the normal BMI range at 1 year. Without bariatric surgery, this reduction in weight likely would not have been possible and unfortunately weight gain may have even resulted if only diet and lifestyle modifications were trialed. Research that focused on extremely obese adults showed that dieting was one of the chief causes of weight gain in these individuals, primarily as a result of frustration and unhealthy attempts at weight loss, which eventually lead to noncompliance poorer outcomes (257). The explosion of fad diets, pills, and powders, seen on the television and in magazines for weight loss has also added to the frustration that many face when trying to make healthy changes and live a better life. Unfortunately these products are not scientifically based and can cost a significant amount of money (258). Furthermore, many men and women do not place weight loss as a top priority, but instead must rank it against work, family, and community obligations (258). Because it takes a great deal of time to organize, plan, and carry out healthy recommendations, long-term adherence to weight loss regiments is difficult to achieve.
CHAPTER V:

CONCLUSION

Based on the results of this retrospective chart review of prior bariatric surgery patients, the Roux-en-Y gastric bypass surgery was able to provide for loss of excess body weight in both premenopausal [Group 1] and postmenopausal [Group 2] women in the study. Resolution of comorbid conditions associated with metabolic syndrome was also seen in both groups, which decreased the diagnosis of metabolic syndrome preoperatively to 1-year post-op. Premenopausal women lost a greater percentage of excess body weight at 2 weeks, 2 months, and 6 months, with a significance between pre- and post- groups at 1 year postoperatively. Because those in the postmenopausal group had less weight loss and less resolution of metabolic syndrome, it may be beneficial to reduce bariatric surgery BMI criteria for future bariatric surgery participants. For those women who are in the perimenopausal or postmenopausal life stage, the current BMI surgery inclusion requirements of 35kg/m² and 40kg/m², based upon presence of comorbid condition, may not be appropriate. Such a shift for perimenopausal or postmenopausal women qualifying for such surgeries may improve their long-range quality of life, especially as life expectancies for both men and women reach into the eighth and ninth decades.

Recommendations for BMI used at present stem from the 1991 National Institute of Health Consensus Development Conference Statement on Gastrointestinal Surgery for Severe Obesity. Utilizing a document that is greater than 20 years old may be somewhat of a disservice to those women who are in need of surgery to help shed excess body weight. The healthcare industry is in a constant state of change, with new research being conducted to help provide insight to various health conditions, as well as, provide a better understanding for their management. Treatment surrounding obesity and weight loss has been given more attention
recently, especially as the waistlines of people worldwide have continued to expand. Therefore, it is reasonable to propose that a change in BMI criteria for bariatric surgeries to include those at a slightly less BMI value be allowed, so that surgery and subsequent weight loss can be attained earlier in the patient’s life. At present, insurance companies still follow the 1991 NIH guidelines, and state that any operation on an individual with a BMI of less than 35kg/m² can be done on strictly investigational grounds. Previous research by Cohen and also Gelonze found success when operating on those with a BMI less than the typical criteria set by the NIH (17, 238). Focusing on those individuals with a BMI between 30 and 35kg/m², and having success with both weight loss and comorbid condition resolution after surgery, indicate that the surgery is effective for those with a BMI in the class I obese category. It is those who are categorized as class I obese who would be eligible for surgery if also in the perimenopausal period.

Even though Gelonze had success with blood sugar normalization in his study, it is not resource feasible to perform bariatric surgery on everyone with type II diabetes, regardless of weight, however it is encouraging to know and understand the beneficial effects the surgery has on those who have issues controlling blood sugars. These two studies are significant in relation to this current research study because they both took atypical patients to undergo bariatric surgery, with both leading to postoperative success. It seems reasonable to assume that if a benefit can be witnessed in the previous two studies, on those with BMI values <35kg/m², those same women who are also perimenopausal would see similar results and health related improvements. Therefore, lower inclusion criteria for surgery could be increasingly important for those women in the perimenopausal period of life.

Current research indicates that weight gain with age is seemingly inevitable, and those women during the menopausal transition have been shown to experience even greater gains and
weight shifts towards the midsection, as a result of hormonal changes. When hormonal shifts occur throughout the menopausal transition, weight gain is not only more pronounced, but it also becomes more difficult to lose. Unfortunately, when excess weight accumulates, the risk of disease also tends to trend upward. Bariatric surgery, specifically the Roux-en-Y procedure has been proven to yield sizeable weight losses and allow for the resolution of weight related comorbid conditions. Therefore by lowering the surgery qualifying BMI inclusion criteria for those in the perimenopausal period, a greater number of women would be eligible for bariatric surgery. Body mass index values of 32kg/m² and 35kg/m² based on diagnosed comorbid condition are not drastically varied from the current criteria of 35kg/m² and 40kg/m², however, this small reduction would allow more women to seek surgery as a method for weight loss. For the most part, healthcare in America is individualized based on specific patient needs. Current BMI requirements are identical for both males and females, throughout all life stages. These criteria do not take into account the inherent differences between genders, especially with each passing decade of life. Adjusting BMI inclusion criteria for women entering the perimenopausal period of life could help to reverse weight gain, and instead, allow for weight reductions. These reductions in weight increase the likelihood of comorbid condition resolution, which over time can both improve quality of life and significantly lower healthcare costs.

Due to the fact that weight is so closely intertwined with comorbid health conditions, it seems logical to aspire for weight loss and then reap the rewards in overall health, thereafter. Future research that focuses on premenopausal bariatric surgery patients throughout the menopausal transition and into the postmenopausal years may provide additional insight into the effects of this change on the patient’s ability to lose weight. Individual components of the metabolic syndrome were more common in premenopausal women pre- and postoperatively, in
relation to blood pressure, triglycerides, blood glucose, and body mass index; however, normal high-density lipoprotein cholesterol was more common in the postmenopausal group. It would be interesting to further research the reasons that caused this benefit in the postmenopausal group, to see if the changes hold true past 1 year time. Delving deeper into the HDL-C particle size may also provide insight into what these values truly represent and if a further focus in the normalization of these lab values should be pursued.

Research that focuses on this specific age group of women is especially significant since there is a paucity of current literature on bariatric surgery in older individuals, and even less in regards to those during and after the menopausal transition. Regardless of BMI inclusion criteria, this current study showed that weight loss and comorbid condition resolution is possible for both pre- and postmenopausal women after the Roux-en-Y bariatric surgery. While surgery may be the last resort for many women to lose weight, it is a noteworthy option, especially as surgical methods have become safer and more commonplace. Tailored BMI inclusion criteria for women in the perimenopausal period would provide for a more proactive health stance in relation to those in the obese category, and help to reverse the negative effects of increased weight in a timelier manner. Until that revered magical pill is crafted to help provide substantial weight loss in those overweight and obese, researchers and potential patients must continue to focus on the first law of thermodynamics; calories in versus calories out, for which gastric bypass surgery acts as the training wheels to complete.
APPENDIX A: BOWLING GREEN STATE UNIVERSITY HSRB APPROVAL LETTER

DATE: January 15, 2013
TO: Ryan Majcher
FROM: Bowling Green State University Human Subjects Review Board
PROJECT TITLE: [314768-3] Efficacy of the Roux-en-Y gastric bypass procedure in pre and postmenopausal women and the resolution of metabolic syndrome, a retrospective chart review.
SUBMISSION TYPE: Revision
ACTION: APPROVED
APPROVAL DATE: January 15, 2013
EXPIRATION DATE: April 13, 2014
REVIEW TYPE: Expedited Review
REVIEW CATEGORY: Expedited review category #5

Thank you for your submission of Revision materials for this project. The Bowling Green State University Human Subjects Review Board has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a project design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

Please note that you are responsible to conduct the study as approved by the HSRB. If you seek to make any changes in your project activities or procedures, those modifications must be approved by this committee prior to initiation. Please use the modification request form for this procedure.

All UNANTICIPATED PROBLEMS involving risks to subjects or others and SERIOUS and UNEXPECTED adverse events must be reported promptly to this office. All NON-COMPLIANCE issues or COMPLAINTS regarding this project must also be reported promptly to this office.

This approval expires on April 13, 2014. You will receive a continuing review notice before your project expires. If you wish to continue your work after the expiration date, your documentation for continuing review must be received with sufficient time for review and continued approval before the expiration date.

Good luck with your work. If you have any questions, please contact the Office of Research Compliance at 419-372-7716 or hsrb@bgsu.edu. Please include your project title and reference number in all correspondence regarding this project.

Comment: The PI will record the Medical Record Number so that participants can be identified. The Bowling Green State University Human Subjects Review Board determined that the three criteria under the Privacy Rule have been satisfied and approved a waiver of authorization under expedited review procedures.
APPENDIX B: BOWLING GREEN STATE UNIVERSITY HSRB CONTINUING REVIEW APPROVAL LETTER

DATE: April 14, 2014
TO: Ryan Majcher
FROM: Bowling Green State University Human Subjects Review Board
SUBMISSION TYPE: Continuing Review/Progress Report
ACTION: APPROVED
APPROVAL DATE: April 14, 2014
EXPIRATION DATE: April 13, 2015
REVIEW TYPE: Expedited Review
REVIEW CATEGORY: Expedited review category #5

Thank you for your submission of Continuing Review/Progress Report materials for this project. The Bowling Green State University Human Subjects Review Board has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a project design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

Please note that you are responsible to conduct the study as approved by the HSRB. If you seek to make any changes in your project activities or procedures, those modifications must be approved by this committee prior to initiation. Please use the modification request form for this procedure.

All UNANTICIPATED PROBLEMS involving risks to subjects or others and SERIOUS and UNEXPECTED adverse events must be reported promptly to this office. All NON-COMPLIANCE issues or COMPLAINTS regarding this project must also be reported promptly to this office.

This approval expires on April 13, 2015. You will receive a continuing review notice before your project expires. If you wish to continue your work after the expiration date, your documentation for continuing review must be received with sufficient time for review and continued approval before the expiration date.

Good luck with your work. If you have any questions, please contact the Office of Research Compliance at 419-372-7716 or hsrb@bgsu.edu. Please include your project title and reference number in all correspondence regarding this project.

This letter has been electronically signed in accordance with all applicable regulations, and a copy is retained within Bowling Green State University Human Subjects Review Board's records.
October 26, 2012

Ryan Majcher
950 West Wooster St
Bowling Green, OH 43402

Dear Ryan,

At the September 11, 2012 Ethics Committee meeting, the Wood County Ethics Committee / IRB approved your project involving the efficacy of the Roux-en-Y gastric bypass procedure between both pre and post menopausal woman and metabolic syndrome in these individuals. The committee would like an opportunity to review your findings at the close of your study.

Should you have questions, please feel free to contact the Medical Staff Office at WCH 419-354-8833.

Sincerely,

Meghan Makley
Manager of Medical Staff Services
REFERENCES


35. STEINER AZ. Predicting age at menopause: Hormonal, familial, and menstrual cycle factors to consider. 2011.


